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Enantioselective Allylic Oxidation of Cycloalkenes by Using Cu(II)-Tris(oxazoline) Complex as a Catalyst

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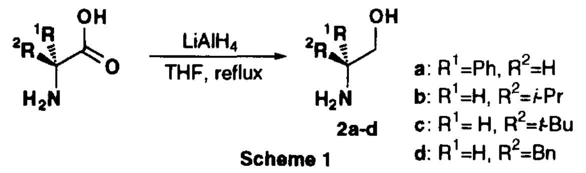
Abstract: Optically active copper(II)-tris(oxazoline) complex that was synthesized as a model compound of the active site of non-heme oxygenase, was found to catalyze allylic oxidation of cycloalkenes to give the corresponding 2-cycloalkenyl benzoates with moderate to excellent enantioselectivity (up to 93% ee) under the Kharash-Sosnovsky reaction conditions.

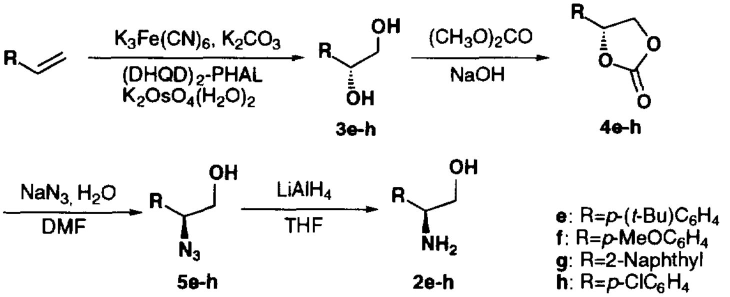
Most of biological reactions proceed with high regio- and stereoselectivities under very mild conditions thanks to the elegant function of enzymes. Some of these enzymes carry metal complex(es) as an active site, wherein the desired reactions are catalyzed with high efficiency. To reproduce these biological reactions in a flask, many efforts have been directed toward the synthesis of model compounds of the active sites of enzymes. For example, cytochrome P-450 which catalyzes the oxidation of alkanes and alkenes, has an iron-porphyrin complex as its active site. Thus, many optically active Mn- and Fe-porphyrin complexes have been synthesized and used as catalysts for enantioselective epoxidation and oxidation of sulfides.[1] Recently, we and others have found that optically active (salen)manganese(III) complexes which have the structure similar to metalloporphyrin complex, serve as highly effective catalysts for enantioselective epoxidation of conjugated olefins and oxidation of sulfides.[2] We have been further interested in the function of non-heme oxidizing enzymes which have an active site bearing metal ion(s) coordinated by imidazoles and carboxylates and catalyze the oxidation of wide variety of substrates. For example, methane monooxygenase (MMO) oxidizes methane to methanol.[3] Kitajima and Moro-oka clarified the function of the active site of this class of enzymes by using model copper and iron complexes bearing hydrotris(pyrazoyl)borate as a ligand.[4] Karlin's and Que's groups also studied the function of these enzymes by using copper or iron-tris[(2-pyridyl)methyl]amine (TPA) complex as the model compound.[5,6] Que *et al.* also reported that a monomeric Fe(III)-TPA complex catalyzes oxidation of alkanes in the presence of an appropriate co-oxidant. On the basis of these studies, we synthesized optically active tris(oxazoline) **1** and found that its copper(II) complex served as an efficient catalyst for enantioselective allylic oxidation under the Kharash-Sosnovsky reaction conditions.[7,8] In the course of our study, enantioselective allylic oxidation using chiral copper(I)-bis(oxazoline) complexes as catalysts under the same reaction conditions was reported by Pfaltz *et al.*[9a] and Andrus *et al.*[9b] The high enantioselectivity (up to 84% ee) has been achieved in the oxidation of cyclopentene.[10a] In this paper, we describe the detailed results of allylic oxidation of cycloalkenes using copper(II)-tris(oxazoline) complexes as catalysts.

Synthesis of tris(oxazoline) ligands

Chiral (2,2'-bisoxazolino)alkanes, which have recently been employed as ligands in a wide variety of metal-catalyzed asymmetric reactions, are generally prepared by the treatment of 1,2-amino alcohols with diacid derivatives.[10] The same is expected for the synthesis of tris(oxazoline). Thus, a series of enantiomerically pure 4-substituted tris(oxazoline) ligands was prepared from amino alcohols and trimethyl nitrilotriacetate in two steps: i) preparation of tris(β-hydroxy amides) from trimethyl nitrilotriacetate and the corresponding amino alcohols and ii) cyclization of the tris(β-hydroxy amides). The starting amino alcohols **2a-d** were easily



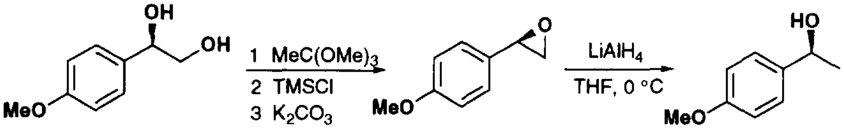
Scheme 1



Scheme 2

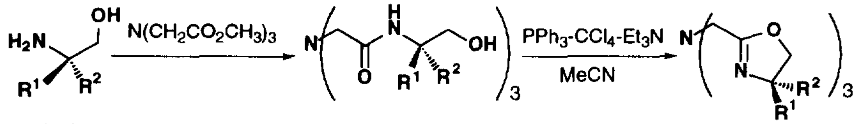
obtained by the reduction of the corresponding α-amino acids, *L*-phenylalanine, *L*-valine, *D*-phenylglycine and *L*-*tert*-leucine, according to the reported procedure (Scheme 1).[11] The amino alcohols **2e-h** were prepared by the sequence: i) Sharpless' asymmetric dihydroxylation, ii) treatment of the resulting diols **3e-h** with dimethyl carbonate, iii) regioselective ring opening of the cyclic carbonate **4e-h** with sodium azide, and iv) reduction of the resulting azido alcohol **5e-h** with lithium aluminum hydride (Scheme 2).[12,13] The enantiomeric excesses of the obtained amino alcohols **2e-h** were determined to be enantiomerically pure (>98% ee) within the detection limits of chiral HPLC analysis of the corresponding cyclic carbamate derivative or *N*-tosyl aziridine derivatives.

The absolute configuration of unknown diol **3f** was determined as follows: **3f** was converted into the epoxide according to the Sharpless' procedure[14] and reduction of the resulting epoxide with lithium aluminum hydride gave 1-(*p*-methoxyphenyl)ethanol (Scheme 3). The reported specific rotation of (*R*)-1-(*p*-methoxyphenyl)ethanol is $[\alpha]_D^{21}$ +41.0° (*c* 1.069, MeOH).[15] The prepared sample showed negative rotation; $[\alpha]_D^{25}$ -10° (*c* 0.41, MeOH). Thus, diol **3f** must have *R* configuration.



Scheme 3

The condensation of amino alcohols and trimethyl nitrilotriacetate which was prepared from commercial nitrilotriacetic acid according to Fisher's method, was effected by heating them at 80 °C to give the corresponding tris(β-hydroxy amide) **6a-h** in good yields. Treatment of **6a-h** with triphenylphosphine, carbon tetrachloride, and triethylamine at room temperature afforded the desired tris(oxazoline) **1a-h**.[16]



2a-h **6a-h** **1a-h**

Table 1. Preparation of **6** and **1**

Amino alcohol	R^1	R^2	Tris(β-hydroxy amide)	Yield (%)	Tris(oxazoline)	Yield (%)
2a	Ph	H	**6a**	67	**1a**	41
2b	H	*i*-Pr	**6b**	94	**1b**	24
2c	H	*t*-Bu	**6c**	39	**1c**	54
2d	H	$PhCH_2$	**6d**	80	**1d**	44
2e	H	*p*-(*t*-Bu)C_6H_4	**6e**	100	**1e**	43
2f	H	*p*-$MeOC_6H_4$	**6f**	74	**1f**	75
2g	H	2-Naphthyl	**6g**	18	**1g**	49
2h	H	*p*-ClC_6H_4	**6h**	85	**1h**	58

The chemical yields of tris(β-hydroxy amide) **6a-h** and the corresponding tris(oxazoline) **1a-h** are summarized in Table 1, respectively.

Enantioselective allylic oxidation of cyclopentene by using copper(II)-tris(oxazoline) complexes as catalysts

Allylic oxidation was first examined by using the iron or copper complex of tris(oxazoline) **1a** as a catalyst. The complexes were prepared in situ by mixing a metal salt and tris(oxazoline) in a molar ratio of 1:1.5 in acetone at room temperature for 30 minutes. The FAB mass analysis of the resulting Cu(II)- and Fe(III)-complexes confirmed that the ligand complexed the metal ions in a ratio of 1 to 1. In the presence of 5 mol% of the metal complex, cyclopentene was treated with the co-oxidant such as *t*-butyl peroxybenzoate, benzoylperoxide and *t*-butyl hydroperoxide in acetone at room temperature. The results are summarized in Table 2.

We first examined the reaction with iron complexes $Fe(ClO_4)_2$-**1a** or $Fe(ClO_4)_3$-**1a** as a catalyst, since the nucleus of MMO bears the same element as a metal ion. However, both Fe complexes did not show any catalytic activity (entries 5, 6). Thus, the central metal ion was replaced by copper ion. Both Cu complexes [CuOTf-**1a** and $Cu(OTf)_2$-**1a**] were found to catalyze the desired oxidation but the Cu(II)-complex showed higher asymmetric induction than the Cu(I)-complex. For example, the reaction using $Cu(OTf)_2$-**1a** and *t*-butyl peroxybenzoate gave (*S*)-2-cyclopentenyl benzoate of 74% ee in 68% yield at room temperature, while the reaction using CuOTf-**1a** and *t*-butyl peroxybenzoate provided the same allylic oxidation product of 66% ee in 67% yield (entries 1 and 2). Neither epoxide nor enone was produced in these reactions. In contrast to our results, Cu(I)-bis(oxazoline) complexes have been reported to be more effective than Cu(II)-bis(oxazoline) complexes, as a catalyst for asymmetric allylic oxidation.[10a] The oxidation with benzoyl peroxide in the

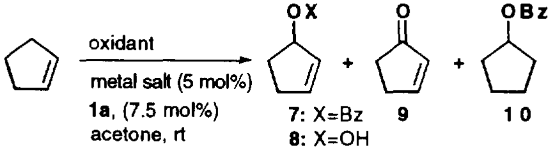


Table 2. Enantioselective allylic oxidation of cyclopentene

Entry	Metal salt	Oxidant	Time (h)	Yield (%)a) 7	8	9	10	% ee b)	Confign. c)
1	CuOTf	$PhCO_3Bu$-*t*	40	67	-	-	-	66	*S*
2	$Cu(OTf)_2$	"	"	68	-	-	-	74	*S*
3	$Cu(OTf)_2$	$(PhCO_2)_2$	"	21	-	-	15	68	*S*
4	$Cu(OTf)_2$	*t*-BuOOH	"	-	29	6	-	13	*S*
5	$Fe(ClO_4)_2$	$PhCO_3Bu$-*t*	24	-	-	-	-	-	-
6	$Fe(ClO_4)_3$	"	"	-	-	-	-	-	-

a) Isolated yield. The yield was calculated based on the peroxide used.

b) Determined by HPLC using optically active column: (DAICEL CHIRALCEL OD; hexane/*i*-PrOH=1000:1).

c) Determined by chiroptical comparison (reference 17).

presence of Cu(OTf)$_2$-**1a** also gave the same product of 68% ee in 21% yield but, in addition to this, the undesired compound **10** was produced in 15% yield (entry 3).[18] Use of *t*-butyl hydroperoxide as an oxidant gave a 83:17 mixture of 2-cyclopentene-1-ol (**8**, 13% ee) and 2-cyclopentene-1-one (**9**).

We next examined the effect of solvent and reaction temperature on enantioselectivity and chemical yield by using cyclopentene as a substrate, Cu(OTf)$_2$-**1a** as a catalyst and *t*-butyl peroxybenzoate as an oxidant. The results are summarized in Table 3.

Table 3. Solvent and temperature effect on allylic oxidation with Cu(OTf)$_2$-**1a** as a catalyst.

Entry	Solvent	Temp.	Time (h)	Yield (%)[a]	% ee	Confign.
1	acetone	rt	40	68	74	*S*
2	"	0 °C	92	44	84	*S*
3	"	-20 °C	111	11	88	*S*
4	AcOEt	rt	40	56	65	*S*
5	"	0 °C	92	2	82	*S*
6	MeCN	rt	40	15	18	*S*
7	EtCN	"	40	25	57	*S*
8	CH_2Cl_2	"	40	48	60	*S*
9	DMF	"	40	16[b]	68	*S*
10	toluene	"	40	27	66	*S*

a) Isolated yield. The yield was based on the amount of *t*-butyl peroxybenzoate used.

b) Peroxyester was completely consumed in 40 h. Oxidation of DMF with peroxyester should be responsible for this undesired low yield (reference 7c).

The desired allylic oxidation proceeded in most polar solvents except for DMF but no clear relationship between enantioselectivity and polarity of solvents was observed. Amongst solvents examined, acetone gave the best result in regard to enantioselectivity as well as chemical yield. Enantioselectivity of the reaction in acetone increased, as the reaction temperature was depressed (entries 1-3). The highest enantioselectivity of 88% ee was achieved at -20 °C, though the reaction was slow. The reaction in ethyl acetate showed the slightly diminished enantioselectivity as compared with acetone. Acetonitrile which was reported to be the best solvent in Pfaltz and Andrus reaction[9a,b] was found to be a poor solvent for our reaction (entry 6).

During these studies, we found that the enantiomeric excess of the product slightly decreased, as the reaction time became longer. This suggested that the partial racemization of the products might occur under the reaction conditions probably due to Lewis acidity of Cu(II)-**1a** complex used as a catalyst.[19] Thus, we examined the stability of 2-cyclopentenyl benzoates to the reaction conditions. Actually, the enantiomeric excess of cyclopentenyl benzoate (75% ee) decreased to 65% ee, when it was exposed to an acetone solution of Cu(OTf)$_2$-**1a** (5 mol% to the benzoate) for 60 h at room temperature.

To suppress the racemization, we examined the effect of several additives (Table 4). We first examined the effect of water, coordination of which to the copper ion was expected to reduce its Lewis acidity. However, no desired reaction occurred in the presence of one equivalent of water to copper ion (entry 1). This result suggested that exhaustive elimination of water from the reaction system would accelerate the reaction, so that reaction time could be shortened and racemization should be minimized. Thus, we examined the reaction in the presence of molecular sieves and found that the reaction rate was enhanced by the addition of molecular sieves. For example, the reaction of cyclopentene in the presence of molecular sieves 4A completed in 16 h and (*S*)-(-)-

Table 4. Allylic oxidation using Cu(II)-**1a** in the presence of additives[a]

Entry	Additive	Temp.	Time (h)	Yield (%)[b]	% ee
1	H_2O	rt	40	-	-
2	MS-4A	rt	16	83	76
3	MS-4A	0 °C	150	81	83
4	MS-4A	-20 °C	200	30	93

a) The reaction was carried out in acetone.

b) Isolated yield. The yield was based on the amount of *t*-butyl peroxybenzoate used.

2-cyclopentenyl benzoate was obtained in 83% yield with ee of 76% (entry 2). The reaction at -20 °C gave the product in 30% yield with excellent enantioselectivity of 93% (entry 4).

Under these optimized conditions, we explored the effect of the ligand on enantioselectivity by using the system of Cu(OTf)$_2$-tris(oxazoline) complex and *t*-butyl peroxybenzoate (Table 5). Complexes of Cu(OTf)$_2$ of **1b**, **1c** and **1d** which have non-aryl substituents in the oxazoline moiety showed no or poor catalytic activity (entries 1-3). However, the sense of asymmetric induction by Cu(II)-**1b** was opposite to that with Cu(II)-**1a** complex. Although the mechanism of asymmetric induction is unclear at present, these results suggested that some attractive interaction between the aryl substituent and the intermediary ally radicals.[20] This was also supported by the fact that the complex Cu(II)-**1e** did not serve as a catalyst, wherein the bulky *t*-butyl group might intercept the interaction between the allyl radical and the aryl ring (entry 4). Introduction of *p*-methoxyphenyl group (**1f**) as an aryl substituent improved enantioselectivity but decreased catalytic activity (entry 5). The reaction with Cu(II)-**1f** complex did not proceed at -20 °C (entry 6). On the other hand, the catalyst derived from **1g** and **1h** showed the diminished enantioselectivities (entries 7 and 8).

Table 5. Effect of the substituent of tris(oxazoline) ligand on enantioselectivity[a)]

Entry	Ligand	Temp.	Time (h)	Yield[b)]	% ee	Confign.
1[c)]	**1b**	rt	40	8	23	*S*
2[c)]	**1c**	"	"	-	-	-
3[c)]	**1d**	"	20	-	-	-
4[c)]	**1e**	"	"	-	-	-
5[d)]	**1f**	"	15	31	81	*R*
6[d)]	**1f**	-20	200	-	-	-
7[d)]	**1g**	0	50	38	50	*R*
8[d)]	**1h**	rt	10	60	20	*R*

a) The reaction was carried out in acetone.

b) Isolated yield. The yield was based on the amount of *t*-butyl peroxybenzoate used. All the products gave satisfactory spectroscopic data.

c) The reaction was carried out without molecular sieves.

d) The reaction was carried out in the presence of molecular sieves.

We also examined the influence of the aryl substituent of peroxyesters on enantioselectivity by using

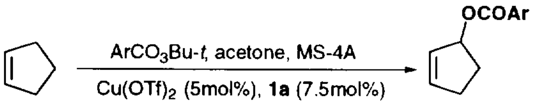


Table 6. Allylic oxidation with various terminal oxidant

Entry	Oxidant (Ar)	Temp.	Time (h)	Yield (%)[a)]	% ee	Confign
1	*p*-MeOC$_6$H$_4$	rt	17	55	68[b)]	*S*
2	*p*-ClC$_6$H$_4$	"	17	63	69[c)]	*S*
3	*p*-NO$_2$C$_6$H$_4$	"	17	-	-	-
4	*o*-MeC$_6$H$_4$	rt	8	16	83[d)]	*S*
5	"	0 °C	27	22	87	*S*
6	"	-20 °C	190	5	91	*S*
7	*m*-MeC$_6$H$_4$	rt	17	61	65[d)]	*S*
8	1-Naphthyl	"	17	53	73[e)]	*S*
9	*o*-ClC$_6$H$_4$	"	17	70	74[d)]	*S*

a) Isolated yield. The yield was based on the amount of the oxidant used. All the products gave satisfactory spectroscopic data.

b) Determined by HPLC using optically active column (DAICEL CHIRALPAK AD; hexane/*i*-PrOH=1000:1).

c) Determined by HPLC using optically active column (DAICEL CHIRALCEL OB-H; hexane).

d) Determined by HPLC using optically active column (DAICEL CHIRALCEL OD; hexane/*i*-PrOH=1000:1).

e) Determined by HPLC using optically active column (DAICEL CHIRALCEL OD; hexane/*i*-PrOH=300:1).

substituted peroxybenzoates as oxidants. We expected that the steric requirement and the electronic nature of the substituent would influence on the transition state geometries and hence on enantioselectivity of the reaction. Thus, a variety of peroxyesters were examined in the oxidation of cyclopentene in the presence of molecular sieves 4A. The results of experiments are summarized in Table 6. Contrary to our expectation, the enantioselectivity was not very influenced by the *m*- or *p*-substituent (entries 1, 2, and 7), though introduction of *p*-nitro group strongly retarded the reaction (entry 3). The presence of an *o*-methyl group affects enantioselectivity to a small extent (entries, 4-6; c.f. Table 4). On the other hand, the presence of an *o*-chloro substituent decreases enantioselectivity, though chemical yield was improved (entry 9).

Oxidation of other olefins

In order to clarify the scope of the present reaction, we examined the oxidation of a series of cycloalkenes and 1-pentene by using Cu(OTf)$_2$-**1a** as a catalyst. The results with cycloalkenes are summarized in Table 7.

Oxidation of cyclohexene, cycloheptene, and cyclooctene in the presence of molecular sieves proceeded with moderate enantioselectivity at room temperature (entries 3, 7, and 9). As the reaction temperature was depressed, enantioselectivity was increased but chemical yield was decreased. For example, oxidation of cyclohexene at -20 °C showed 72% ee but the yield of cyclohexenyl benzoate was only 4%, even after 255 h (entry 5). Oxidation of cycloheptene and cyclooctene did not occur at - 20 °C.

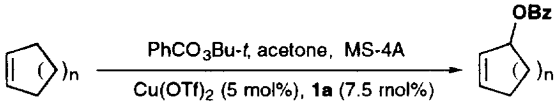
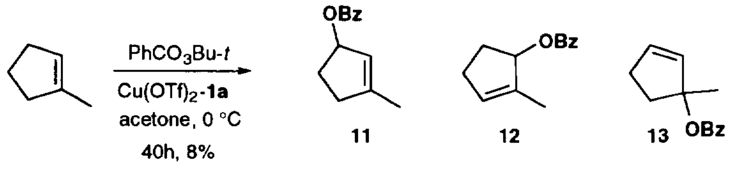


Table 7. Asymmetric allylic oxidation of cycloalkenes in the presence of MS-4A.

Entry	n	Additive	Temp.	Time (h)	Yield (%)[a]	% ee
1	2	-	rt	48	10	56
2	2	MS-4A	rt	20	19	42
3	2	MS-4A	rt	10	3	58
4	2	MS-4A	0 °C	250	14	66
5	2	MS-4A	-20 °C	255	4	72
6	3	-	rt	90	34	14
7	3	MS-4A	rt	90	5	60
8	4	-	rt	90	18	54
9	4	MS-4A	rt	50	11	64

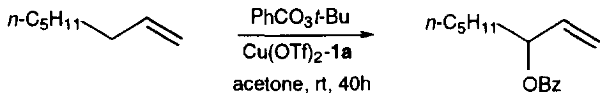
a) Isolated yield. The yield was based on the amount of *t*-butyl peroxybenzoate used. All the products gave satisfactory spectroscopic data. All products have (*S*)-configuration.

Oxidation of 1-methyl-1-cyclopentene at 0 °C was also examined (Scheme 4). The reaction gave a mixture of **11** (42% ee), **12** (1% ee), and **13** (93% ee) in a ratio of 67:25:8.



Scheme 4

Oxidation of 1-octene was also examined but enantioselectivity was only modest at room temperature (Scheme 5). The reaction did not proceed at 0 °C.



Scheme 5 23% ee, 12%

In conclusion, the authors could demonstrate that the copper(II)-tris(oxazoline) complex newly designed on the basis of the active site structure of non-heme monooxygenase catalyzed enantioselective allylic C-H hydroxylation, though substrates are so far limited to cycloalkenes. Construction of the more sophisticated model compounds which enable the higher enantioselective C-H oxidation will be the future study.

Experimental

General. NMR spectra were recorded in $CDCl_3$ on a JEOL EX-270 (270MHz) instrument at ambient temperature unless otherwise mentioned. All signals were expressed as ppm down field from tetramethylsilane used as an internal standard (δ-value in $CDCl_3$). IR spectra were obtained with a SHIMADZU FTIR-8600 instrument. Optical rotation was measured with a JASCO DIP-360 automatic digital polarimeter. High resolution mass spectra were recorded on a JEOL JMS-SX/SX 102A instrument. HPLC analysis of enantiomeric excess was carried out using Hitachi L-4000 equipped with an appropriate optically active column, as described in the footnote to Tables. Column chromatography was conducted on Silica Gel BW-820MH, 70-200 mesh ASTM, available from FUJI SILYSIA CHEMICAL LTD. Preparative thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). All solvents were purified before use: tetrahydrofuran (THF) and toluene were dried over sodium benzophenone ketyl radical; dichloromethane, acetonitrile, propionitrile and carbon tetrachloride were distilled from calcium hydride; acetone and ethyl acetate were distilled from P_2O_5. Reactions were carried out under an atmosphere of nitrogen or argon, if necessary. Reagents were purified prior to use at need. All olefins were distilled prior to use. CuOTf and $Cu(OTf)_2$ were purchased from the Fluka Chemical Co. and Kanto Chemical Co. respectively, dried under vaccum with an electric heat gun, and handled under an atmosphere of nitrogen. For known compounds obtained in this study, only the specific rotations are given.

Trimethyl nitrilotriacetate

To a suspension of nitrilotriacetic acid (30 g, 157 mmol) in methanol (250 ml) was added conc. H_2SO_4 (9 ml) and the resulting mixture was refluxed for 10 h. The reaction mixture was cooled to room temperature and K_2CO_3 (20g) was added as portions and stirred for 1 h. Then, the suspension was filtered through a pad of Celite and concentrated *in vaccuo* to give a yellow oil. The residue was distilled under reduced pressure (75 °C, 2.5 mmHg) to give a pure material as a colorless oil (22.0 g, 60%). ^1H NMR: δ 3.66 (s, 9H), 3.61 (s, 6H). IR (KBr): 1732, 1437, 1271, 1155, 1013 cm^{-1}. Calcd for $C_9H_{15}NO_6$: C, 46.35; H, 6.48; N, 6.01%. Found: C, 46.23; H, 6.44; N, 5.98%.

Compounds **3**,**4**, and **5** were prepared according to the reportrd procedure.[12,13]

(*R*)-1-(*p*-*tert*-Butylphenyl)ethane-1,2-diol (**3e**); Mp 110-112 °C. $[\alpha]_D^{17}$ -37.8° (*c* 0.83, EtOH). ^1H NMR: δ 7.40 (d, *J*=8.6 Hz, 2H), 7.30 (d, *J*=8.6 Hz, 2H), 4.78 (ddd, *J*=3.6, 3.6, 7.9 Hz, 1H), 3.65-3.81 (m, 2H), 2.39 (d, *J*=3.3 Hz, 1H), 2.02 (dd, *J*=4.6, 7.6 Hz, 1H), 1.32 (s, 9H). IR (KBr): 3406, 1508, 1458, 1339, 1229, 1086, 1065, 1039, 889, 831, 579 cm^{-1}. Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34%. Found: C, 74.10; H, 9.25%. The absolute configuration of **3e** was determined in a same manner described for **3f**. The reported specific rotation of (*R*)-1-(*p*-*tert*-butylphenyl)ethanol (51.4% ee) is $[\alpha]_D^{20}$ +17.81° (*c* 3.94, EtOH).[15b] The prepared sample showed negative rotation; $[\alpha]_D^{17}$ -33.1° (*c* 2.16, EtOH). Thus, diol **3e** must have *R* configuration.

(*R*)-1-(*p*-Methoxyphenyl)ethane-1,2-diol (**3f**); Mp 95-96 °C. $[\alpha]_D^{17}$ -36.9° (*c* 1.48, EtOH). ^1H NMR: δ 7.29 (d, *J*=8.9 Hz, 2H), 6.89 (d, *J*=8.9 Hz, 2H), 4.78 (ddd, *J*=3.0, 3.6, 3.6 Hz, 1H), 3.81 (s, 3H), 3.61-3.77 (m, 2H), 2.45 (d, *J*=3.0 Hz, 1H), 2.06 (dd, *J*=4.9, 7.3 Hz, 1H). IR (KBr): 3315, 1612, 1514, 1246, 1182, 1086, 1026, 893, 833 cm^{-1}. Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19%. Found: C, 64.21; H, 7.20%.

(*R*)-1-(β-Naphthyl)ethane-1,2-diol (3g); $[\alpha]_D^{17}$ -36.5° (*c* 2.01, EtOH). Lit.[22] (*R*)-isomer; $[\alpha]_D^{21}$ -33.7° (*c* 1.2, EtOH).

(*R*)-1-(*p*-Chlorophenyl)ethane-1,2-diol (3h); $[\alpha]_D^{18}$ -38.2° (*c* 1.81, EtOH). Lit.[23] $[\alpha]_D$ -31.4° (*c* 0.97, EtOH).

(*R*)-4-(*p*-*tert*-Butylphenyl)-1,3-dioxolane-2-one (4e); Mp 72-73 °C. $[\alpha]_D^{17}$ -37.2° (*c* 0.58, $CHCl_3$). ^1H NMR: δ 7.46 (d, *J*=8.6 Hz, 2H), 7.29 (d, *J*=8.6 Hz, 2H), 5.65 (dd, *J*=7.9, 8.3 Hz, 1H), 4.77 (dd, *J*=8.3, 8.6 Hz, 1H), 4.36 (dd, *J*=8.3, 8.6 Hz, 1H), 1.34 (s, 9H). IR (KBr): 1791, 1477, 1362, 1163, 1059, 964, 827, 777, 581 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32%. Found: C, 70.89; H, 7.32%.

(*R*)-4-(*p*-Methoxypheny)-1,3-dioxolane-2-one (4f); Mp 71-72 °C. $[\alpha]_D^{16}$ -29.3° (*c* 1.13, $CHCl_3$). ^1H NMR: δ 7.30 (d, *J*=8.6 Hz, 2H), 6.96 (d, *J*=8.6 Hz, 2H), 5.62 (dd, *J*=7.9, 8.3 Hz, 1H), 4.75 (dd, *J*=8.3, 8.6 Hz, 1H), 4.35 (dd, *J*=7.9, 8.6 Hz, 1H), 3.83 (s, 3H). IR (KBr): 1796, 1614, 1512, 1256, 1171, 1071, 835, 770 cm^{-1}. Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%. Found: C, 61.78; H, 5.25%.

(*R*)-4-(β-Naphthyl)-1,3-dioxolane-2-one (4g); Mp 130-131 °C. $[\alpha]_D^{16}$ -31.0° (*c* 1.22, $CHCl_3$). ^1H NMR: δ 7.85-7.95 (m, 4H), 7.41-7.57 (m, 3H), 5.84 (dd, *J*=7.9, 8.6 Hz, 1H), 4.87 (dd, *J*=8.3, 8.6 Hz, 1H), 4.43 (dd, *J*=7.9, 8.3 Hz, 1H). IR (KBr): 1773, 1178, 1053, 827, 752 cm^{-1}. Anal. Calcd for $C_{13}H_{10}O_3$: C, 72.89; H, 4.70%. Found: C, 72.87; H, 4.76%.

(*R*)-4-(*p*-Chlorophenyl)-1,3-dioxolane-2-one (4h); Mp 99-100 °C. $[\alpha]_D^{17}$ -45.0° (*c* 0.63, $CHCl_3$). ^1H NMR: δ 7.45 (d, *J*=8.6 Hz, 2H), 7.29 (d, *J*=8.6 Hz, 2H), 5.66 (dd, *J*=7.9, 8.2 Hz, 1H), 4.81 (dd, *J*=8.2, 8.6 Hz, 1H), 4.31 (dd, *J*=7.9, 8.6 Hz, 1H). IR (KBr): 2964, 2912, 1865, 1821, 1799, 1597, 1549, 1491, 1475, 1420, 1385, 1350, 1327, 1209, 1182, 1105, 1094, 1053, 1094, 1053, 1013, 957, 908, 829, 775, 719 cm^{-1}. Anal. Calcd for $C_9H_7O_3Cl$: C, 54.43; H, 3.55%. Found: C, 54.55; H, 3.67%.

(*S*)-2-Azido-2-(*p*-*tert*-butylphenyl)ethanol (5e); $[\alpha]_D^{16}$ +194° (*c* 1.42, $CHCl_3$). ^1H NMR: δ 7.41 (d, *J*=8.6 Hz, 2H), 7.25 (d, *J*=8.6 Hz, 2H), 4.65 (t, *J*=6.3 Hz, 1H), 3.73 (d, *J*=6.3 Hz, 2H), 2.04 (b s, 1H), 1.32 (s, 9H). IR (KBr): 3420 , 2964, 2104, 1269, 1076, 1041, 831, 571 cm^{-1}. Anal. Calcd for $C_{12}H_{17}N_3O$: C, 65.73; H, 7.81; N, 19.16%. Found: C, 65.71; H, 7.83; N, 19.11%.

(*S*)-2-Azido-2-(*p*-methoxyphenyl)ethanol (5f); Mp 110-112 °C. $[\alpha]_D^{17}$ +239° (*c* 0.33, $CHCl_3$). ^1H NMR: δ 7.25 (d, *J*=8.6 Hz, 2H), 6.92 (d, *J*=8.6 Hz, 2H), 4.63 (t, *J*=6.6 Hz, 1H), 3.82 (s, 3H), 3.73 (dd, *J*=6.3, 6.6 Hz, 2H), 2.88 (t, *J*=6.3 Hz, 1H). IR (KBr): 3356, 2127, 2081, 1614, 1514, 1466, 1340, 1308, 1267, 1244, 1184, 829 cm^{-1}. Anal. Calcd for $C_9H_{11}N_3O_2$: C, 55.95; H, 5.74; N, 21.75%. Found: C, 55.92; H, 5.70; N, 21.69%.

(*S*)-2-Azido-2-(β-naphthyl)ethanol (5g); Mp 67-68 °C. $[\alpha]_D^{18}$ +229° (*c* 0.48, $CHCl_3$). ^1H NMR: δ 7.82-7.90 (m, 4H), 7.42-7.55 (m, 3H), 4.85 (t, *J*=6.3 Hz, 1H), 3.84 (dd, *J*=6.3, 6.6 Hz, 2H), 2.27 (t, *J*=6.6 Hz, 1H). IR (KBr): 3420, 2135, 2098, 1373, 1337, 1273, 1034, 822, 748, 484 cm^{-1}. Anal. Calcd for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71%. Found: C, 67.54; H, 5.22; N, 19.69%.

(*S*)-2-Azido-2-(*p*-chlorophenyl)ethanol (5h); Mp 85-86 °C. $[\alpha]_D^{17}$ +216° (*c* 0.43, $CHCl_3$). ^1H NMR: δ 7.38 (d, *J*=8.6 Hz, 2H), 7.28 (d, *J*=8.6 Hz, 2H), 4.66 (dd, *J*=5.3, 7.3 Hz, 1H), 3.70-3.78 (m, 2H), 1.94 (dd, *J*=5.9, 6.9 Hz, 1H). IR (KBr): 3358, 2137, 2087, 1493, 1339, 1304, 1263, 1092, 1059, 1034, 1009, 870, 824 cm^{-1}. Anal. Calcd for $C_8H_8N_3OCl$: C, 48.62; H, 4.08; N, 21.26%. Found: C, 48.63; H, 4.12; N, 21.15%.

(*S*)-2-Amino-2-(*p*-methoxyphenyl)ethanol (2f)

To a solution of **5f** (412 mg, 2.13 mmol) in THF (8.4 ml) was slowly added lithium aluminum hydride (160 mg, 237 µmol) at 0 °C. After being stirred at room temperature for 2 h, the mixture was diluted with diethyl ether (10 ml) and quenched with aqueous KF (1.6 N, 474 µl). The suspension was filtered through a pad of Celite, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to give the crude **13f** as white solids (354 mg). Recrystallization from toluene afforded pure **2f** as white crystals (200 mg, 56%). Mp 92-93 °C. Enantiomeric excess was determined to be >99% ee by HPLC analysis of the corresponding cyclic carbamate derived from **2f** (DAICEL CHIRALPAK AD, *i*-PrOH/hexane=1:9, 0.5 ml/min; 36.46, 40.27). $[\alpha]_D^{18}$ +38.3° (*c* 0.43, $CHCl_3$). ^1H NMR: δ 7.22 (d, *J*=8.6 Hz, 2H), 6.85 (d, *J*=8.6 Hz, 2H), 3.96 (dd, *J*=4.3, 8.6 Hz, 1H), 3.77 (s, 3H), 3.65 (dd, *J*=4.3, 10.9 Hz, 1H), 3.50 (dd, *J*=8.6, 10.9 Hz, 1H), 2.79 (b s, 3H). IR (KBr): 3144, 1614, 1587, 1516, 1462, 1352, 1298, 1250, 1178, 1062, 974, 837, 818 cm^{-1}. Anal. Calcd for $C_9H_{13}NO_2$: C, 64.65; H, 7.84; N, 8.38%. Found: C, 64.65; H, 7.84; N, 8.24%.

In a similar manner, coupounds **2e,g-h** were prepared from the corresponding azido alcohols.

(*S*)-2-Amino-2-(β-naphthyl)ethanol (2g); Mp 97-98 °C. $[\alpha]_D^{16}$ +31.0° (*c* 1.41, $CHCl_3$). Enantiomeric excess was determined to be >98% ee by HPLC analysis of the corresponding *N*-*p*-tolylsulfonyl-2-(β-naphthyl)aziridine derived from **2g** (DAICEL CHIRALCEL OF, *i*-PrOH/hexane=1:1). ^1H NMR: δ 7.71-7.79 (m, 4H), 7.23-7.48 (m, 3H), 4.12 (dd, *J*=4.3, 8.3 Hz, 1H), 3.76 (dd, *J*=4.3, 10.9 Hz, 1H), 3.59 (dd, *J*=8.3, 10.9 Hz, 1H), 2.67 (b s, 3H). IR (KBr): 3354, 1600, 1508, 1458, 1366, 1047, 951, 858, 822, 746, 478 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48%. Found: C, 76.83; H, 7.05; N, 7.45%.

(*S*)-2-Amino-2-(*p*-*tert*-butylphenyl)ethanol (2e); Mp 113-114 °C. $[\alpha]_D^{18}$ +37.5° (*c* 0.47, $CHCl_3$). Enantiomeric excess was determined to be >98% ee by HPLC analysis with the corresponding *N*-*p*-tolylsulfonyl-2-(*p*-*tert*-butylphenyl)aziridine derived from **2e** (DAICEL CHIRALCEL OJ, *i*-PrOH/hexane=1:1). ^1H NMR: δ 7.29 (d, *J*=8.3 Hz, 2H), 7.18 (d, *J*=8.3 Hz, 2H), 3.94 (dd, *J*=4.6, 8.3 Hz, 1H), 3.65 (dd, *J*=4.6, 19.6 Hz, 1H), 3.47 (dd, *J*=8.3, 10.6 Hz, 1H), 1.24 (s, 9H). IR (KBr): 3337, 2958, 1462, 1362, 1271, 1082, 1045, 955, 829 cm^{-1}. Anal. Calcd for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25%. Found: C, 74.48; H, 9.87; N, 7.28%.

(*S*)-2-Amino-2-(*p*-chlorophenyl)ethanol (2h); Mp 74-75 °C. $[\alpha]_D^{18}$ +39.7° (*c* 0.69, $CHCl_3$). Enantiomeric excess was determined to be >98% ee by HPLC analysis of the corresponding *N*-*p*-tolylsulfonyl-2-(*p*-chlorophenyl)aziridine derived from **2h** (DAICEL CHIRALCEL OF, *i*-PrOH/hexane=1:4). ^1H NMR: δ 7.29–7.46 (m, 4H), 4.04 (dd, *J*=4.3, 7.9 Hz, 1H), 3.71 (dd, *J*=4.3, 10.9 Hz, 1H), 3.52 (dd, *J*=7.9, 10.9 Hz, 1H). IR (KBr): 3063, 1620, 1497, 1412, 1092, 1090, 1016, 984, 891, 827, 806, 484 cm^{-1}. Anal. Calcd for $C_8H_{10}NOCl$: C, 55.99; H, 5.87; N, 8.16%. Found: C, 55.93; H, 5.85; N, 8.12%.

_N,N',N''_-Tris[(1*R*)-(2-hydroxy-1-phenylethyl)]nitrilotriacetamide (6a)

(*R*)-Phenylglycinol (2.00 g, 14.6 mmol) was added to trimethyl nitrilotriacetate (1.11g, 4.78 mmol) and the resulting mixture was heated at 80 °C for 40 h. The mixture was cooled to room temperature and chromatographed on silica gel ($CHCl_3$/MeOH=19:1) to give **6a** as white solids (1.75 g, 67% based on the amount of trimethyl nitrilotriacetate used). $[\alpha]_D^{18}$ -72.8° (*c* 1.22, $CHCl_3$). ^1H NMR: δ 8.48 (d, *J*=8.3 Hz, 3H), 7.16-7.26 (m, 15H), 5.10 (m, 3H), 4.58 (b s, 3H), 3.70-3.80 (m, 6H), 3.32 (d, *J*=16.5 Hz, 3H), 3.23 (d, *J*=16.5 Hz, 3H). IR (KBr): 3403, 1655, 1556, 1070, 1041, 760, 702, 527 cm^{-1}. Anal. Calcd for $C_{30}H_{36}N_4O_6$: C, 65.68; H, 6.61; N, 10.21%. Found: C, 65.37; H, 6.67; N, 10.32%.

In a similar manner, coupounds **6b-h** were prepared from trimethyl nitrilotriacetate and the corresponding amino alcohols.

_N,N',N''_-Tris[(1*S*)-2-hydroxy-1-*i*-propylethyl]nitrilotriacetamide (6b); White solids. $[\alpha]_D^{18}$ -7.1° (*c* 0.79, $CHCl_3$). ^1H NMR: δ 7.44 (d, *J*=8.9 Hz, 3H), 4.30 (b s, 3H), 3.51-3.79 (m, 9H), 3.46 (m, 3H), 3.36 (d, *J*=16.5 Hz, 3H), 1.81 (m, 3H), 0.93 (d, *J*=16.5 Hz, 9H), 0.90 (d, *J*=6.9 Hz, 9H). IR (KBr): 3433, 2964, 2877, 1650, 1550 cm^{-1}. Anal. Calcd for $C_{21}H_{42}N_4O_6$: C, 56.48; H, 9.48; N, 12.55%. Found: C, 56.35; H, 9.51; N, 12.48%.

_N,N',N''_-Tris[(1*S*)-2-hydroxy-1-*tert*-butylethyl]nitrilotriacetamide (6c); White solids. $[\alpha]_D^{18}$ +16.5° (*c* 0.38, EtOH). ^1H NMR (CD_3OD): δ 3.80-3.84 (m, 6H), 3.30-3.78 (m, 9H), 0.93 (s, 9H). IR (KBr): 3406, 2964, 1740, 1657, 1545, 1477, 1367, 1261, 1053 cm^{-1}. Anal. Calcd for $C_{24}H_{48}N_4O_6$: C, 58.99; H, 9.90; N, 11.47%. Found: C, 58.94; H, 9.95; N, 11.41%.

_N,N',N''_-Tris[(1*S*)-2-hydroxy-1-benzylethyl]nitrilotriacetamide (6d); White solids. $[\alpha]_D^{18}$ -50.7° (*c* 2.93, EtOH). ^1H NMR: δ 8.61 (d, *J*=8.9 Hz, 3H), 7.24-7.82 (m, 21H), 5.29 (m, 3H), 3.81-3.84 (m, 9H), 3.33 (ABq, *J*=16.2 Hz, 6H), 2.54 (b s, 3H). IR (KBr): 3491, 1651, 1543, 1039, 748, 702 cm^{-1}. Anal. Calcd for $C_{33}H_{42}N_4O_6$: C, 67.10; H, 7.17; N, 9.48%. Found: C, 66.87; H, 7.05; N, 9.35%.

***N,N',N''*-Tris[(1*S*)-2-hydroxy-1-(*p*-*tert*-butylphenyl)ethyl]nitrilotriacetamide (6e)**; White solids $[\alpha]_D^{18}$ +54.4° (*c* 1.86, EtOH). ^{1}H NMR: δ 8.31 (d, *J*=8.3 Hz, 3H), 7.31 (d, *J*=8.6 Hz, 6H), 7.22 (d, *J*=8.6 Hz, 6H), 5.12 (m, 3H), 4.35 (b s, 3H), 3.70-3.78 (m, 6H), 3.39 (ABq, *J*=16.2 Hz, 6H), 1.25 (s, 27H). IR (KBr): 3292, 2963, 1653, 1545, 1269, 1043, 831, 575 cm^{-1}. Anal. Calcd for $C_{42}H_{60}N_4O_6$: C, 70.36; H, 8.43; N, 7.81%. Found: C, 70.35; H, 8.51; N, 7.88%.

***N,N',N''*-Tris[(1*S*)-2-hydroxy-1-(*p*-methoxyphenyl)ethyl]nitrilotriacetamide (6f)**; White solids. $[\alpha]_D^{18}$ +76.3° (*c* 1.28, $CHCl_3$). ^{1}H NMR: δ 8.41 (d, *J*=8.3 Hz, 3H), 7.17 (d, *J*=8.6 Hz, 6H), 6.75 (d, *J*=8.6 Hz, 6H), 5.06 (m, 3H), 3.47-3.79 (m, 6H), 3.71 (s, 9H), 3.31 (ABq, *J*=16.5 Hz, 6H), 2.79 (d, *J*=7.3 Hz, 6H), 2.40 (b s, 3H). IR (KBr): 3381, 1663, 1614, 1543, 1514, 1462, 1304, 1250, 1180, 1034, 833 cm^{-1}. Anal. Calcd for $C_{33}H_{42}N_4O_9$: C, 62.06; H, 6.63; N, 8.77%. Found: C, 61.68; H, 6.70; N, 8.62%.

***N,N',N''*-Tris[(1*S*)-2-hydroxy-1-(β-naphthyl)ethyl]nitrilotriacetamide (6g)**; White solids. $[\alpha]_D^{18}$ +45.4° (*c* 1.02, EtOH). ^{1}H NMR: δ 8.41 (d, *J*=8.3 Hz, 3H), 7.17 (d, *J*=8.6 Hz, 6H), 6.75 (d, *J*=8.6 Hz, 6H), 5.06 (m, 3H), 3.47-3.79 (m, 6H), 3.71 (s, 9H), 3.31 (ABq, *J*=16.5 Hz, 6H), 2.79 (d, *J*=7.3 Hz, 6H), 2.40 (b s, 3H). IR (KBr): 3381, 1663, 1614, 1543, 1514, 1250, 1180, 833 cm^{-1}. Anal. Calcd for $C_{42}H_{42}N_4O_6$: C, 72.19; H, 6.06; N, 8.02%. Found: C, 72.35; H, 6.13; N, 7.98%.

***N,N',N''*-Tris-[(1*S*)-2-hydroxy-1-(*p*-chlorophenylethyl]nitrilotriacetamide (6h)**; White solids. $[\alpha]_D^{18}$ +74.5° (*c* 1.41, $CHCl_3$). ^{1}H NMR: δ 8.26 (d, *J*=7.9 Hz, 3H), 7.29 (d, *J*=5.6 Hz, 6H), 7.21 (d, *J*=5.6 Hz, 6H), 5.08 (m, 3H), 3.52-3.83 (m, 6H), 3.38 (ABq, *J*=15.8 Hz, 6H), 2.14 (b s, 3H). IR (KBr): 3366, 1665, 1541, 1493, 1458, 1092, 1045, 1015, 823, 529 cm^{-1}. Anal. Calcd for $C_{30}H_{33}N_4O_6Cl_3$: C, 55.27; H, 5.10; N, 8.59%. Found: C, 55.26; H, 5.10; N, 8.59%.

Tri{[2-(4*R*)-(4-phenyl-1,3-oxazolinyl)]methyl}amine (1a)

To a solution of **6a** (360 mg, 656 μmol), triethylamine (1.43 ml) and CCl_4 (1.43 ml) in dry MeCN (7 ml) was added triphenylphosphine (680 mg, 2.59 mmol) under nitrogen at room temperature. After 2 h, the mixture was diluted with ethyl acetate (20 ml) and washed with saturated aqueous $NaHCO_3$ (5 ml). After the organic layer was separated, the aqueous layer was extracted with ethyl acetate (5 ml). The combined organic extracts were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification by short column chromatography (SiO_2, $CHCl_3/NEt_3$=100:0 to 100:1) afforded crude **1a**. The oil was further purified by flash column chromatography (Chromatorex-NH®, CH_2Cl_2) to give pure **1a** as a pale yellow oil (134 mg, 41%). $[\alpha]_D^{18}$ +63.2° (*c* 1.58, $CHCl_3$). IR (KBr): 1664, 1491, 1456, 1144, 984, 762, 700 cm^{-1}. ^{1}H NMR: δ 7.27-7.35 (m, 15H), 5.22 (dd, *J*=8.6, 10.2 Hz, 3H), 4.65 (dd, *J*=8.6, 10.2 Hz, 3H), 4.11 (dd, *J*=8.6, 8.6 Hz, 3H), 3.91 (s, 6H). HRFABMS m/z. Calcd. for $C_{30}H_{30}N_4O_3H$ (MH$^+$): 495.2396. Found 495.2392.

In a similar manner, coupounds **1b-h** were prepared from the corresponding tris(β-hydroxy amide) **6b-h**.

Tri{[2-(4*S*)-(4-(*i*-propyl)-1,3-oxazolinyl)]methyl}amine (1b); $[\alpha]_D^{18}$ -57.3° (*c* 0.66, $CHCl_3$). ^{1}H NMR: δ 4.25 (m, 3H), 3.78-4.01 (m, 6H), 3.64 (s, 6H), 1.73 (m, 3H), 0.96 (d, *J*=6.6 Hz, 9H), 0.88 (d, *J*=6.6 Hz, 9H). IR (KBr): 2960, 2931, 2906, 2873, 1670 cm^{-1}. HRFABMS m/z. Calcd. for $C_{21}H_{36}N_4O_3H$ (MH$^+$): 393.2866. Found 393.2862.

Tri{[2-(4*S*)-(4-(*tert*-butyl)-1,3-oxazolinyl)]methyl}amine (1c); $[\alpha]_D^{18}$ -44.6° (*c* 1.08, $CHCl_3$). ^{1}H NMR: δ 4.19 (dd, *J*=8.9, 10.2 Hz, 3H), 4.05 (dd, *J*=8.3, 10.2 Hz, 3H), 3.86 (dd, *J*=8.3, 8.9 Hz, 3H) 3.64 (ABq, *J*=17.0 Hz, 6H), 0.07 (s, 27H). IR (KBr): 2961, 1672, 1479, 1366, 1194, 1148, 980 cm^{-1}. HRFABMS m/z. Calcd. for $C_{24}H_{42}N_4O_3H$ (MH$^+$): 435.3335. Found 435.3339.

Tri{[2-(4*S*)-(4-benzyl-1,3-oxazolinyl)]methyl}amine (1d); $[\alpha]_D^{18}$ -30.7° (*c* 1.05, $CHCl_3$). ^{1}H NMR: δ 7.18-7.32 (m, 15H), 4.40 (dddd, *J*=7.6, 8.3, 8.6, 9.6 Hz, 3H), 4.21 (dd, *J*=8.3, 9.6 Hz, 3H), 3.97 (dd, *J*=7.6, 8.3 Hz, 3H), 3.59 (s, 6H), 2.90 (ABdq, *J*=5.3, 8.6, 13.9 Hz, 6H). IR (KBr): 2901, 1666, 1495, 1452, 1192, 1146, 980, 754, 702 cm^{-1}. HRFABMS m/z. Calcd. for $C_{33}H_{36}N_4O_3H$ (MH$^+$): 537.2866. Found 537.2866.

Tri{[2-(4*S*)-(4-(*p*-*tert*-butylphenyl)-1,3-oxazolinyl)]methyl}amine (1e); $[\alpha]_D^{18}$ -51.8° (*c* 1.48, $CHCl_3$). IR (KBr): 2963, 1510, 1364, 1269, 984, 833, 571 cm^{-1}. ^{1}H NMR: δ 7.35 (d, *J*=8.6 Hz, 6H), 7.20

(d, *J*=8.6 Hz, 6H), 5.20 (dd, *J*=8.3, 10.2 Hz, 3H), 4.65 (dd, *J*=8.6, 10.2 Hz, 3H), 4.07 (dd, *J*=8.3, 8.6 Hz, 3H), 3.87 (s, 6H). HRFABMS m/z. Calcd. for $C_{42}H_{54}N_4O_3H$ (MH^+): 663.4274. Found 663.4272.

Tri{[2-(4*S*)-(4-(*p*-methoxyphenyl)-1,3-oxazolinyl)]methyl}amine (1f); $[\alpha]_D^{18}$ -61.0° (*c* 0.79, $CHCl_3$). ^1H NMR: δ 7.18 (d, *J*=8.6 Hz, 6H), 6.86 (d, *J*=8.6 Hz, 6H), 5.17 (dd, *J*=8.6, 9.9 Hz, 3H), 4.62 (dd, *J*=8.3, 9.9 Hz, 3H), 4.10 (dd, *J*=8.3, 8.6 Hz, 3H), 3.87 (s, 6H), 3.79 (s, 9H). IR (KBr): 1665, 1514, 1464, 1302, 1248, 1178, 1032, 982, 833 cm^{-1}. HRFABMS m/z. Calcd. for $C_{33}H_{36}N_4O_6H$ (MH^+): 585.2713. Found 585.2718.

Tri{[2-(4*S*)-(4-(β-naphthyl)-1,3-oxazolinyl)]methyl}amine (1g); $[\alpha]_D^{21}$ -72.8° (*c* 1.58, $CHCl_3$). ^1H NMR: δ 7.76-7.82 (m, 12H), 7.34-7.45 (m, 9H), 5.42 (dd, *J*=8.3, 10.2 Hz, 3H), 4.63 (dd, *J*=8.6, 10.2 Hz, 3H), 4.15 (dd, *J*=8.3, 8.6 Hz, 3H), 3.88 (s, 6H), 1.30 (s, 27H). IR (KBr): 1666, 1541, 1373, 1271, 1192, 1144, 978, 895, 750, 478 cm^{-1}. HRFABMS m/z. Calcd. for $C_{42}H_{36}N_4O_3H$ (MH^+): 645.2866. Found 645.2862.

Tri{[2-(4*S*)-(4-(*p*-chlorophenyl)-1,3-oxazolinyl)]methyl}amine (1h); $[\alpha]_D^{21}$ -47.2° (*c* 1.92, $CHCl_3$). ^1H NMR: δ 7.29 (d, *J*=8.6 Hz, 6H), 7.19 (d, *J*=8.6 Hz, 6H), 5.20 (dd, *J*=8.3, 10.2 Hz, 3H), 4.65 (dd, *J*=8.6, 10.2 Hz, 3H), 4.07 (dd, *J*=8.3, 8.6 Hz, 3H), 3.87 (s, 6H). IR (KBr): 1665, 1493, 1412, 1350, 1182, 1092, 1015, 984, 827, 754 cm^{-1}. HRFABMS m/z. Calcd. for $C_{30}H_{27}N_4O_3Cl_3H$ (MH^+): 597.1227. Found 597.1221.

$Cu(OTf)_2$-1a complex; HRFABMS m/z. Calcd. for $C_{30}H_{30}N_4O_3CuCF_3SO_3$ (**1a**-$CuOTf^+$): 706.1134. Found 706.1139.

$Fe(ClO_4)_3$-1a complex; HRFABMS m/z. Calcd. for $C_{30}H_{30}N_4O_3FeClO_4$ (**1a**-$FeClO_4^{2+}$): 649.8908. Found 649.8902.

tert-Butyl peroxy-*p*-methoxybenzoate

To a solution of *p*-anisoyl chloride (1.30 g, 7.59 mmol), triethylamine (1.27 ml, 9.10 mmol) and 4-(*N,N*-dimethylamino)pyridine (10 mg, 80 μmol) in CH_2Cl_2 (10 ml), was added dry *tert*-butyl hydroperoxide (3.3 N in toluene, 2.5 ml) dropwise at 0 °C and stirred for 2 h. Usual work up followed by column chromatography (SiO_2, hexane/AcOEt=19:1) gave a colorless oil (1.51 g, 89%). ^1H NMR: δ 7.91 (d, *J*=8.9 Hz, 2H), 6.93 (d, *J*=8.9 Hz, 2H), 3.87 (s, 3H), 1.41 (s, 9H). IR (KBr): 1753, 1607, 1512, 1367, 1317, 1250, 1167, 1055, 1026, 843, 760, 692, 611 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19%. Found: C, 64.06; H, 7.19%.

***tert*-Butyl peroxy-*p*-chlorobenzoate**; 86% yield. ^1H NMR: δ 7.89 (d, *J*=8.6 Hz, 2H), 7.43 (d, *J*=8.6 Hz, 2H), 1.41 (s, 9H). IR (KBr): 1757, 1367, 1244, 1094, 1061, 1015, 748. Anal. Calcd for $C_{11}H_{13}O_3Cl$: C, 57.78; H, 5.73%. Found: C, 57.76; H, 5.78%.

***tert*-Butyl peroxy-*p*-nitrobenzoate**; Mp 68-70 °C; 75% yield. ^1H NMR: δ 8.33 (d, *J*=8.9 Hz, 2H), 8.14 (d, *J*=8.9 Hz, 2H), 1.44 (s, 9H). IR (KBr): 1755, 1524, 1346, 1246, 1067, 714 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48%. Found: C, 55.01; H, 5.35%.

***tert*-Butyl peroxy-*o*-metylbenzoate**; 73% yield. ^1H NMR: δ 7.73-7.76 (m, 2H), 7.30-7.41 (m, 2H), 2.40 (s, 3H), 1.42 (s, 9H). IR (KBr): 1757, 1477, 1460, 1367, 1261, 1173, 1078, 1053, 854, 735 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%. Found: C, 69.12; H, 7.72%.

***tert*-Butyl peroxy-*m*-metylbenzoate**; 89% yield. ^1H NMR: δ 7.72 (d, *J*=7.9 Hz, 1H), 7.22-7.44 (m, 3H), 2.57 (s, 3H), 1.41 (s, 9H).IR (KBr): 2984, 1761, 1458, 1367, 1231, 1190, 1132, 1022, 735 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74%. Found: C, 69.11; H, 7.70%.

***tert*-Butyl peroxy-1-naphthoate**; 64% yield. ^1H NMR: δ 8.62 (d, *J*=9.4 Hz, 1H), 8.04 (d, *J*=8.3 Hz, 1H), 7.98 (d, *J*=6.3 Hz, 1H), 7.94 (d, *J*=14.5 Hz, 1H), 7.47-7.88 (m, 3H), 1.46 (s, 9H). IR (KBr): 2982, 1753, 1510, 1391, 1367, 1236, 1182, 1107, 978, 849, 810, 779, 748 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%. Found: C, 73.78; H, 6.62%.

***tert*-Butyl peroxy-*o*-chlorobenzoate**; 72% yield. ^1H NMR: δ 7.70 (ddd, *J*=1.0, 2.6, 8.3 Hz, 1H), 7.42-7.49 (m, 2H), 7.34 (ddd, *J*=2.6, 5.3, 7.6 Hz, 1H), 1.43 (s, 9H). IR (KBr): 1773, 1591, 1275, 1231, 1188, 1090, 1024, 755 cm^{-1}. Anal. Calcd for $C_{11}H_{13}O_3Cl$: C, 57.78; H, 5.73%. Found: C, 57.76; H, 5.78%.

General procedure for asymmetric allylic oxidation using Cu(OTf)$_2$-1a complex as a catalyst

A 5 ml round-bottomed flask was charged with pre-dried Cu(OTf)$_2$ (4.0 mg, 11 μmol). To the flask was added a solution of ligand **1a** (8.2 mg, 17 μmol) in CH_2Cl_2 (90 μl) under N_2. The solution was stirred at room temperature for 1 h. The resulted emerald green solution was transferred to the another flask containing acetone (0.34 ml) and molecular sieves 4A (85 mg) and cyclopentene (60 mg, 0.88 mmol). After being stirred for 30 min, the whole mixture was cooled to -20 °C. *tert*-Butyl peroxybenzoate (42 mg, 0.22 mmol, 1.0 eq) was added dropwise and the reaction mixture was left at -20 °C. After being stirred for 200 h, the reaction mixture was passed through a short silica gel column (hexane/AcOEt=9:1) to remove molecular sieves and the copper catalyst. The filtrate was concentrated and purified by column chromatography (hexane/AcOEt=100:1) to give (*S*)-2-cyclopentenyl benzoate as an oil (12.4 mg, 30%). The optical purity of this sample was determined to be 93% ee by HPLC (DAICEL CHIRALCEL OD, hexane/*i*-propanol=1000/1).

Spectroscopic data of the allyl benzoates obtained.

(*S*)-2-Cyclopentenyl benzoate (93% ee); $[\alpha]_D^{17}$ -179° (*c* 0.37, $CHCl_3$). Lit.[9c] (54% ee); $[\alpha]_D^{20}$ -103° (*c* 1.0, $CHCl_3$).

(*S*)-2-Cyclohexenyl benzoate (66% ee); $[\alpha]_D^{17}$ -118° (*c* 0.45, $CHCl_3$). Lit.[9c] (48% ee); $[\alpha]_D^{20}$ -87° (*c* 1.0, $CHCl_3$).

(*S*)-2-Cycloheptenyl benzoate (60% ee); $[\alpha]_D^{17}$ -29° (*c* 0.24, $CHCl_3$). Lit.[9f] (25% ee); $[\alpha]_D$ -11.5° ($CHCl_3$).

(*S*)-2-Cyclooctenyl benzoate (64% ee); $[\alpha]_D^{17}$ +55° (*c* 0.11, $CHCl_3$). Lit.[9c] (4% ee); $[\alpha]_D^{20}$ +3.1° ($CHCl_3$).

(*S*)-3-Benzoyloxy-1-octene (23% ee); $[\alpha]_D^{17}$ -4.8° (*c* 0.10, $CHCl_3$). Lit.[9c] (9% ee); $[\alpha]_D^{20}$ -2.0° ($CHCl_3$).

(*S*)-2-Cyclopentenyl *p*-methoxybenzoate (68% ee); $[\alpha]_D^{19}$ -71° (*c* 0.75, $CHCl_3$). ^1H NMR: δ 7.98 (d, *J*=8.9 Hz, 2H), 6.90 (d, *J*=8.9 Hz, 2H), 6.13-6.16 (m, 1H), 5.90-5.96 (m, 2H), 3.86 (s, 3H), 2.33-2.63 (m, 3H), 1.91-2.05 (m, 1H). IR (KBr): 1717, 1637, 1595, 1273, 1117, 1103, 1014 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47%. Found: C, 71.48; H, 6.52%.

(*S*)-2-Cyclopentenyl *p*-chlorobenzoate (69% ee); $[\alpha]_D^{19}$ -77° (*c* 1.02, $CHCl_3$). ^1H NMR: δ 7.95 (d, *J*=8.6 Hz, 2H), 7.40 (d, *J*=8.6 Hz, 2H), 6.17 (dd, *J*=2.3, 4.6 Hz, 1H), 5.92-5.95 (m, 2H), 2.32-2.66 (m, 3H), 1.90-2.02 (m, 1H). IR (KBr): 1717, 1595, 1487, 1271, 1117, 1103, 1010, 1015, 760 cm^{-1}. Anal. Calcd for $C_{12}H_{11}O_2Cl$: C, 64.73; H, 4.98%. Found: C, 64.58; H, 5.06%.

(*S*)-2-Cyclopentenyl *o*-methylbenzoate (82% ee); $[\alpha]_D^{19}$ -116° (*c* 1.14, $CHCl_3$). ^1H NMR: δ 7.82 (d, *J*=6.6 Hz, 1H), 7.27-7.36 (m, 3H), 6.14-6.18 (m, 1H), 5.92-5.95 (m, 2H), 2.34-2.64 (m, 3H), 2.39 (s, 3H), 1.93-2.05 (m, 1H). IR (KBr): 1715, 1336, 1293, 1142, 1076, 1030, 739 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Found: C, 77.15; H, 6.99%.

(*S*)-2-Cyclopentenyl *m*-methylbenzoate (65% ee); $[\alpha]_D^{19}$ -53° (*c* 0.90, $CHCl_3$). ^1H NMR: δ 7.87 (dd, *J*=1.7, 8.3 Hz, 1H), 7.19-7.41 (m, 3H), 6.16 (dd, *J*=2.3, 4.3 Hz, 1H), 5.91-5.97 (m, 2H), 2.32-2.70 (m, 3H), 2.59 (s, 3H), 1.80-2.04 (m, 1H). IR (KBr): 1713, 1609, 1340, 1277, 1200, 1109, 1082, 1030, 746 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Found: C, 77.15; H, 7.10%.

(*S*)-2-Cyclopentenyl 1-naphthoate (73% ee); $[\alpha]_D^{19}$ -72° (*c* 0.80, $CHCl_3$). ^1H NMR: δ 8.89 (d, *J*=8.2 Hz, 1H), 8.14 (d, *J*=7.3 Hz, 1H), 7.99 (d, *J*=7.9 Hz, 1H), 7.87 (d, *J*=8.3 Hz, 1H), 7.45-7.63 (m, 3H), 6.19-6.21 (m, 1H), 6.02-6.06 (m, 2H), 2.37-2.66 (m, 3H), 2.01-2.06 (m, 1H). IR (KBr): 1709, 1277, 1244, 1196, 1134, 1072, 1030, 783 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92%. Found: C, 80.59; H, 5.95%.

(*S*)-2-Cyclopentenyl *o*-chlorobenzoate (74% ee); $[\alpha]_D^{21}$ -107° (*c* 2.41, $CHCl_3$). ^1H NMR: δ 7.77 (dd, *J*=1.7, 7.6 Hz, 1H), 7.27-7.44 (m, 3H), 6.16-6.19 (m, 1H), 5.95-5.98 (m, 2H), 2.32-2.64 (m, 3H), 1.95-2.06 (m, 1H). IR (KBr): 1726, 1290, 1252, 1132, 1049, 1028, 748 cm^{-1}. Anal. Calcd for $C_{12}H_{11}O_2Cl$: C, 64.73; H, 4.98%. Found: C, 64.71; H, 5.03%.

1-Methyl-2-cyclopentenyl benzoate (93% ee); Enantiomeric exccess was analyzed by HPLC using DAICEL CHIRALCEL OJ (hexane, 0.5 ml/min; 37.76, 39.59). ^1H NMR: δ 8.06 (d, *J*=8.3 Hz, 2H), 7.56 (t, *J*=7.6 Hz 1H), 7.44 (dd, *J*=7.6, 8.3 Hz, 2H), 5.26 (d, *J*=1.32 Hz, 1H), 5.13 (m, 1H), 2.37-2.50 (m, 2H), 2.10-2.17 (m, 1H), 1.73-1.94 (m, 1H), 1.65 (s, 3H). IR (KBr): 1719, 1271, 1113, 1069, 1026, 712 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Found: C, 76.96; H, 7.13%.

2-Methyl-2-cyclopentenyl benzoate (42% ee); Enantiomeric excess was analyzed by HPLC using DAICEL CHIRALCEL OJ (hexane, 0.5 ml/min; 30.29, 33.05). ^{1}H NMR: δ 8.05 (d, *J*=7.9 Hz, 2H), 7.55 (t, *J*=7.6 Hz, 1H), 7.43 (dd, *J*=7.6, 7.9 Hz, 2H), 5.84 (d, *J*=4.9 Hz, 1H), 5.71 (s, 1H), 2.30-2.59 (m, 3H), 1.92 (m, 1H), 1.80 (s, 3H). IR (KBr): 1715, 1452, 1273, 1177, 1111, 1069, 1024, 953, 712 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Found: C, 77.18; H, 7.12%.

3-Methyl-2-cyclopentenyl benzoate (1% ee); Enantiomeric exccess was analyzed by HPLC using DAICEL CHIRALPAK AD connected to DAICEL CHIRALCEL OD (hexane/*i*-PrOH=1000:1, 0.5 ml/min; 41.23, 45.44). ^{1}H NMR: δ 8.02 (d, *J*=7.9 Hz, 2H), 7.53 (t, *J*=7.6 Hz, 1H), 7.41 (dd, *J*=7.6, 7.9 Hz, 2H), 5.89 (d, *J*=4.9 Hz, 1H), 5.57 (s, 1H), 2.52-1.95 (m, 4H), 1.84 (s, 3H). IR (KBr): 1713, 1603, 1452, 1425, 1329, 1274, 1111, 710 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98%. Found: C, 77.05; H, 7.02%.

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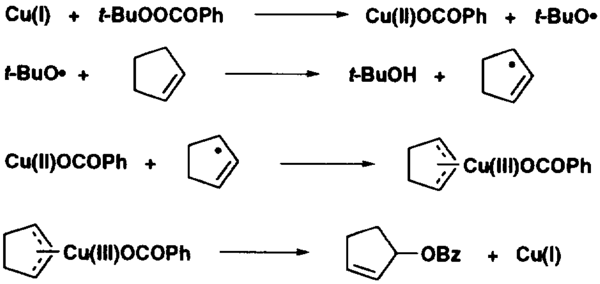

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