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Enantioselective Protonation of Samarium Enolates Derived from α-Heterosubstituted Ketones and Lactone by SmI_2-Mediated Reduction

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Abstract: *SmI_2-mediated reductive cleavage of α-hetero substituents of α-alkyl or α-aryl ketones and lactone gave the corresponding "thermodynamic samarium enolates". Enantioselective protonation of the samarium enolates with C_2-symmetric chiral diols afforded the corresponding ketones and lactone in moderate to high enantioselectivities.* © 1999 Elsevier Science Ltd. All rights reserved.

Enantioselective protonation has been demonstrated to be an effective method for preparing chiral carbonyl compounds, carboxylic acid derivatives and phosphine oxide bearing a stereogenic center at the α-position[1-4] and allenic compounds as well.[5] The reaction must be the most simple method to obtain such chiral compounds. Therefore, it has become a challenging area in asymmetric reaction to find a new protonation reaction and to convert it to a catalytic process. Chiral carbonyl compounds and carboxylic acid derivatives, for example, were prepared in very high enantioselectivities by enantioselective protonation of metal enolates with chiral proton sources not only stoichiometrically but also catalytically. However, it is not so easy to prepare a thermodynamically stable metal enolate in pure form, which is a prerequisite for getting high enantioselectivity, directly from the corresponding ketone such as 2-alkyl or 2-aryl-cyclohexanone. Thus, it is usual to prepare the metal enolates by a reaction of regiochemically pure silyl enol ether with metal alkyl such as alkyl lithium. Very recently, Yamamoto and coworkers have reported a highly regio- and stereoselective isomerization of a kinetic silyl enol ether to a thermodynamic one followed by enantioselective protonation catalyzed by chiral Lewis acid-assisted Brønsted acids.[3a]

In 1986, Molander and coworkers reported that a wide range of α-substituted carbonyl compounds are rapidly reduced under mild conditions by samarium iodide in the presence of a proton source such as methanol and proposed a reaction mechanism in which reductive cleavage of the carbon and hetero atom bond takes place by two equivalent of samarium iodide to give the samarium enolate.[6] Consequently, a thermodynamically stable 2-alkyl or 2-aryl-cyclic ketone enolate, for example, was expected to form regiospecifically from the corresponding 2-heterosubstituted cyclic ketones by the reaction. Since then we had examined the reaction to convert it to an enantioselective version and found that a moderate enantioselectivity was obtained in the following reaction (eq. 1). Although other chiral proton sources,

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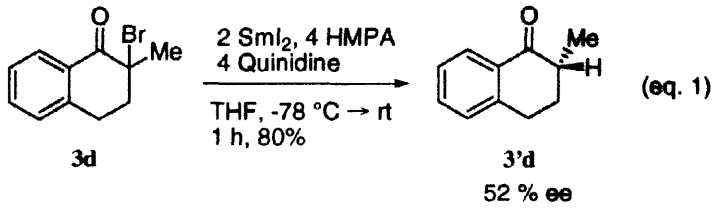
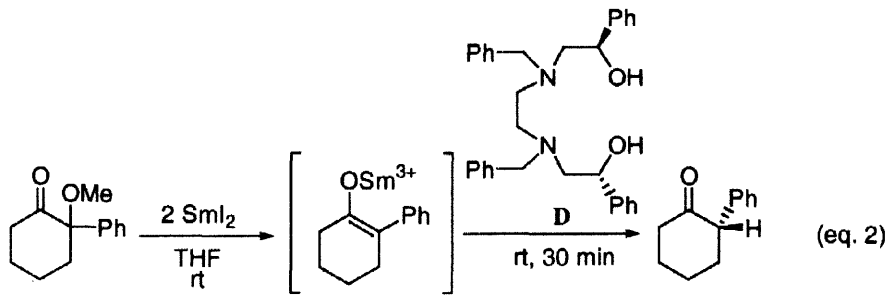
additives, and reaction conditions were screened to get higher enantioselectivity, all the trial turned out unsuccessful.



3d 3'd
52 % ee

In 1996, Mikami and coworkers broke through the deadlock by getting a high enantioselectivity in the following reaction (eq. 2).[7] The results demonstrated that the substrate underwent the reductive elimination of methoxy group by two equivalent of samarium iodide to give the corresponding samarium enolate regiospecifically and the following protonation of the enolate by the C_2-symmetric chiral diaminodiol (**D**) took place effectively to give such a high enantiomeric excess at room temperature. Unfortunately, however, the enantiomeric excess was reduced to a lower level when the reaction was carried out at lower temperature.



1a 1a'
76% ee

Based upon the background, we have investigated the reaction to get higher enantioselectivity for more general substrates. We wish to describe herein the results obtained by the examination to establish a general preparation method of substrates and to find more effective chiral proton sources.

Results and Discussion

Preparation of the substrates

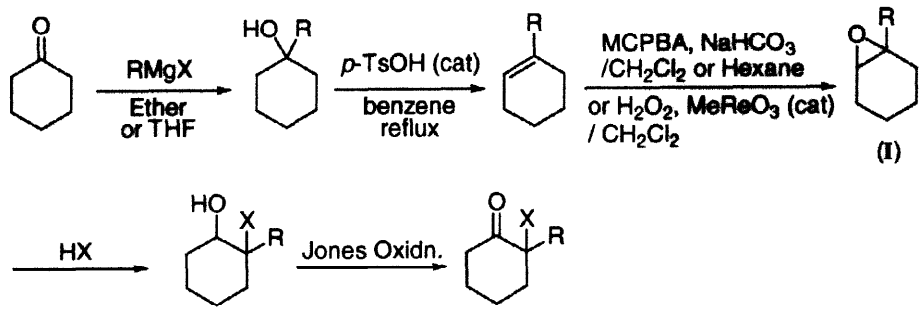
2-alkyl or 2-aryl-2-heterosubstituted cyclohexanone can be prepared from cyclohexan-1,2-dione by Grignard reaction. However, it is rather difficult to introduce substituents such as methoxy, acetoxy or halogen at the α-position via a common precursor by the route. Thus, we employed the following process to get the desired compounds from cyclohexanone (Scheme 1).

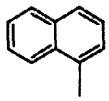
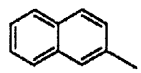
2-Methoxy (**1a**, **1e-i**, **2c** and **2e**), 2-acetoxy (**1d**), 2-chloro (**1c**) and 2-bromo (**1b**, **1j**, **1k** and **2d**) derivatives of 2-alkyl or 2-arylcyclohexanone (**II**) were obtained by the reaction of the corresponding epoxide (**I**) with methanol/sulfuric acid, acetic acid, hydrochloric acid and hydrobromic acid, respectively.[8]

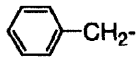
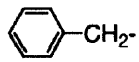
2-Bromo-2-methyl (**2a**) and 2-propylcyclohexanone (**2b**) and 2-bromo-2-methyl-1-tetralone (**3d**) were prepared by bromination of the corresponding precursor with bromine.[9]

2-Methoxy-1,2-diphenyl-1-propanone (**3a**) [10] and 2-Bromo-2-phenyl-δ-lactone (**3c**) [11] were prepared

according to the literatures.

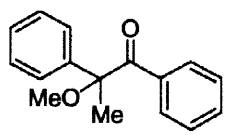


1a: X=OMe, R=Ph
1b: X=Br, R=Ph
1c: X=Cl, R=Ph
1d: X=OAc, R=Ph
1e: X=OMe, R=*p*-MeO-C_6H_4-
1f: X=OMe, R=*p*-Me-C_6H_4-
1g: X=OMe, R=*p*-Cl-C_6H_4-
1h: X=OMe, R= 
1i: X=OMe, R= 
1j: X=Br, R=*p*-Me-C_6H_4-
1k: X=Br, R=*p*-Cl-C_6H_4-

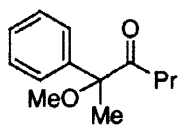
2a: X=Br, R=Me
2b: X=Br, R=*n*-Pr
2c: X=OMe, R=*i*-Bu
2d: X=Br, R= 
2e: X=OMe, R= 

Scheme 1

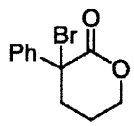
2-Methoxy-2-phenyl-hexan-3-one (**3b**) was prepared by the similar route to that in Scheme 1 via 2-phenyl-2-hexene which was obtained by Wittig reaction of acetophenone with triphenylbutylphosphorane.



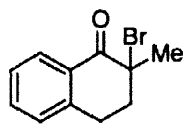
3a



3b



3c

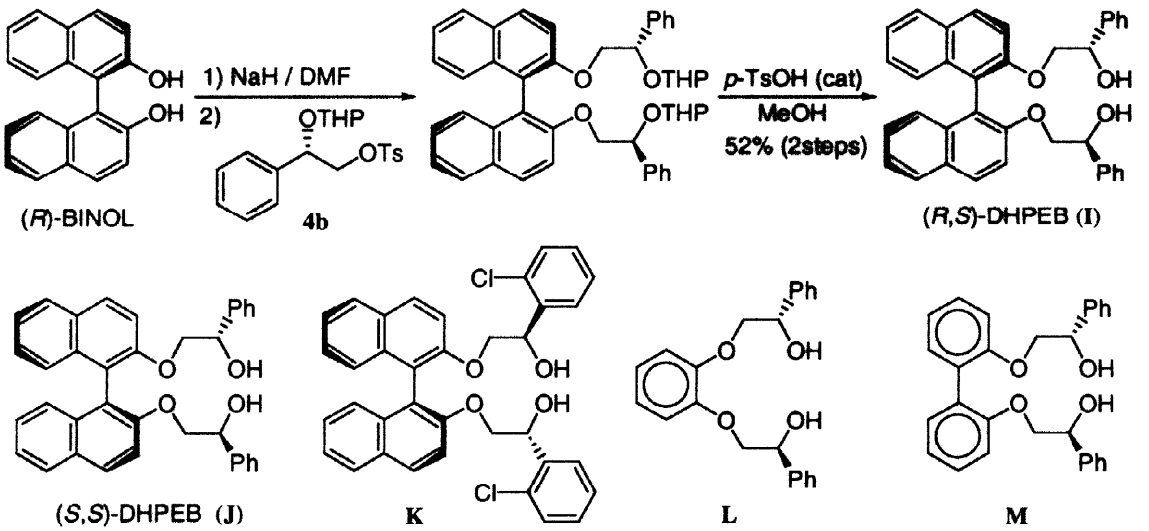


3d

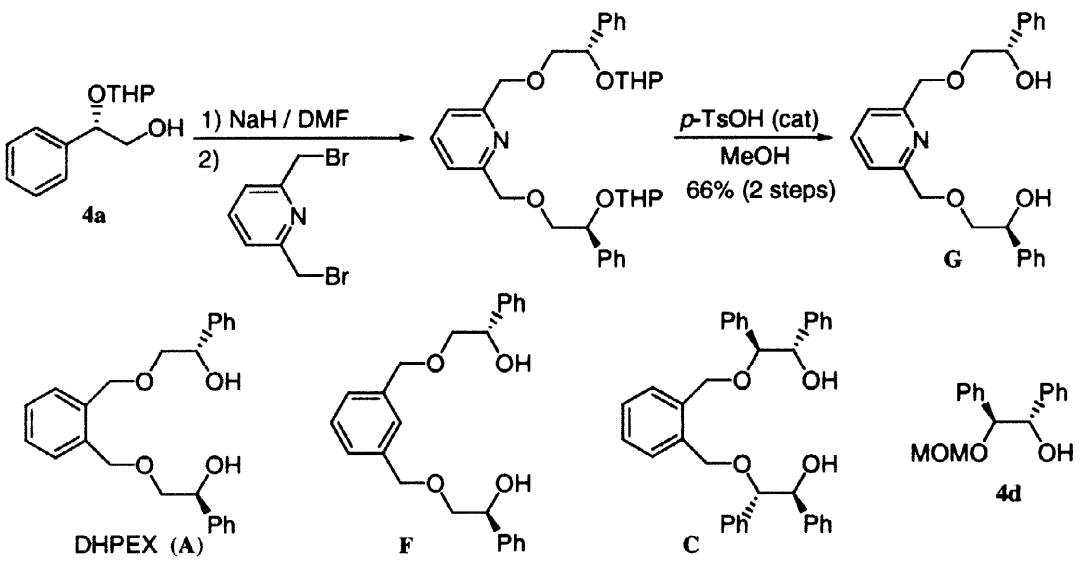
Preparation of the chiral proton sources:

Since C_2-symmetric chiral diol which has a multidentate ligand structure such as **D** was expected to be effective for this enantioselective protonation, a variety of C_2-symmetric chiral diols were prepared from (2*S*)-2-phenyl-2(2'-tetrahydropyranyloxy)ethanol (**4a**)[12] or its tosyl derivative (**4b**), (*R*)-styreneoxide (**4c**) and (1*S*,2*S*)-1,2-diphenyl-2-methoxymethyloxyethanol (**4d**) as the starting materials.

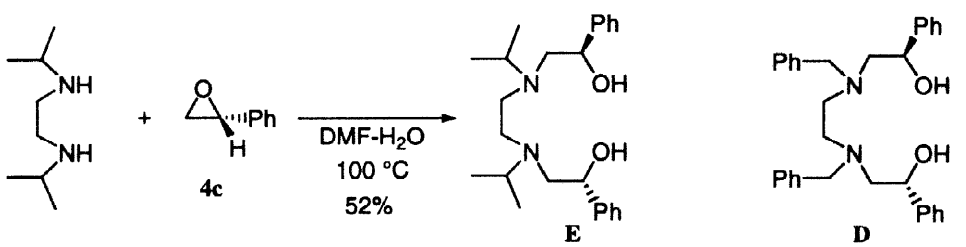
For example, (*R*)-2,2'-di[(*S*)-2-hydroxy-2-phenylethoxy]-1,1'-binaphthyl ((*R*,*S*)-DHPEB; **I**) was obtained in 52% overall yield by the following route. (*S*,*S*)-DHPEB (**J**), **K**, **L** and **M** were prepared by the similar process from the corresponding aryloxy precursor and **4b**.



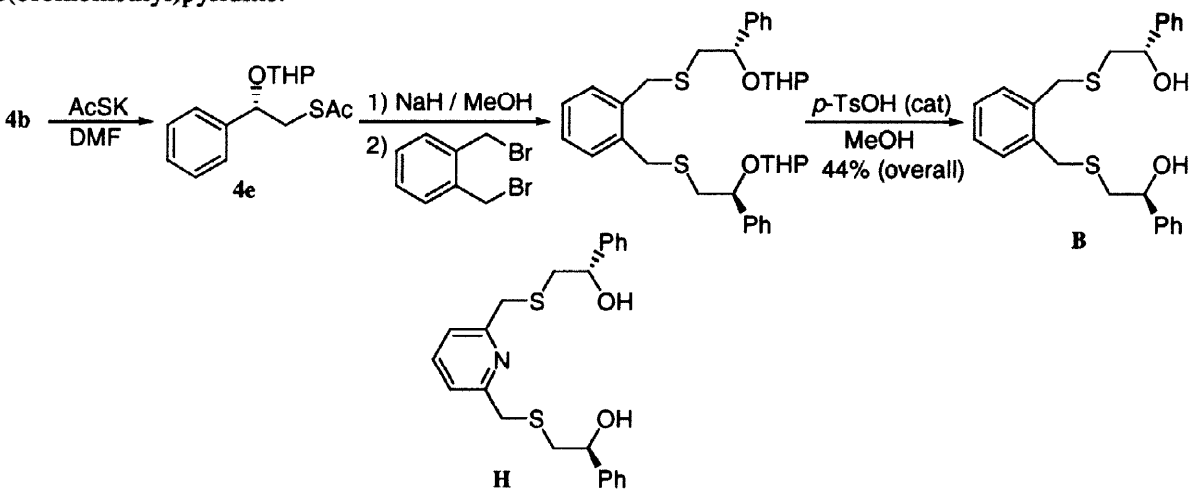
Di-[(*S*)-2-hydroxy-2-phenylethoxy]-2,6-dimethylenepyridine (**G**) was obtained by the reaction of **4a** with 2,6-bis(bromomethyl)pyridine followed by deprotection of THP group in 66% overall yield as follows. DHPEX (**A**)[2u] and **F** were prepared by the similar route and **C** was obtained similarly from **4d** and the corresponding dibromide precursor.



N,N'-di[(*S*)-2-hydroxy-2-phenylethyl]-*N,N'*-diisopropylethylenediamine (**E**) was prepared by the reaction of (*R*)-styreneoxide (**4c**) with *N,N'*-diisopropylethylenediamine in 52% yield according to the similar way as **D**.



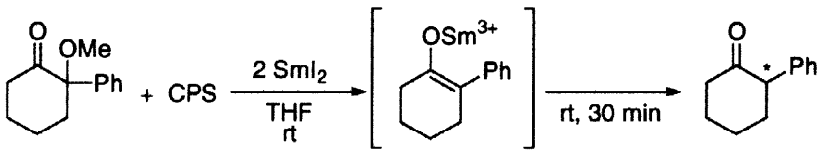
Di-[(*S*)-2-hydroxy-2-phenylethylthio]-1,2-dimethylenebenzene (**B**) was obtained by the following process in 44% overall yield. **H** was prepared similarly by the reaction of **4e** with 2,6-bis(bromomethyl)pyridine.



Enantioselective protonation:

At the outset, the enantioselective protonation of the samarium enolate derived from 2-methoxy-2-phenylcyclohexanone (**1a**) was examined by using the C_2-symmetric chiral diols obtained above and the results were summarized in Table 1.

Table 1. Enantioselective protonation of the samarium enolate derived from 2-methoxy-2-phenylcyclohexanone with C_2-symmetric chiral diols.[a]



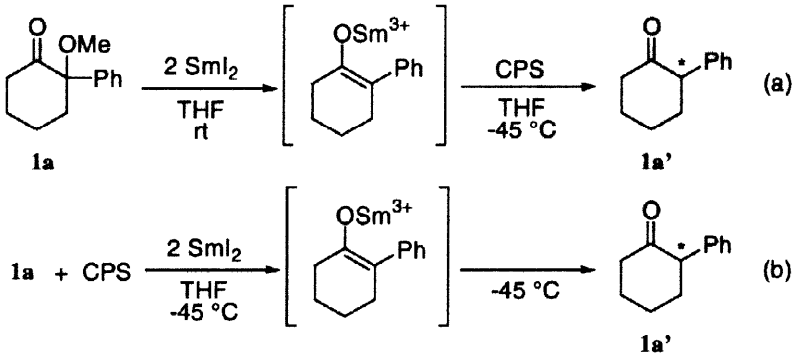
1a **1a'**

Entry	CPS[b]	Product		
		Yield (%)	% ee[c]	Config.[d]
1	DHPEX (A)	89	58	*R*
2	**B**	94	13	*R*
3	**C**	90	13	*R*
4	**D**	86	76	*S*
5	**E**	90	43	*S*
6	**F**	86	33	*R*
7	**G**	96	49	*R*
8	**H**	52	44	*R*
9	(*R*,*S*)-DHPEB (**I**)	88	65	*R*
10	(*S*,*S*)-DHPEB (**J**)	85	34	*R*
11	**K**	63	65	*S*
12	**L**	86	67	*R*
13	**M**	86	82	*R*

[a] The reactions were carried out using 2.0 mol *equiv.* of the chiral proton source and 2.4 mol *equiv.* of SmI_2. [b] CPS=chiral proton source. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H. [d] The configuration of **1a'** was determined by specific rotation.

As seen from Table 1, the configuration of the product was determined by that of the stereogenic center of 2-hydroxy-2-phenylethyl moiety of the chiral diols and DHPEX (**A**), **D**, (*R*,*S*)-DHPEB (**I**), **K**, **L** and **M** gave moderate to high enantiomeric excesses (Entries 1, 4, 9, 11, 12 and 13). Thus, we next examined the reaction temperature and time and the effect of additive HMPA with the use of **A**, **D**, **I**, **L** and **M** to get optimal reaction conditions and to know the most effective proton source. The results were summarized in Table 2 together with the data of Table 1 for comparison.

Table 2. Examination of the reaction conditions of the enantioselective protonation.[a]



Entry	CPS[b]	Addition mode of CPS	HMPA (mol equiv.)	Temp (°C)	Time (min)	Product		
						Yield (%)	% ee[c]	Config.[d]
1	**D**	a		rt	30	91	76	*S*
2	**D**	a		rt	120	80	53	*S*
3	**D**	a		-40	120	79	35	*S*
4	**D**	b		-45	120	83	67	*S*
5	(*R*,*S*)-DHPEB (**I**)	a		rt	30	88	72	*R*
6	(*R*,*S*)-DHPEB (**I**)	a		-45	120	73	58	*R*
7	(*R*,*S*)-DHPEB (**I**)	b		-45	120	78	87	*R*
8	(*R*,*S*)-DHPEB (**I**)	b	2.2	-45	120	72	89	*R*
9	(*R*,*S*)-DHPEB (**I**)	b	4.3	-45	120	63	82	*R*
10	DHPEX (**A**)	b		rt	30	89	58	*R*
11	DHPEX (**A**)	b		-45	120	84	84	*R*
12	**L**	b		rt	30	86	67	*R*
13	**L**	b		-45	120	78	86	*R*
14	**M**	b		rt	30	84	82	*R*
15	**M**	b		-45	120	88	85	*R*

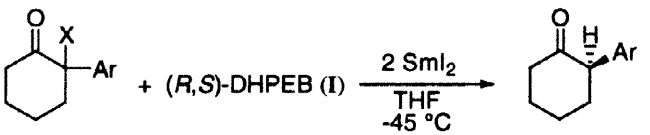
[a] The reactions were carried out using 2.0 mol *equiv.* of the chiral proton source and 2.4 mol *equiv.* of SmI_2. [b] CPS=chiral proton source. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H. [d] The configuration of **1a'** was determined by specific rotation.

In the case of **D**, the enantioselectivity was highest when the chiral diol was added to the samarium enolate solution at room temperature (Entry 1). However, the enantiomeric excess was decreased even in low temperature when the reaction time was prolonged to complete the reaction (Entries 2, 3 and 4). The similar tendency was observed in the case of (*R*,*S*)-DHPEB (**I**), when the chiral proton source was added to the samarium enolate solution (Entries 5 and 6). By contrast with the case of **D**, however, the

enantioselectivity was increased dramatically to 87% ee, when a samarium iodide solution was added to the solution of the substrate and **I** in THF at -45 °C (Entry 7). Since the effect by HMPA was not significant (Entries 8 and 9) the reaction for other chiral proton sources was carried out under the same reaction conditions as those in Entry 7 (Entries 11, 13 and 15). It is noteworthy that the enantioselectivities were increased remarkably in all cases compared to those at room temperature except for **D**, although the difference was not so large in the case of **M**. As seen from the results in Entries 1-4, it is clear that racemization of the product occurred in the reaction mixture in the case of **D**.[13a]

Among these chiral proton sources, **I** gave the best results at -45 °C in the addition mode of chiral proton source, b. Thus, the effect of 2-aryl substituents on enantioselectivity was examined by using the substrates prepared above under the same reaction conditions as those in Entry 7 of Table 2 and the results were summarized in Table 3.

Table 3. The effect of the 2-aryl substituents to the enantioselective protonation.[a]



1a-k **1'a-k**

Entry	Ar	X	Substrate No.	Product		
				Yield (%)	% ee[b]	Config.[c]
1	Ph	OMe	**1a**	70	87	*R* (+)
2	Ph	Br	**1b**	87	91	*R* (+)
3	Ph	Cl	**1c**	79	82	*R* (+)
4	Ph	OAc	**1d**	83	83	*R* (+)
5	*p*-MeO-C_6H_4-	OMe	**1e**	79	87	*R* (+)[d]
6	*p*-Me-C_6H_4-	OMe	**1f**	75	94	*R* (+)[d]
7	*p*-Cl-C_6H_4-	OMe	**1g**	78	83	*R* (+)[d]
8	1-Naphthyl	OMe	**1h**	81	16	*R* (-)[d]
9	2-Naphthyl	OMe	**1i**	86	90	*R* (+)[d]
10	*p*-Me-C_6H_4-	Br	**1j**	84	92	*R* (+)[d]
11	*p*-Cl-C_6H_4-	Br	**1k**	77	84	*R* (+)[d]

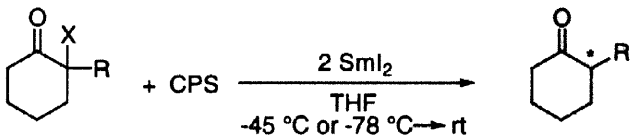
[a] The reactions were carried out using 2.0 mol *equiv.* of the chiral proton source and 2.4 mol *equiv.* of SmI_2. [b] Determined by HPLC analysis using DAICEL CHIRALCEL OD-H (Entries 1-6, 9 and 10) and OJ (Entries 7, 8 and 11). [c] Specific rotation was measured in benzene. [d] The configuration was determined by comparing the CD spectra of the product to that of (*R*)-(+)-**1a'**.

As seen from Table 3, high enantiomeric excesses were obtained in general except for 1-naphthyl derivative (**1h**) (Entry 8) and *p*-methyl derivative (**1f**) gave the best result (94% ee, Entry 6).[13b] The large difference in enentioselectivity between **1h** and **1i** may be ascribable to the different steric demand of the naphthyl groups of the substrates at the protonating transition state as will be mentioned later. The variation of the leaving groups (X) resulted in small and unpredictable difference in enantioselectivity. Bromo derivative **1b** gave the higher enantioselectivity than methoxy derivative **1a** in Entries 2 and 1, respectively. However, the tendency was reversed in the case of **1f** *vs.* **1j** (Entries 6 *vs.* 10).

Since it was demonstrated that 2-heterosubstituted-2-arylcyclohexanone (**1a-g, 1i-k**) gave the high

enantioselectivities in general, we next examined the reaction by using 2-alkylcyclohexanone derivatives obtained above and the results were summarized in Table 4.

Table 4. The effect of the 2-alkyl substituents to the enantioselective protonation.[a]



2a-e 2'a-e

Entry	R	X	Substrate No.	CPS[b]	Temp (Time)	Product		
						Yield (%)	% ee[c]	Config.[d]
1	Me	Br	**2a**	**L**	-45 °C (2 h)	69	12	*S* (+)
2	Me	Br	**2a**	(*R*,*S*)-DHPEB (**I**)	-45 °C (2 h)	55	55	*S* (+)
3	*n*-Pr	Br	**2b**	**L**	-45 °C (2 h)	63	31	*S* (+)
4	*n*-Pr	Br	**2b**	(*R*,*S*)-DHPEB (**I**)	-45 °C (2 h)	75	65	*S* (+)
5	*i*-Bu	OMe	**2c**	**L**	-45 °C (2 h)	79	22	*R* (+)
6	*i*-Bu	OMe	**2c**	(*R*,*S*)-DHPEB (**I**)	-45 °C (2 h)	81	65	*R* (+)
7	Bn	Br	**2d**	**L**	-45 °C (2 h)	72	20	*R* (+)
8	Bn	Br	**2d**	(*R*,*S*)-DHPEB (**I**)	-45 °C (2 h)	71	72	*R* (+)
9	Bn	OMe	**2e**	**L**	-45 °C (2 h)	74	25	*R* (+)
10	Bn	OMe	**2e**	(*R*,*S*)-DHPEB (**I**)	-45 °C (2 h)	70	80	*R* (+)
11	Bn	OMe	**2e**	DHPEX (**A**)	-45 °C (2 h)	76	23	*R* (+)
12	Bn	OMe	**2e**	**M**	-45 °C (2 h)	72	81	*R* (+)
13	Bn	OMe	**2e**	(*R*,*S*)-DHPEB (**I**)	-78 °C→rt (40 min)	66	76	*R* (+)
14	Bn	OMe	**2e**	(*R*,*S*)-DHPEB (**I**)	-78 °C→rt (2 h)	67	83	*R* (+)

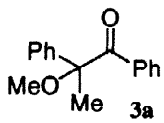
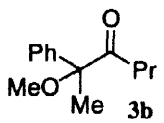
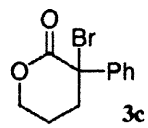
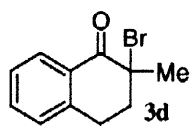
[a] The reactions were carried out under the same conditions as those in Entry 7 of Table 2 except for Entries 13 and 14. [b] CPS=chiral proton source. [c] Determined by comparison of the specific rotation with reported data (Entries 1-6) and by HPLC analysis using DAICEL CHIRALCEL OJ (Entries 7-11). [d] The configuration of the product was determined by specific rotation.

The enantioselectivity was increased with increasing bulkiness of the substituent R and high enantioselectivities were brought about when benzyl substrate **2e** and the proton sources **I** and **M** were used for the reactions (Entries 10 and 12). The highest enantiomeric excess was obtained when the reaction was carried out from -78 °C to room temperature for 2 h by using **I** and **2e** (83% ee, Entry 14). In contrast to the results in Table 2, the chiral proton sources **L** and DHPEX (**A**) resulted in the low enantiomeric excesses even in the case of substrate **2e**. The different configuration of the products in Entries 1-4 is due to the

priority of the substituents at the stereogenic center in Cahn-Ingold-Prelog sequence rules and the stereochemistry upon the protonation of the samarium enolates are the same in all substrates in both Table 3 and Table 4.

Finally, we examined the reaction by using the substrates such as acyclic 2-heterosubstituted ketones (**3a** and **3b**), 2-heterosubstituted tetralone (**3d**) and 2-bromo-2-aryl-δ-valerolactone (**3c**) under the same reaction conditions as those in Entry 7 of Table 2 and the results were summarized in Table 5.

Table 5. Enantioselective protonation of the samarium enolate derived from ketones and δ-lactone.[a]

Entry	Substrate	CPS[b]	Product		
			Yield (%)	% ee[c]	Config.[d]
1	 **3a**	L	42	20	*R* (-)
2	**3a**	(*R*,*S*)-DHPEB (I)	35	35	*S* (+)
3	 **3b**	L	79	30	*R* (-)
4	**3b**	(*R*,*S*)-DHPEB (I)	81	45	*S* (+)
5	 **3c**	DHPEX (A)	84	49	*R* (+)[e]
6	**3c**	(*R*,*S*)-DHPEB (I)	81	28	*R* (+)[e]
7	**3c**	L	88	72	*R* (+)[e]
8	 **3d**	(*R*,*S*)-DHPEB (I)	91	24	*S* (-)
9	**3d**	L	79	13	*S* (-)

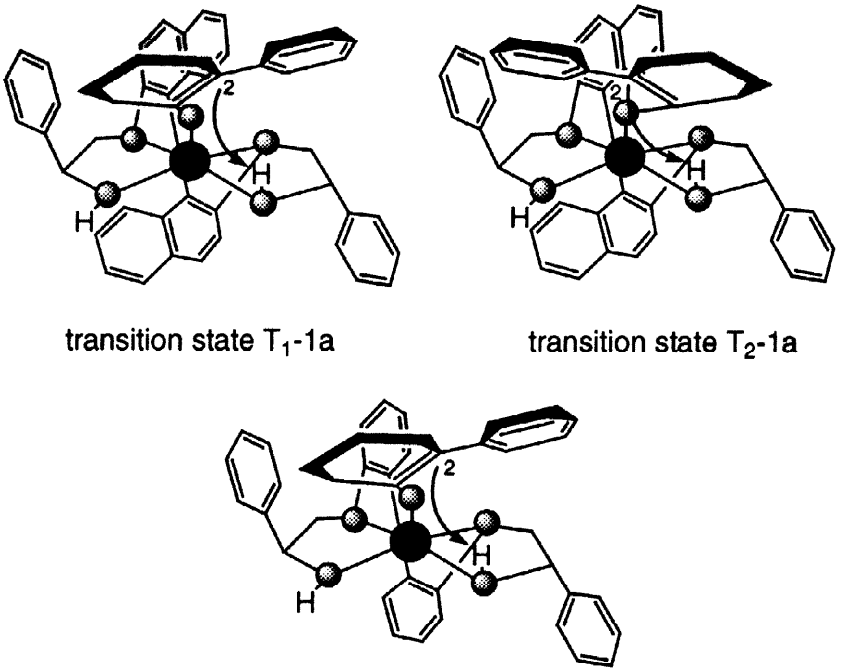
[a] The reactions were carried out under the same conditions as those in Entry 7 of Table 2. [b] CPS=chiral proton source. [c] Determined by HPLC analysis using DAICEL CHIRALCEL OD (Entries 1 and 2), OB' (Entries 3, 4, and 5-7) and OD-H (Entries 8 and 9). [d] The configuration of the product was determined by specific rotation except for **3c'**. [e] The configuration was determined by specific rotation of 1,5-diol derived from the product by reduction: See Ref. 27.

Acyclic ketones **3a** and **3b** gave low enantiomeric excesses probably because of low *E*/*Z* selectivities of the samarium enolates (Entries 1-4). It is interesting that the δ-valerolactone (**3c**) afforded rather high enentiomeric excess (72% ee, Entry 7) when **L** was used as the chiral proton source, although **I** was ineffective (Entry 6).

Stereochemistry at the protonating transition state:

We have already proposed a model of the protonating transition state in which a chiral proton source was coordinated to samarium (III) ion as a tetradentate ligand.[13a] The model explains clearly the

enantioselectivities observed in Tables 3 and 4 and for δ-lactone derivative (**3c**) in Table 5. In Fig. 1, the two transition states for the substrate **1a** and the chiral proton source (*R,S*)-DHPEB (**I**) are depicted as a typical model.



transition state T_1-1a transition state T_2-1a

transition state T_3-1a

Fig. 1

In the transition state T_1-1a, the substituent at C-2 position of the enolate is far apart from the benzene ring at the left side of (*R,S*)-DHPEB (**I**) and thus has no repulsive interaction with it. Consequently, protonation by OH group at the right side takes place from the *si* face at C-2 position of the enolate to give the product of (*R*)-configuration, for example in the case of the substrate **1a**. On the contrary, in transition T_2-1a, the repulsive interaction between the benzene rings at C-2 position of the enolate and on the left side of **I** makes the conformation unstable. On the other hand, the circumstances are different from those above in the case of **1h** in Entry 8 of Table 3, because the steric hindrance due to C-8 hydrogen of naphthyl ring of **1h** against the enolate plane forces the naphthyl ring orthogonal to the enolate plane. Therefore, the transition state T_1 for the substrate **1h** must be more unstable compared to T_1-1a because the steric repulsion between the naphthyl ring and the right side framework of **I** becomes serious in transition T_1. The lower enantioselectivities in Table 4 compared to those in Table 3 can be explained in the same way for the smaller substituents of the substrates. If the substituent at C-2 position is small, then the difference in free energy between T_1 and T_2 becomes small to result in a low enantioselectivity. The biphenyl auxiliary in **M** is chirally flexible[13a,c,d] and hence, easily adjustable to the favorable conformation T_3-1a in Fig. 1.

However, the model can not explain the enantioselectivities of the products of the tetralone substrate **3d**. **3d** has a benzene ring in tetralone skeleton and a small substituent at the C-2 position. Thus, it is expected that T_2 is rather stable than T_1 to give the product of (*R*)-configuration. In addition, the high enantiomeric excesses were brought about in all cases only when a samarium iodide solution was added to

the solution of the substrates and the chiral proton sources. This means that the chiral proton sources play an important role to construct a highly ordered transition state during the formation of the samarium enolate. The fact that two equivalent of samarium iodide are required to form the samarium enolate also raises a question about the role of the samarium ion other than the one coordinated to the chiral proton source in T_1 and T_2.

Therefore, we are now reexamining the reaction pathway from the different view points in order to get a more precise model at the transition state which can explain the enantioselectivity even in the case of tetralone substrate and answer the question about the role of samarium ions.

Experimental Section

General. The melting point was determined by a Yanagimoto micro-melting point apparatus and was uncorrected. The IR spectra were recorded on a Perkin-Elmer 1720-X FT-IR spectrometer. The ^{1}H NMR spectra were obtained on a JEOL-FX 200 and JEOL JNM-A400 spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. The optical rotations were measured with a Perkin Elmer 241 polarimeter and CD spectra were recorded on a JASCO J-40C spectrometer. Mass spectra were measured on a Hitachi M-2500 double focusing mass spectrometer. HPLC analysis was performed with Hitachi L-7100 flow system and L 7400 detector using DAICEL CHIRALCEL OB', OD, OJ, or OD-H column. Preparative TLC were run on Wakogel B-5F and column chromatography was performed using Wakogel C-300. Dimethylformamide (DMF) was distilled from CaH_2 *in vacuo*. Tetrahydrofuran (THF) was distilled prior to use from sodium benzophenone ketyl under argon. Jones reagent was prepared according to his literature.[14] 0.1 M samarium iodide THF solution was prepared from samarium metal and diiodoethane according to Kagan's method.[15] 1-Phenyl-1-cyclohexene and 2-methyl-1-tetralone were purchased from Aldrich Chemical Co., Inc. 2-Propylcyclohexanone was purchased from Tokyo Kasei Kogyo Co., Ltd. 1-(4-Methylphenyl)1-cyclohexene,[2q] 1-(4-Methoxyphenyl)-1-cyclohexene,[2q] 1-(2-Naphthyl)-1-cyclohexene,[2q] 1-phenyl-1,2-epoxycyclohexane,[8a] 2-chloro-2-phenylcyclohexanone (**1c**),[8b] 2-bromo-2-methylcyclohexanone (**2a**),[9] 2-methoxy-1,2-diphenyl-1-propanone (**3a**),[10] and 2-bromo-2-phenyl-δ-valerolactone (**3c**)[11] were prepared according to the literatures.

Preparation of olefins: typical procedure for 1-(4-chlorophenyl)-1-cyclohexene[16]

To a solution of cyclohexanone (1.70 g, 17.3 mmol) in ether (50 mL) was added 4-chlorolphenyl magnesium bromide (generated from Mg (0.88 g, 36.2 mmol) and 4-bromochlorobenzene (6.7 g, 35.0 mmol) in ether (20 mL)) at 0 °C. After stirring overnight at room temperature, the reaction mixture was poured onto ice. 3 N-hydrochloric acid was added to the mixture until a homogeneous solution of water layer was obtained. The aqueous layer was separated and extracted with ether (30 mL×2). The combined organic layer was washed successively with saturated sodium bicarbonate (20 mL) and with brine (20 mL), dried over anhydrous $MgSO_4$, filtered and concentrated to give an oil. To a solution of the resulting oil in benzene (40 mL) was added a catalytic amount of *p*-toluenesulfonic acid monohydrate (*ca* 0.1 g). The mixture was refluxed in a Dean-Stark apparatus for 1 h while water was removed. The solvent of the mixture was removed *in vacuo*. The product was purified by column chromatography on silica gel to give

1-(4-chlorolphenyl)-1-cyclohexene as a colorless solid (3.06 g, 92% yield): mp 65-66 °C (crude crystals); IR (KBr) 3048, 3026, 2923, 2858, 2832, 1485, 1449, 1436, 1403, 1137, 1093, 920, 819, 799, 759, 543 cm^{-1}; ^1H NMR (400 MHz) δ 1.62-2.39 (m, 8H, (-CH_2-)$_4$), 6.10 (m, 1H, =C*H*-), 7.25 (d, 2H, Ar*H*, *J*=8.8 Hz), 7.30 (d, 2H, Ar*H*, *J*=8.8 Hz).

1-(1-Naphthyl)-1-cyclohexene: 79% yield; mp 40-43 °C (crude crystals); IR (KBr) 3049, 2925, 2854, 2834, 1590, 1504, 1436, 1390, 797, 778, 478 cm^{-1}; ^1H NMR (400 MHz) δ 1.54-2.39 (m, 8H, (-CH_2-)$_4$), 5.76 (m, 1H, =C*H*-), 7.25-7.47 (m, 4H, Ar*H*), 7.71-8.02 (m, 3H, Ar*H*).

1-(*i*-Butyl)-1-cyclohexene: 1-(*i*-Butyl)-1-cyclohexanol was prepared according to the procedure described above except that cyclohexanone (1.7 g, 17 mmol) and *i*-butylmagnesium bromide (prepared from Mg (0.99 g, 41 mmol) and 1-bromo-2-methylpropane (4.8 g, 35 mmol) in THF (30 mL)) were used. The alcohol was dehydrated for 1 h at 160 °C in the presence of catalytic amount of *p*-toluenesulfonic acid monohydrate (*ca* 0.1 g) without solvent. Purification of the product on a silica gel column (pentane) yielded the olefin as a colorless oil (0.68 g, 28% yield). 15% of *i*-butylidenecyclohexane was included in the oil; IR (neat) 2995, 2927, 2836, 1463, 1383, 1366, 920, 793 cm^{-1}; ^1H NMR (200 MHz) δ 0.84 (d, 5.1 H, *endo* olefin's –CH_3, *J*=6.4 Hz), 0.92 (d, 0.9H, *exo* olefin's –CH_3, *J*=6.8 Hz), 1.40-2.60 (m, 11H, *exo* olefin's (-CH_2-)$_5$ and –C*H*-(CH_3)$_2$, and *endo* olefin's (-CH_2-)$_4$ and -CH_2-C*H*-(CH_3)$_2$) 4.89 (d, 0.15H, *exo* olefin's =C*H*-, *J*=9.0 Hz), 5.37 (s, 0.85H, *endo* olefin's =C*H*-).

1-Benzyl-1-cyclohexene: 1-Benzyl-1-cyclohexanol was prepared according to the procedure described above except that cyclohexanone (1.7 g, 17 mmol) and benzyl magnesium chloride (prepared from Mg (0.88 g, 36 mmol) and benzyl chloride (4.4 g, 35 mmol) in THF (20 mL)) were used. The alcohol was dehydrated for 1 h at 160 °C in the presence of catalytic amount of *p*-toluenesulfonic acid monohydrate (*ca* 0.1 g) without solvent. Purification of the product on a silica gel column (hexane) yielded the olefin as a colorless oil (1.22g, 41% yield). 16% of benzylidenecyclohexane was included in the oil; IR (neat) 3026, 2998, 2926, 2856, 2835, 1494, 1453, 1438, 1081, 919, 738, 699 cm^{-1}; ^1H NMR (400 MHz) δ 1.51-2.02 (m, 8.32H, benzylidene derivative's (-CH_2-)$_5$ and cyclohexene's (-CH_2-)$_4$), 3.24 (s, 1.68H, -CH_2Ph), 5.46 (m, 0.84H, cyclohexene's =C*H*-), 6.23 (s, 0.16H, benzylidene derivative's =C*H*-), 7.16-7.32 (m, 5H, Ar*H*).

Epoxidation of olefins: typical procedure for 1-(4-methylphenyl)-1,2-epoxycyclohexane

A solution of 1-(4-methylphenyl)-1-cyclohexene (0.86 g, 5.0 mmol) in hexane (10 mL) was added to a mixture of *m*-chloroperbenzoic acid (70% purity, 1.36 g, 5.5 mmol) and $NaHCO_3$ (0.84 g, 10 mmol) in hexane (20 mL) at 0 °C. The mixture was stirred at room temperature for 1.5 h and then was filtered. The filtrate was concentrated to give an oil. The product was purified by short column chromatography on silica gel (deactivated with Et_3N) to give 1-(4-methylphenyl)-1,2-epoxycyclohexane as a colorless liquid (0.5 g, 53% yield): IR (neat) 3055, 3029, 2989, 2941, 2861, 1730, 1515, 1445, 1435, 1362, 1258, 1130, 1114, 996, 975, 920, 855, 828, 814, 792, 763, 558, 537 cm^{-1}; ^1H NMR (400 MHz) δ 1.28-2.31 (m, 8H, (-CH_2-)$_4$), 2.33 (s, 3H, -CH_3), 3.06 (m, 1H, -C*H*O-), 7.14 (d, 2H, Ar*H*, *J*=8.3 Hz), 7.26 (d, 2H, Ar*H*, *J*=8.3 Hz).

1-(4-Chlorophenyl)-1,2-epoxycyclohexane: 98% yield; colorless prisms from hexane at –20 °C, mp 46-48 °C; IR (KBr) 3087, 3045, 2979, 2954, 2931, 2862, 1488, 1456, 1445, 1433, 1401, 1360, 1106, 1089, 1013, 995, 975, 852, 827, 812, 768, 722, 547, 502, 465, 423 cm^{-1}; ^1H NMR (400 MHz) δ 1.28-2.27 (m, 8H, (-CH_2-)$_4$), 3.03 (m, 1H, -C*H*O-), 7.30 (s, 4H, Ar*H*).

1-(1-Naphthyl)-1,2-epoxycyclohexane: 91% yield; colorless prisms from hexane at –20 °C, mp 61-63 °C; IR (KBr) 3054, 2980, 2938, 2912, 2856, 1509, 1435, 958, 859, 802, 775, 757, 738, 564, 541, 450, 427 cm^{-1}; ^1H NMR (400 MHz) δ 1.50-2.19 (m, 8H, (-C*H*$_2$-)$_4$), 3.26 (m, 1H, -C*H*O-), 7.42-7.56 (m, 4H, Ar*H*), 7.76-8.03 (m, 3H, Ar*H*).

1-(2-Naphthyl)-1,2-epoxycyclohexane: 86% yield; colorless prisms from hexane, mp 56-58 °C; IR (KBr) 3057, 2978, 2940, 2913, 2855, 1601, 1505, 1430, 1361, 1353, 1193, 1135, 979, 963, 900, 965, 854, 821, 803, 763, 750, 653, 542, 512, 480 cm^{-1}; ^1H NMR (400 MHz) δ 1.32-2.44 (m, 8H, (-C*H*$_2$-)$_4$), 3.16 (m, 1H, -C*H*O-), 7.43-7.49 (m, 3H, Ar*H*), 7.80-7.85 (m, 4H, Ar*H*).

1-(*i*-Butyl)-1,2-epoxycyclohexane: 78% yield; colorless oil, IR (neat) 2937, 2868, 1466, 1386, 986, 922, 877, 844, 764 cm^{-1}; ^1H NMR (200 MHz) δ 0.91 and 0.94 (d×2, 3H×2, -CH$_3$×2, *J*=9.3 Hz), 1.20-2.00 (m, 11H, (-C*H*$_2$-)$_4$ and –C*H*$_2$-C*H*-(CH$_3$)$_2$), 2.90 (dd, 1H, -C*H*O-, *J*=1.2 and 3.4 Hz).

1-Benzyl-1,2-epoxycyclohexane: 68% yield; colorless oil, IR (neat) 3028, 2935, 2857, 1729, 1496, 1455, 1435, 1295, 1284, 1259, 1031, 986, 973, 945, 928, 870, 847, 752, 677 cm^{-1}; ^1H NMR (400 MHz) δ 0.88-1.96 (m, 8H, (-C*H*$_2$-)$_4$), 2.80 and 2.87 (d×2, -C*H*$_2$Ph, *J*=14.2 Hz), 3.02 (d, 1H, -C*H*O-, *J*=2.9 Hz), 7.17-7.40 (m, 5H, Ar*H*).

2-Phenyl-2,3-epoxyhexane:

To a suspension of *n*-butyltriphenylphosphonium bromide (10 g, 25 mmol) in THF (50 mL) was added dropwise 1.47 M *n*-BuLi solution in hexane (17 mL, 25 mmol) at 0 °C under argon. After stirring 30 min, a solution of acetophenone (3 g, 25 mmol) in THF (20 mL) was added to the reaction mixture. After stirring for 30 min at 0 °C, the reaction was quenched with saturated aqueous NH_4Cl solution (50 mL). The reaction mixture was extracted with Et_2O (50 mL×3), and the organic layer was washed with brine (30 mL×2), dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to give an oil. The oil was passed through a short silica gel column (hexane) to give crude 2-phenyl-2-hexene as a colorless oil (3.6 g, 90% yield). To a suspension of the oil (3.6 g, 23 mmol) and $NaHCO_3$ in hexane (50 mL) was added *m*-chloroperbenzoic acid (70% purity, 6.6 g, 27 mmol) at 0 °C. The reaction mixture was stirred for 2 h at room temperature, and then the insoluble material was filtered off. The filtrate was concentrated *in vacuo* to give an oil, which was purified on a silica gel column (hexane:Et_2O=20:1) to afford 2-phenyl-2,3-epoxyhexane as an oil (3.6g, 91% yield). The product was a mixture of (*R**,*R**)- and (*R**, *S**)-isomers (major isomer:minor isomer=82:18): IR (neat) 3030, 2962, 2931, 2874, 1732, 1497, 1446, 1295, 1284, 1259, 1075, 1058, 1027, 859, 766, 702, 579 cm^{-1}; ^1H NMR (400 MHz) δ 0.83 (t, 2.46H, major isomer's -C*H*$_3$, *J*=7.3 Hz), 1.01 (t, 0.54H, minor isomer's -C*H*$_3$, *J*=7.3 Hz), 1.12-1.71 (m, 4H, (-C*H*$_2$-)$_2$), 1.65 (s, 2.46H, major isomer's -C*H*$_3$), 1.65 (s, 0.54H, minor isomer's -C*H*$_3$), 2.82 (t, 0.18H, minor isomer's –C*H*O-, *J*=5.9 Hz), 3.04 (t, 0.82H, major isomer's –C*H*O-, *J*=5.9 Hz), 7.24-7.40 (m, 5H, Ar*H*).

1-(4-Methoxyphenyl)-1,2-epoxycyclohexane:[17]

To a solution of 1-(4-methoxy)-1-cyclohexene (377 mg, 2.00 mmol) and methyltrioxorhenium (2.5 mg, 0.01 mmol) in CH_2Cl_2 (1 mL) was added pyridine (19 mg, 0.24 mmol) followed by an addition of 30% aq. H_2O_2 (0.3 mL, 15 mmol) dropwise at 20-25 °C. The reaction mixture was stirred at room temperature for 3 h, and then the aqueous layer was separated. The remaining H_2O_2 in the organic phase was decomposed by stirring with a catalytic amount of MnO_2 (*ca* 5 mg). The mixture was dried over anhydrous $MgSO_4$, and

concentrated *in vacuo*. The residue was purified by short column chromatography on silica gel (deactivated with Et_3N) to give 1-(4-methoxyphenyl)-1,2-epoxycyclohexane as a colorless solid (354 mg, 87% yield): colorless plates from pentane at –20 °C, mp 47-49 °C; IR (KBr) 3040, 2934, 2857, 1513, 1450, 1439, 1183, 1173, 1036, 830, 572 cm^{-1}; ^1H NMR (400 MHz) δ 1.27-2.28 (m, 8H, (-C*H*$_2$-)$_4$), 3.07 (m, 1H, -C*H*O-), 3.80 (s, 3H, -OC*H*$_3$), 6.87 (d, 2H, Ar*H*, *J*=9.0 Hz), 7.28 (d, 2H, Ar*H*, *J*=9.0 Hz).

Preparation of 2-aryl- and 2-alkyl-2-methoxyketones: typical procedure for 2-methoxy-2-phenylcyclohexanone

A solution of 1-phenyl-1,2-epoxycyclohexane (349 mg, 2.0 mmol) and catalytic amount of conc. H_2SO_4 (*ca* 50 mg) in methanol (10 mL) was stirred at 0 °C for 30 min. Methanol was removed *in vacuo* in the presence of $NaHCO_3$ (300 mg). The residue was dissolved with ether (30 mL), and then after filtration of the mixture, the filtrate was concentrated *in vacuo*. A solution of the residue in acetone (10 mL) was treated with Jones reagent (0.4 mL) at 0 °C for 1 h and then excess Jones reagent was quenched with 2-propanol (1 mL). The precipitates were filtered off, and the filtrate was added to a saturated aqueous $NaHCO_3$ solution (20 mL). After removing the organic solvent *in vacuo*, the aqueous solution was extracted with ether (20 mL×3). The organic layer was washed with brine (20 mL) and dried over anhydrous $MgSO_4$. Concentration of the ether solution *in vacuo* gave an oil, which was purified on a silica gel column (hexane: ether=10:1) to give 2-methoxy-2-phenylcyclohexanone (**1a**) as colorless syrup (342 mg, 84% yield): IR (neat) 3027, 2942, 2865, 2828, 1724, 1495, 1447, 1428, 1257, 1127, 1104, 1065, 1005, 895, 800, 756, 703, 580, 554 cm^{-1}; ^1H NMR (400 MHz) δ 1.66-2.68 (m, 8H, (-C*H*$_2$-)$_4$), 3.07 (s, 3H, -OC*H*$_3$), 7.31-7.41 (m, 5H, Ar*H*); HRMS *m/z* calcd for $C_{13}H_{16}O_2$: 204.1150, found 204.1163.

2-Methoxy-2-(4-methoxyphenyl)cyclohexanone (1e): 78% yield; colorless plates from hexane at -20 °C, mp 31-33 °C; IR (KBr) 3066, 2998, 2988, 2935, 2867, 2830, 1719, 1617, 1519, 1459, 1441, 1311, 1284, 1261, 1176, 1130, 1103, 1080, 1061, 1049, 1035, 1014, 996, 829, 806, 560, 540 cm^{-1}; ^1H NMR (400 MHz) δ 1.68-2.63 (m, 8H, (-C*H*$_2$-)$_4$), 3.05 (s, 3H, -OC*H*$_3$), 3.82 (s, 3H, -OC*H*$_3$), 6.92 (d, 2H, Ar*H*, *J*=8.8 Hz), 7.26 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{14}H_{18}O_3$: 234.1256, found 234.1242.

2-Methoxy-2-(4-methylphenyl)cyclohexanone (1f): 76% yield; colorless syrup; IR (neat) 3027, 2941, 2864, 2827, 1723, 1515, 1450, 1428, 1257, 1187, 1126, 1102, 1064, 896, 817, 563, 552 cm^{-1}; ^1H NMR (400 MHz) δ 1.68-2.88 (m, 8H, (-C*H*$_2$-)$_4$), 2.35 (s, 3H, -C*H*$_3$), 3.06 (s, 3H, -OC*H*$_3$), 7.20 (d, 2H, Ar*H*, *J*=8.8 Hz), 7.23 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{14}H_{18}O_2$: 218.1307, found 218.1336.

2-(4-Chlorophenyl)-2-methoxycyclohexanone (1g): 88% yield; colorless syrup; IR (neat) 3065, 3025, 2942, 1723, 1492, 1129, 1094, 1063, 926 cm^{-1}; ^1H NMR (200 MHz) δ 1.61-2.78 (m, 8H, (-C*H*$_2$-)$_4$), 3.08 (s, 3H, -OC*H*$_3$), 7.28 (d, 2H, Ar*H*, *J*=8.8 Hz), 7.37 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{13}H_{15}ClO_2$: 238.0761, found 238.0758.

2-Methoxy-2-(1-naphthyl)cyclohexanone (1h): 87% yield; colorless prisms from EtOAc-hexane, mp 136-138 °C; IR (KBr) 3051, 2982, 2948, 2861, 2827, 1718, 1442, 1432, 1247, 1153, 1124, 1098, 1084, 1067, 1056, 808, 793, 793, 784, 773, 587, 529 cm^{-1}; ^1H NMR (200 MHz) δ 1.80-2.90 (m, 8H, (-C*H*$_2$-)$_4$), 2.99 (s, 3H, -OC*H*$_3$), 7.43-7.58 (m, 4H, Ar*H*), 7.82-7.87 (m, 2H, Ar*H*), 8.12-8.17 (m, 1H, Ar*H*); HRMS *m/z* calcd for $C_{17}H_{18}O_2$: 254.1307, found 254.1330.

2-Methoxy-2-(2-naphthyl)cyclohexanone (1i): 84% yield; colorless syrup; IR (neat) 3057, 2940,

2864, 1723, 1506, 1448, 1274, 1259, 1186, 1125, 1101, 1063, 898, 855, 822, 798, 748, 479 cm^{-1}; ^1H NMR (200 MHz) δ 1.68-2.75 (m, 8H, (-CH_2-)$_4$), 3.10 (s, 3H, -OCH_3), 7.41-7.53 (m, 3H, Ar*H*), 7.83-7.89 (m, 4H, Ar*H*); HRMS *m/z* calcd for $C_{17}H_{18}O_2$: 254.1307, found 254.1293.

2-(*i*-Butyl)-2-methoxycyclohexanone (2c): 54 % yield; colorless oil; IR (neat) 2953, 2829, 1718, 1463, 1367, 1168, 1119, 1075, 807 579, 543 cm^{-1}; ^1H NMR (400 MHz) δ 0.94 and 0.95 (d×2, 3H×2, -CH_3 ×2, *J*=6.3 Hz), 1.44-2.19 (m, 9H, -CH_2-×4 and –CH-$(CH_3)_2$) 2.31 (m, 1H, -CH_2-), 2.62 (m, 1H, -CH_2-), 3.15 (s, 3H, -OCH_3); HRMS *m/z* calcd for $C_{11}H_{20}O_2$: 184.1463, found 184.1454.

2-Benzyl-2-methoxycyclohexanone (2e): 52% yield; colorless oil; IR (neat) 3029, 2942, 2864 2828, 1714, 1497, 1454, 1432, 1312, 1112, 1095, 1068, 1051, 755, 703, 518 cm^{-1}; ^1H NMR (400 MHz) δ 1.36-1.66 (m, 3H,-CH_2- and one proton of another –CH_2-), 1.84-2.02 (m, 3H, -CH_2- and one proton of another –CH_2-), 2.35 (m, 1H, one proton of -CH_2-), 2.68 (m, 1H, another proton of -CH_2-), 2.84 and 2.15 (d×2, 1H×2, -CH_2Ph, *J*=14.9 Hz), 3.31 (s, 3H, -OCH_3), 7.17-7.29 (m, 5H, Ar*H*); HRMS *m/z* calcd for $C_{14}H_{18}O_2$: 218.1307, found 218.1312.

2-Methoxy-2-phenylhexan-3-one (3b): 76% yield; colorless oil; IR (neat) 3060, 3027, 2962, 2937, 2876, 2830, 1718, 1494, 1448, 1369, 1295, 1284, 1259, 1197, 1182, 1135, 1112, 1077, 1050, 1013, 753, 702 cm^{-1}; ^1H-NMR (400 MHz) δ 0.75 (t, 3H, -CH_3, *J*=7.6 Hz), 1.43 (m, 2H, -CH_2-), 1.65 (s, 3H, -CH_3), 2.46 (m, 2H, -CH_2-), 3.28 (s, 3H,- OCH_3), 7.25-7.41 (m, 5H, Ar*H*).

Preparation of 2-aryl- and 2-alkyl-2-bromocyclohexanone: typical procedure for 2-bromo-2-phenylcyclohexanone (1b)

A solution of 1-phenyl-1,2-epoxycyclohexane (1.74 g, 10.0 mmol) in chloroform (70 mL) was stirred with 48% hydrobromic acid (30 mL) at room temperature for 30 min. The organic layer was separated and the aqueous layer was extracted with chloroform (10 mL×2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL), and dried over anhydrous $MgSO_4$. After concentration of the solvent *in vacuo*, a solution of the residue in acetone (40 mL) was treated with Jones reagent (4 mL) at 0 °C for 1 h, and then the reaction was quenched with 2-propanol (4 mL). The precipitates were filtered off, and the filtrate was added to a saturated aqueous $NaHCO_3$ (50 mL). After removing the organic solvent *in vacuo*, the aqueous solution was extracted with ether (30 mL×3). The organic layer was washed with brine (30 mL) and dried over anhydrous $MgSO_4$. Concentration of the ether solution *in vacuo* gave an oil, which was purified on a silica gel column (hexane: ether=10:1) to give colorless crystals. Recrystallization from heptane gave 2-bromo-2-phenylcyclohexanone (**1b**) as a colorless prisms (1.41 g, 59% yield): mp 59-60 °C (lit. mp 74-77 °C or 98-101 °C[8b]); IR (KBr) 3059, 2944, 2866, 1707, 1498, 1446, 1255, 1233, 1206, 1138, 1119, 1069, 956, 838, 775, 708, 696, 681, 640, 557 cm^{-1}; ^1H NMR (400 MHz) δ 1.81-3.03 (m, 8H, (-CH_2-)$_4$), 7.26-7.44 (m, 5H, Ar*H*); HRMS *m/z* calcd for $C_{12}H_{13}BrO$: 252.0150, found 252.0124.

2-Bromo-2-(4-methylphenyl)cyclohexanone (1j): 71% yield; colorless prisms from hexane, mp 73-75 °C; IR (KBr) 3028, 2962, 2948, 2876, 1723, 1511, 1446, 1421, 1053, 981, 939, 777, 747, 606, 542, 511 cm^{-1}; ^1H NMR (400 MHz) δ 1.82-3.05 (m, 8H, (-CH_2-)$_4$), 2.35 (s, 3H, -CH_3), 7.19 (d, 2H, Ar*H*, *J*=8.5 Hz), 7.31 (d, Ar*H*, *J*=8.5 Hz); MS (EI) *m/z* (relative intensity) 266 (M^+, 39), 184 (88), 158 (100), 131 (51), 106 (77).

2-Bromo-2-(4-chlorophenyl)cyclohexanone (1k): 76% yield; colorless plates from hexane, mp 67-

69 °C; IR (KBr) 3065, 2953, 2934, 1720, 1496, 1469, 1446, 1406, 1221, 1115, 1101, 1071, 1012, 980, 829, 767, 718, 698, 569, 507 cm^{-1}; ^1H NMR (400 MHz) δ 1.57-3.12 (m, 8H, (-CH_2-)$_4$), 7.34 (d, 2H, Ar*H*, *J*=8.8 Hz), 7.38 (d, 2H, Ar*H*, *J*=8.8 Hz); MS (EI) *m/z* (relative intensity) 286 (M^+, 2), 207 (100), 179 (75), 125 (82).

2-Benzyl-2-bromocyclohexanone (2d): 42% yield; colorless oil, IR (neat) 3030, 2943, 2865, 2837, 1713, 1496, 1453, 1430, 1256, 1232, 1124, 1083, 766, 756, 726, 702, 583, 524 cm^{-1}; ^1H NMR (400 MHz) δ 1.40-2.18 (m, 6H, -CH_2-×3), 2.40 (m, 1H, one proton of -CH_2-), 3.25 (m, 1H, another proton of -CH_2-), 3.44 (s, 2H, -CH_2Ph), 7.23-7.47 (m, 5H, Ar*H*); HRMS *m/z* calcd for $C_{13}H_{15}BrO$: 266.0306, found 266.0305.

2-Acetoxy-2-phenylcyclohexanone (1d):

A solution of 1-phenyl-1,2-epoxycyclohexane (1.0 g, 5.7 mmol) in acetic acid (20 mL) was treated with three 4 mL portions of 5% CrO_3 solution in acetic acid at 10 min intervals at 80 °C. After 30 min, the reaction solution was diluted with water (100 mL), and extracted with ether (30 mL×3). The combined extract was washed with saturated aqueous $NaHCO_3$ (30 mL×3), and dried over anhydrous $MgSO_4$. Concentration of the ether solution *in vacuo* to give an oil, which was purified on a silica gel column (benzene:acetone=10:1) gave 2-acetoxy-2-phenylcyclohexanone (**1d**) as a colorless syrup (255 mg, 19% yield): IR (neat) 3061, 3028, 2943, 2868, 1742, 1723, 1496, 1449, 1369, 1230, 1200, 1123, 1041, 955, 757, 700, 610, 554 cm^{-1}; ^1H NMR (400 MHz) δ 1.75-2.69 (m, 8H, (-CH_2-)$_4$), 2.13 (s, 3H, -COCH_3), 7.28-7.45 (m, 5H, Ar*H*); MS (EI) *m/z* (relative intensity) 232 (M^+, 0.5), 173 (100), 144 (58), 116 (47).

2-Bromo-2-(*n*-propyl)cyclohexanone (2b):[9]

To a solution of 2-propylcyclohexanone (1.4g, 10 mmol) in dry Et_2O (30 mL) was slowly added bromine (1.6 g, 10 mmol) at –40 °C. The reaction mixture was stirred for 30 min at –40 °C, and washed with a 5% aqueous $NaHCO_3$ solution (10 mL×3). The organic layer was dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified on a silica gel column (pentane:Et_2O=20:1) to give α-bromo derivative **2b** as a pale yellowish oil (1.46 g, 67% yield): IR (neat) 2960, 2875, 1714, 1450, 1430, 1318, 1247, 1229, 1125, 1102, 906, 838, 815, 547 cm^{-1}; ^1H NMR (400 MHz) δ 0.98 (t, 3H, -CH_3, *J*=7.3 Hz), 1.38-2.40 (m, 11H, one proton of -CH_2-, (-CH_2-)$_4$ and -CH_2-), 3.21 (m, 1H, another proton of -CH_2-); MS (EI) *m/z* (relative intensity) 218 (M^+, 2), 177 (63), 138 (100), 110 (78).

2-Bromo-2-methyl-1-tetralone (3d):

To a solution of 2-methyl-1-tetralone (1.68 g, 10.5 mmol) in dry Et_2O (35 mL) was added bromine (1.67g, 10.5 mmol) at –40 °C. The reaction mixture was stirred for 20 min, washed with a 5% aqueous $NaHCO_3$ solution (10 mL×3) and then dried over anhydrous Na_2SO_4. Concentration of the solution *in vacuo* gave an oil, which was purified on a silica gel column (hexane:EtOAc=100:1) to give α-bromo derivative **3d** as crystals (1.94 g, 77% yield). Colorless prisms from hexane, mp 65-66 °C; IR (KBr) 3060, 3004, 2971, 2951, 2901, 1684, 1600, 1448, 1420, 1380, 1356, 1301, 1230, 1179, 1065, 854, 803, 743, 636, 472 cm^{-1}; ^1H-NMR (200 MHz) δ 2.03 (s, 3H, -CH_3), 2.19 (ddd, 1H, -CH_2-, *J*=4.6, 11.5 and 14.9 Hz), 2.51 (ddd, 1H, -CH_2-, *J*=2.4, 4.6 and 14.9 Hz), 2.91 (ddd, 1H, -CH_2-, *J*=2.4, 4.6 and 17.3 Hz), 3.35 (ddd, 1H, -CH_2-, *J*=4.6, 11.5 and 17.3 Hz), 7.26 (d, 1H, Ar*H*, *J*=7.6 Hz), 7.35 (dd, 1H, Ar*H*, *J*=7.6 and 7.8 Hz), 7.51 (ddd, 1H, Ar*H*, *J*=1.5, 7.6 and 7.6 Hz), 8.12 (dd, 1H, Ar*H*, *J*=1.5 and 7.8 Hz); MS (EI) *m/z* (relative

intensity) 238 (M^+, 0.5), 222 (100), 193 (34), 118 (68).

(*S*)-2-Phenyl-2-tetrahydropyranyloxy-1-*p*-toluenesulfonyloxyethane (4b):

To a solution of **4a**[11] (6.5 g, 29.2 mmol) in pyridine (20 mL) was added *p*-toluenesulfonyl chloride (6.1g, 32.0 mmol) and stirred for 5 h at room temperature. The reaction mixture was poured onto ice and extracted with $CHCl_3$ (50mL×3). The organic layer was washed with brine (30 mL×3) and dried over anhydrous $MgSO_4$. Concentration of the solution *in vacuo* gave tosylate **4b** as a colorless crystals (9.0g, 82% yield): IR (KBr) 3032, 3009, 1986, 2956, 2937, 1456, 1441, 1378, 1353, 1205, 1193, 1173, 1123, 1099, 1040, 1020, 964, 933, 922, 874, 858, 820, 782, 706, 664, 557, 546 cm^{-1}; ^1H NMR (400 MHz) δ 1.40-1.85 (m, 6H, THP's -C*H*$_2$-×3), 2.44 and 2.45 (s×2, 3H, Ts's -C*H*$_3$), 3.40-4.05 (m, 2H, THP's -OC*H*$_2$-), 4.06-4.23 (m, 2H, -C*H*$_2$O-), 4.23-4.50 (m, 1H, THP's –OC*H*O-), 4.82-5.00 (m, 1H, -C*H*O-), 7.23-7.32 (m, 7H, Ar*H*), 7.72-7.80 (m, 2H, Ar*H*).

(*R*)-2,2'-Di[(*S*)-2-hydroxy-2-phenylethoxy]-1,1'-binaphthyl (I):

To a solution of (*R*)-1,1'-binaphthyl-2,2'-diol (100 mg, 0.349 mmol) in DMF (1 mL) was slowly added sodium hydride (60%, 28 mg, 0.70 mmol) at 0 °C, and stirred for 30 min at room temperature. To the suspension was added tosylate **4b** (289 mg, 0.768 mmol) at room temperature. After stirring for 7 h at 80 °C, Et_2O (50 mL) was added to the reaction mixture at room temperature, and then the mixture was washed with water (10 mL) and then with brine (10 mL×2). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo* to give syrup. The syrup was purified on a silica gel column (hexane:EtOAc=10:1) to provide bis *O*-THP derivative of **I**. A solution of the product in methanol (5 mL) and *p*-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol) was stirred for 2 h at room temperature. After removing methanol in the presence of $NaHCO_3$ (1 g), Et_2O (50 mL) was added to the residue and the insoluble material was filtered off. The filtrate was concentrated *in vacuo* to give a syrup, which was purified on a silica gel column (benzene:acetone=4:1) to afford the diol **I** as a colorless solid (95 mg, 52% yield): colorless prisms from EtOAc-hexane, mp 171-172 °C; $[\alpha]_D^{24}$ +31.9° (*c* 1.03, $CHCl_3$); IR (KBr) 3438, 3031, 2930, 1621, 1591, 1510, 1452, 1265, 1242, 1089, 1058, 1019, 810, 756, 746, 700 cm^{-1}; ^1H NMR (400 MHz) δ 3.07 (d, 2H, -O*H*, *J*=2.5 Hz), 4.02 (dd, 2H, one proton of -OC*H*$_2$-, *J*=8.8 and 9.8 Hz), 4.14 (dd, 2H, another proton of -OC*H*$_2$-, *J*=2.7 and 9.8 Hz), 4.64 (ddd, 2H, -C*H*O-, *J*=2.5, 2.7 and 8.8 Hz), 7.09-7.29 (m, 14H, Ar*H*), 7.39 (dd, 2H, Ar*H*, *J*=6.8 and 8.0 Hz), 7.43 (d, 2H, Ar*H*, *J*=9.0 Hz), 7.92 (d, 2H, Ar*H*, *J*=8.3 Hz), 8.00 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{36}H_{30}O_4$: 526.2144, found 526.2111.

(*S*)-2,2'-Di[(*S*)-2-hydroxy-2-phenylethoxy]-1,1'-binaphthyl (J):

According to the procedure described for **I**, tosylate **4b** (868 mg, 2.31 mmol) and (*S*)-1,1'-binaphthyl-2,2'-diol (300 mg, 1.05 mmol) reacted with sodium hydride (60%, 92 mg, 2.3 mmol) yielded diol **J** as an amorphous solid (370 mg, 51% yield): $[\alpha]_D^{22}$ +9.0° (*c*0.55, $CHCl_3$); IR (neat) 3544, 3401, 3058, 2922, 2873, 1592, 1508, 1454, 1331, 1272, 1244, 1224, 1089, 1019, 809, 749, 700 cm^{-1}; ^1H NMR (400 MHz) δ 2.56 (d, 2H, -OH, *J*=3.2 Hz), 3.92 (dd, 2H, one proton of -C*H*$_2$O-, *J*=8.4 and 9.8 Hz), 4.29 (dd, 2H, another proton of -C*H*$_2$O-, *J*=2.8 and 9.8 Hz), 4.69 (ddd, 2H, -C*H*O-, *J*=2.8, 3.2 and 8.4 Hz), 7.08-7.12 (m, 4H, Ar*H*), 7.18-7.26 (m, 8H, Ar*H*), 7.32 (ddd, 2H, Ar*H*, *J*=1.6, 6.8 and 8.4 Hz), 7.38-7.44 (m, 4H, Ar*H*), 7.93 (d, 2H, Ar*H*, *J*=8.0 Hz), 8.01 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{36}H_{30}O_4$: 526.2144, found 526.2111.

(*R*)-2-(2-Chlorophenyl)-2-tetrahydropyranyloxy-1-*p*-toluenesulfonyloxyethane:

Methyl (*R*)-2-chloromanderate was obtained by reaction of (*R*)-2-chloromanderic acid (2.0g, 10.7 mmol) with methanol (10 mL) in the presence of *p*-toluenesulfonic acid monohydrate (204 mg, 1.07 mmol) in carbon tetrachloride (40 mL) by azeotropic dehydration using Soxhlet's extractor type column packed with MS3A for 4 h. After usual work up to give the ester. To a solution of the ester in dichloromethane (30 mL) were added 2,3-dihydropyran (1.35 g, 16.1 mmol) and pyridinium *p*-toluenesulfonate (200 mg, 0.796 mmol) with stirring at room temperature. After 3 h, the mixture was purified on a silica gel column (hexane: EtOAc=10:1) to give THP ether as a colorless oil. A solution of the oil in THF (30 mL) was treated with lithium aluminum hydride (610 mg, 16.1 mmol) for 12 h at room temperature. Usual work up provided (*R*)-2-(2-chlorophenyl)-2-tetrahydropyranyloxyethanol. The alcohol was reacted with *p*-toluenesulfonyl chloride (2.3 g, 12 mmol) in pyridine (15 mL) for 6 h at room temperature. The reaction mixture was diluted with Et_2O (100 mL), and washed with brine (25 mL×4). The organic layer was dried over anhydrous $MgSO_4$ and evaporated *in vacuo*. The resulting oil was purified on a silica gel column (hexane:EtOAc=10:1) to afford the tosylate as a colorless syrup (3.95 g, 90% overall yield): IR (neat) 3067, 2946, 2872, 1364, 1178, 1121, 1098, 1080, 1035, 980, 816, 760, 554 cm^{-1}; ^1H NMR (400 MHz) δ 1.40-1.85 (m, 6H, THP's –C*H*$_2$-×3), 2.44 (s, 3H, Ts's –C*H*$_3$), 3.25-3.60 (m, 2H, THP's –OC*H*$_2$-), 3.98-4.23 (m, 2H, -OC*H*$_2$-), 4.48 (t, 0.5H, THP's –OC*H*O-, *J*=2.9 Hz), 4.91 (t, 0.5H, THP's –OC*H*O-, *J*=3.4 Hz), 5.28 (dd, 0.5H, -C*H*O-, *J*=2.9 and 7.8 Hz), 5.36 (dd, 0.5H, -C*H*O-, *J*=3.4 and 7.3 Hz), 7.20-7.31 (m, 6H, Ar*H*), 7.42 (dd, 0.5H, Ar*H*, *J*=2.4 and 7.3 Hz), 7.59 (dd, 0.5H, Ar*H*, *J*=2.0 and 7.8 Hz), 7.73 (d, 0.5H, Ar*H*, *J*=8.8 Hz), 7.74 (d, 0.5H, Ar*H*, *J*=8.3 Hz).

(*S*)-2,2'-Di[(*R*)-2-hydroxy-2-(2-chlorophenyl)ethoxy]-1,1'-binaphthyl (K):

K was prepared according to the procedure described for **I** except that (*R*)-2-(2-chlorophenyl-2-tetrahydropyranyloxy-1-*p*-toluenesulfonyloxyethane (1.72 g, 4.19 mmol) and (*S*)-1,1'-binaphthyl-2,2'-diol (500 mg, 1.75 mmol) were used. Purification of the crude product on a silica gel column (benzene) yielded diol **K** as a colorless solid (500 mg, 48% yield): colorless prisms from EtOAc-hexane, mp 150-152 °C; $[\alpha]_D^{22}$ –74.4° (*c*0.524, $CHCl_3$); IR (KBr) 3431, 3056, 2928, 1592, 1508, 1474, 1438, 1329, 1271, 1244, 1148, 1088, 1034, 1019, 809, 751 cm^{-1}; ^1H NMR (400 MHz) δ 2.88 (d, 2H, -O*H*, *J*=3.4 Hz), 3.84 (dd, 2H, one proton of -C*H*$_2$O-, *J*=8.3 and 9.8 Hz), 4.29 (dd, 2H, another proton of -C*H*$_2$O-, *J*=2.4 and 9.8 Hz), 5.04 (ddd, 2H, -C*H*O-, *J*=2.4, 3.4 and 8.3 Hz), 7.11-7.45 (m, 16H, Ar*H*), 7.92 (d, 2H, Ar*H*, *J*= 8.4 Hz), 8.01 (d, 2H, Ar*H*, *J*=8.8 Hz); HRMS *m/z* calcd for $C_{36}H_{28}Cl_2O_4$: 594.1365, found 594.1345.

1,2-Di[(*S*)-2-hydroxy-2-phenylethoxy]benzene (L):

To a suspension of cesium carbonate (3.25 g, 9.98 mmol) in DMF (5 mL) was added catechol (500 mg, 4.54 mmol) at room temperature and the reaction mixture was stirred vigorously for 30 min. To the suspension was added tosylate **4b** (3.76 g, 9.99 mmol) at room temperature and the reaction mixture was stirred for 6 h at 80 °C. After cooling, the reaction mixture was diluted with Et_2O (100 mL) and washed with water (20 mL) and then with brine (20 mL×2). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo*. A solution of the residue and of *p*-toluenesulfonic acid monohydrate (300 mg, 1.58 mmol) in methanol (30 mL) was stirred at room temperature for 2 h. After removing methanol in the presence of $NaHCO_3$ (2 g), Et_2O (100 mL) was added to the residue and the insoluble material was filtered off. The filtrate was concentrated *in vacuo* to give syrup, which was purified on a silica gel column (hexane:EtOAc=10:1) to afford diol **L** as a colorless solid (1.24 g, 78% yield): colorless needles from

EtOAc-hexane, mp 100-101 °C; $[\alpha]_D^{22}$ +85.7° (*c*1.00, $CHCl_3$); IR (KBr) 3684, 3664, 3642, 3058, 3026, 2930, 1599, 1499, 1363, 1244, 1199, 1116, 1066, 1003, 741, 700, 637 cm^{-1}; ^1H NMR (400 MHz) δ 3.87 (d, 2H, -O*H*, *J*=2.4 Hz), 4.06 (dd, 2H, one proton of -CH_2O-, *J*=8.8 and 9.8 Hz), 4.16 (dd, 2H, another proton of -CH_2O-, *J*=2.9 and 9.8 Hz), 5.11 (ddd, 2H, -C*H*O-, *J*=2.4, 2.9 and 8.8 Hz), 6.98 (s, 4H, Ar*H*), 7.25-7.44 (m, 10H, Ar*H*); HRMS *m/z* calcd for $C_{22}H_{22}O_4$: 350.1518, found 350.1504.

2,2'-Di[(*S*)-2-hydroxy-2-phenylethoxy]-1,1'-biphenyl (M):

According to the procedure described for **L**, 2,2'-biphenol (1.50 g, 8.06 mmol) and tosylate **4b** (6.75 g, 17.9 mmol) were reacted with cesium carbonate (5.77 g, 17.7 mmol) in DMF (20 mL) for 6 h at 90 °C. Purification of the product on a silica gel column (hexane:EtOAc=4:1) yielded diol **M** as an amorphous solid (2.04 g, 59% yield): $[\alpha]_D^{22}$ +40.1° (*c*0.551, $CHCl_3$); IR (neat) 3436, 3062, 3030, 2926, 2868, 1594, 1504, 1483, 1441, 1284, 1262, 1111, 1053, 1027, 1003, 754, 701, 681 cm^{-1}; ^1H NMR (400 MHz) δ 3.64 (bs, 2H, -O*H*), 3.97 (dd, 2H, one proton of -OCH_2-, *J*=9.3 and 9.3 Hz), 4.12 (dd, 2H, another proton of -OCH_2-, *J*=2.4 and 9.3 Hz), 4.89 (dd, 2H, -C*H*O-, *J*=2.4 and 9.3 Hz), 7.01 (d, 2H, Ar*H*, *J*=8.1 Hz,), 7.12 (dd, 2H, Ar*H*, *J*=7.6 and 7.6 Hz), 7.25-7.39 (m, 14H, Ar*H*); HRMS *m/z* calcd for $C_{28}H_{26}O_4$: 426.1831, found 426.1771.

(*S*,*S*)-1,2-Diphenyl-2-methoxymethyloxyethanol (4d):

To a solution of (*S*,*S*)-1,2-diphenylethane-1,2-diol (200 mg, 0.933 mml) and Et_3N (0.38g, 3.76 mmol) in THF (2 mL) was added a solution of chloromethylmethylether (90 mg, 1.12 mmol) in THF (1 mL) at 0 °C and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was diluted with EtOAc (30 mL) and washed successively with water (10 mL) and with brine (10 mL×2). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo*. The resulting oil was purified on silica gel column (hexane:EtOAc=1:1) to afford mono ether **4d** as a colorless syrup (176 mg, 73% yield): $[\alpha]_D^{22}$ +63.0° (*c*0.506, $CHCl_3$); IR (neat) 3462, 3031, 2891, 2845, 2824, 1495, 1455, 1198, 1150, 1102, 1068, 1022, 970, 918, 765, 700, 566 cm^{-1}; ^1H NMR (400 MHz) δ 3.31 (d, 1H, -O*H*, *J*=1.5 Hz), 3.33 (s, 3H, -OCH_3), 4.61 (s, 2H, -OCH_2O-), 4.62 (d, 1H, -C*H*OCH_2-, *J*=7.8 Hz), 4.77 (dd, 1H, -C*H*OH, *J*=1.5 and 7.8 Hz), 7.06-7.26 (m, 10H, ArH).

α,α'-Di[(1*S*,2*S*)-2-hydroxy-1,2-diphenylethyl]-*o*-xylenedioxide (C):

To a suspension of sodium hydride (60%, 30 mg, 0.75 mmol) in THF (0.5 mL) was added a solution of alcohol **4d** (176 mg, 0.68 mmol) in THF (0.5 mL) at 0 °C and the reaction mixture was stirred for 30 min at room temperature under argon. To the suspension was added α,α'-*o*-xylyldibromide (90 mg, 0.34 mmol) and stirred for 30 min. After refluxing for 10 min, EtOAc (30 mL) was added to the reaction mixture at room temperature and the solution was washed successively with water (5 mL) and with brine (5 mL). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo*. A solution of the residue and catalytic amount of *p*-toluenesulfonic acid monohydrate (*ca* 20 mg) in methanol (5 mL) was refluxed for 2 h. After removing methanol in the presence of $NaHCO_3$ (100 mg), EtOAc (30 mL) was added to the residue and the mixture was filtered. The filtrate was concentrated *in vacuo* to give syrup, which was purified on a silica gel column (hexane:EtOAc=4:1) to afford diol **C** as an amorphous solid (124 mg, 67% yield): $[\alpha]_D^{22}$ +63.4° (*c*0.435, $CHCl_3$); IR (neat) 3436, 3062, 3030, 2874, 1454, 1198, 1118, 1072, 1024, 766, 699, 566 cm^{-1}; ^1H NMR (400 MHz) δ 4.42 (d, 2H, -C*H*O-, *J*=8.4 Hz), 4.52 and 4.73 (d×2, 2H×2, -CH_2O-, *J*=11.2 Hz), 4.76 (s, 2H, -O*H*), 4.82 (d, 2H, -C*H*O-, *J*=8.4 Hz), 6.98-7.42 (m, 24H, Ar*H*).

α,α'-Di[(*S*)-2-hydroxy-2-phenylethyl]-*m*-xylenedioxide (F):

To a suspension of sodium hydride (60%, 762 mg, 19.1 mmol) in THF (20 mL) was added a solution of alcohol **4a** (3.85 g, 17.3 mmol) in THF (0.5 mL) at 0 °C and the reaction mixture was stirred for 40 min at room temperature under argon. To the suspension was added α,α'-*m*-xylyldichloride (1.46 g, 8.31 mmol) and stirred for 2 min. After refluxing for 5 h, Et_2O (100 mL) was added to the reaction mixture at room temperature and the solution was washed successively with water (20 mL) and with brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo*. A solution of the residue and *p*-toluenesulfonic acid monohydrate (300 mg, 1.58 mmol) in methanol (30 mL) was stirred at room temperature for 2 h. After removing methanol in the presence of $NaHCO_3$ (1 g), Et_2O (100 mL) was added to the residue and the mixture was filtered. The filtrate was concentrated *in vacuo* to give syrup, which was purified on a silica gel column (hexane:EtOAc=4:1) to afford diol **F** as a colorless syrup (2.5 g, 79% yield): $[\alpha]_D^{22}$ +42.4° (*c*0.571, $CHCl_3$); IR (neat) 3420, 3062, 3031, 2902, 2861, 1494, 1454, 1359, 1198, 1157, 1109, 1028, 757, 701 cm^{-1}; ^1H NMR (400 MHz) δ 2.85 (s, 2H, -O*H*), 3.52 (dd, 2H, one proton of -CH_2O-, *J*=8.8 and 9.8 Hz), 3.65 (dd, 2H, another proton of -CH_2O-, *J*=3.4 and 9.8 Hz), 4.60 (s, 4H, Ph-CH_2O-), 4.93 (dd, 2H, -C*H*O-, *J*=3.4 and 8.8 Hz), 7.25-7.45 (m, 14H, Ar*H*).

2,6-Di[(*S*)-2-hydroxy-2-phenylethyloxy]pyridine (G):

According to the procedure described for **F**, alcohol **4a** (923 mg, 4.15 mmol) and 2,6-bis(bromomethyl)pyridine (500 mg, 1.89 mmol) were reacted with sodium hydride (60%, 166 mg, 4.15 mmol) in THF (10 mL) at room temperature to yield diol **G** (469 mg, 66% yield) as crystals: colorless needles from EtOAc-hexane, mp 104-105 °C; $[\alpha]_D^{22}$ +136° (*c*1.06, $CHCl_3$); IR (KBr) 3361, 3197, 3059, 3029, 2900, 2872, 1598, 1579, 1494, 1461, 1362, 1340, 1237, 1199, 1137, 1117, 1096, 1083, 1063, 1024, 998, 905, 885, 803, 766, 751, 699, 639, 542 cm^{-1}; ^1H NMR (400 MHz) δ 3.65 (dd, 2H, one proton of -OCH_2-, *J*=9.0 and 10.3 Hz), 3.85 (dd, 2H, another proton of -OCH_2-, *J*=2.7 and 10.3 Hz), 4.76 (d, 2H, one proton of -OCH_2-Py, *J*=13.4 Hz), 4.82 (d, 2H, another proton of -OCH_2-Py *J*=13.4 Hz), 5.03 (dd, 2H, -C*H*O-, *J*=2.7 and 9.0 Hz), 5.51 (bs, 2H, -O*H*), 7.21-7.42 (m, 12H, Ar*H*), 7.71 (t, 1H, Ar*H*, *J*=7.6 Hz).

***N,N'*-Di[(*S*)-hydroxy-2-phenylethyl]-*N,N'*-diisopropylethylenediamine (E):**

A solution of *N,N'*-diisopropylethylenediamine (600 mg, 4.16 mmol) and (*R*)-styrene oxide (1.00 g, 8.32 mmol) in DMF-H_2O (10:1, 3.3 mL) was stirred for 14 h at 100 °C. The reaction mixture was diluted with EtOAc (50 mL) and the solution was washed with brine (15 mL×2) and then dried over anhydrous $MgSO_4$. Concentration of the solution *in vacuo* gave an oil, which was purified on a silica gel column (hexane: EtOAc=5:1) to afford diamino diol **E** as a viscous syrup (835 mg, 52% yield); $[\alpha]_D^{22}$ −137° (*c*0.448, $CHCl_3$); IR (neat) 3333, 3064, 3030, 2970, 2932, 2836, 1452, 1387, 1366, 1337, 1202, 1162, 1083, 1059, 895, 763, 700 cm^{-1}; ^1H NMR (400 MHz) δ 1.07 (d, 6H, -CH_3, *J*=6.8 Hz), 1.11 (d, 6H, -CH_3, *J*=6.8 Hz), 2.46 (dd, 2H, one proton of -CH_2N-, *J*=10.3 and 13.7 Hz), 2.56-2.85 (m, 4H, -NCH_2CH_2N-), 2.68 (dd, 2H, another proton of -CH_2N-, *J*=2.9 and 13.7 Hz), 3.10 (heptet, 2H, -C*H*C-, *J*=6.8 Hz), 4.78 (dd, 2H, -C*H*O-, *J*=2.9 and 10.3 Hz), 5.90 (bs, 2H, -O*H*), 7.24-7.41 (m, 10H, Ar*H*).

(*S*)-2-Phenyl-2-tetrahydropyranyloxy-*S*-acetyl-1-ethanethiol (4e):

A solution of tosylate **4b** (2.0 g, 5.3 mmol) and potassium thioacetate (1.54g, 13.5 mmol) in DMF (5 mL) was stirred for 2 h at 80 °C. Et_2O was added to the reaction mixture at room temperature and the solution was washed with brine (15 mL×2). The organic layer was dried over anhydrous $MgSO_4$ and then

concentrated *in vacuo*. The residue was purified on a silica gel column (hexane:EtOAc=10:1) to give thioacetate **4e** as a yellowish syrup (1.41 g, 95% yield): IR (neat) 3063, 3031, 2942, 2873, 1695, 1455, 1354, 1202, 1118, 1079, 1023, 978, 918, 871, 733, 701, 631 cm^{-1}; ^1H NMR (400 MHz) δ 1.18-1.90 (m, 6H, THP's $-CH_2-$×3), 2.32 (s, 1.05H, $-COCH_3$), 2.33 (s, 1.95H, $-COCH_3$), 3.16-4.07 (m, 4H, THP's $-CH_2O-$ and $-CH_2S-$), 4.45 (t, 0.65H, THP's $-OCHO-$, *J*=2.9 Hz), 4.72 (dd, 0.35H, -C*H*O-, *J*=4.9 and 6.8 Hz), 4.77 (dd, 0.65H, -C*H*O-, *J*=4.4 and 8.8 Hz), 4.93 (t, 0.35H, THP's $-OCHO-$, *J*=3.4 Hz), 7.26-7.41 (m, 5H, Ar*H*).

α,α'-Di[(*S*)-2-hydroxy-2-phenylethyl]-*o*-xylenedithioate (B):

To a solution of thiolacetate **4e** (1.0 g, 3.6 mmol) in dry methanol (4 mL) was added sodium hydride (60%, 157 mg, 3.93 mmol) at 0 °C and the reaction mixture was stirred for 1 h at room temperature. After removing methanol azeotoropic distillation was carried out with benzene (2 mL×3) *in vacuo*. To a solution of the residue in THF (4 mL) was added α,α'-*o*-xylyldibromide (470 mg, 1.78 mmol) at 0 °C and stirred for 1h at room temperature. The reaction mixture was diluted with Et_2O (60 mL) and the mixture was washed successively with water (20 mL) and with brine (20 mL×2). The organic layer was dried over anhydrous $MgSO_4$ and then concentrated *in vacuo* to give a syrup. The syrup was purified on a silica gel column (hexane:EtOAc=10:1) to provide bis THP ether derivative (945 mg). A solution of the bis THP ether derivative and *p*-toluenesulfonic acid monohydrate (100 mg, 0.526 mmol) in methanol (15 mL) was stirred at room temperature for 3 h. After removing methanol in the presence of $NaHCO_3$ (1 g), Et_2O (100 mL) was added to the residue and the mixture was filtered. The filtrate was concentrated *in vacuo* to give syrup, which was purified on a silica gel column (hexane:EtOAc=4:1) to afford diol **B** as an amorphous solid (639 mg, 44% yield): $[\alpha]_D^{22}$ +78.1° (*c*0.558, $CHCl_3$); IR (neat) 3258, 3029, 2949, 2913, 2879, 1493, 1455, 1434, 1422, 1411, 1284, 1228, 1201, 1029, 1012, 770, 750, 723, 699, 929, 599, 543 cm^{-1}; ^1H NMR (400 MHz) δ 2.73 (dd, 2H, one proton of $-CH_2S-$, *J*=9.0 and 13.9 Hz), 2.86 (dd, 2H, another proton of $-CH_2S-$, *J*=3.7 and 13.9 Hz), 2.93 (d, 2H, -OH, *J*=2.4 Hz), 3.90 and 3.95 (d×2, 2H×2, Ph-CH_2S-, *J*=12.9 Hz), 4.71 (ddd, 2H, -C*H*O-, *J*=2.4, 3.7 and 9.3 Hz), 7.22-7.36 (m, 14H, Ar*H*).

2,6-Di[(*S*)-2-hydroxy-2-phenylethylthiomethyl] pyridine (H):

According to the procedure described for **B**, thiolacetate **4e** (923 mg, 4.15 mmol) and 2,6-bis(bromomethyl)pyridine (500 mg, 1.89 mmol) were reacted with sodium hydride (60%, 166 mg, 4.15 mmol) in THF (10 mL) at room temperature to provide diol **H** (469 mg, 66% yield) as a viscous syrup. The syrup was gradually crystallized: $[\alpha]_D^{22}$ +97.2° (*c*0.631, $CHCl_3$); IR (neat) 3388, 3083, 2909, 2780, 1595, 1573, 1459, 1339, 1203, 1086, 1061, 1003, 810, 763, 730, 721, 702, 517 cm^{-1}; ^1H NMR (400 MHz) δ 2.82 (dd, 2H,one proton of $-CH_2S-$, *J*=8.8 and 14.4 Hz), 2.94 (dd, 2H, another proton of $-CH_2S-$, *J*=3.6 and 14.4 Hz), 3.98 (s, 4H, Py-CH_2S-), 4.86 (dd, 2H, -C*H*O-, *J*=3.6 and 8.8 Hz), 5.08 (bs, 2H, -O*H*), 7.20-7.37 (m, 12H, Ar*H*), 7.67 (t, 1H, Ar*H*, *J*=7.6 Hz).

Typical procedure for the enantioselective protonation of the samarium enolate derived from 1a with (*R,S*)-DHPEB (I):

A SmI_2 solution (0.1 $mol \cdot dm^{-3}$, 6.3 mL, 0.63 mmol) was added to a solution of α-methoxy ketone **1a** (54.0 mg, 0.264 mmol) and (*R,S*)-DHPEB (**I**) (278 mg, 0.529 mmol) in THF (5 mL) with stirring under argon at –45 °C. After stirring for 2 h at the temperature, the reaction mixture was quenched with 0.1 N hydrochloric acid (4 mL) and extracted with Et_2O (15 mL×3). The organic layer was washed with brine

(15 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (hexane:EtOAc=8:1) to give 2-phenylcyclohexane (**1'a**) (32.2 mg, 70% yield) in 87% ee as a colorless solid: $[\alpha]_D^{20}$ +84.1° (*c*0.350, benzene). The absolute configuration was determined to be *R* by comparison of its optical rotation with the reported one (*lit.* $[\alpha]_D^{26}$ +114.7° (*c*0.17, benzene) for (*R*)-**1'a**,[18] $[\alpha]_D^{29}$ –88.9° (*c*1.0, $CHCl_3$) for 87% ee of (*S*)-**1'a**[2q]). CD spectrum of the product (*c*0.091, MeOH) λext 289 nm, Δε +1.2. The enantiomeric excess (ee) was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD-H, hexane:2-propanol=95:5, flow rate=0.5 mL/min): t_R=14.7 min (*S*-isomer); t_R=15.8 min (*R*-isomer). The chiral diol **I** was recovered almost quantitatively without a loss of optical purity.

2-(4-Methoxyphenyl)cyclohexanone (1'e): $[\alpha]_D^{20}$ +80.9° (*c*0.346, benzene) for the product of 87% ee (*lit.*$[\alpha]_D^{29}$ -70° (*c*1.0, $CHCl_3$) for (-)-**1'e** of 81% ee[2q]); CD (*c*0.023, MeOH) λext 287 nm, Δε +2.2 for the product of 86% ee. The absolute configuration was assigned to be *R* based on the similarity of the CD spectrum to that of (*R*)-**1'a**. The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD-H, hexane:2-propanol=95:5, flow rate=0.6 mL/min): t_R=21.9 min (*S*-isomer); t_R=28.1 min (*R*-isomer).

2-(4-Methylphenyl)cyclohexanone (1'f): $[\alpha]_D^{20}$ +75.4° (*c*0.349, benzene) for the product of 94% ee (*lit.*$[\alpha]_D^{27}$ –60.0° (*c*0.75, $CHCl_3$) for (-)-**1'f** of 75% ee[2q]); CD (*c*0.090, MeOH) λext 289 nm, Δε +1.5 for the product of 92% ee. The absolute configuration was assigned to be *R* based on the similarity of the CD spectrum to that of (*R*)-**1'a**. The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD-H, hexane:2-propanol=95:5, flow rate=0.4 mL/min): t_R=18.7 min (*S*-isomer); t_R=22.0 min (*R*-isomer).

2-(4-Chlorophenyl)cyclohexanone (1'g):[19] $[\alpha]_D^{20}$ +47.7° (*c*0.346, benzene) for the product of 83% ee; CD (*c*0.086, MeOH) λext 288 nm, Δε +1.0 for the product of 80% ee. The absolute configuration was assigned to be *R* based on the similarity of the CD spectrum to that of (*R*)-**1'a**. The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OJ, hexane:2-propanol=9:1, flow rate=1.0 mL/min): t_R=10.1 min (*R*-isomer); t_R=14.1 min (*S*-isomer).

2-(1-Naphthyl)cyclohexanone (1'h):[20] $[\alpha]_D^{20}$ –8.0° (*c*0.21, benzene) for the product of 14% ee; CD (*c*0.017, MeOH) λext 286 nm, Δε +0.64 for the product of 67% ee. The absolute configuration was assigned to be *R* based on the similarity of the CD spectrum to that of (*R*)-**1'a**. The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OJ, hexane:2-propanol=8:2, flow rate=1.0 mL/min): t_R=16.0 min (*R*-isomer); t_R= 23.0 min (*S*-isomer).

2-(2-Naphthyl)cyclohexanone (1'i): $[\alpha]_D^{20}$ +70.5° (*c*0.380, benzene) for the product of 90% ee (*lit.*$[\alpha]_D^{27}$ –97.9° (*c*0.64, $CHCl_3$) for (-)-**1'i** of 99% ee[2q]); CD (*c*0.017, MeOH) λext 285 nm, Δε +1.5 for the product of 90% ee. The absolute configuration was assigned to be *R* based on the similarity of the CD spectrum to that of (*R*)-**1'a**. The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD-H, hexane:2-propanol=9:1 flow rate=0.5 mL/min): t_R=18.3 min (*S*-isomer); t_R= 21.7 min (*R*-isomer).

2-Methylcyclohexanone (2'a): $[\alpha]_D^{22}$ +7.7° (*c*0.285, MeOH). The absolute configuration and ee were determined by comparison of its optical rotation with the reported one.[21]

2-Propylcyclohexanone (2'b): $[\alpha]_D^{22}$ +18.4° (*c*0.423, MeOH). The absolute configuration and ee

were determined by comparison of its optical rotation with the reported one.[22]

2-(*i*-Butyl)cyclohexanone (2'c): $[\alpha]_D^{22}$ +29.7° (*c*0.417, MeOH). The absolute configuration and ee were determined by comparison of its optical rotation with the reported one.[23]

2-Benzylcyclohexanone (2'e): $[\alpha]_D^{22}$ +36.8° (*c*0.332, MeOH) for the product of 80% ee. The absolute configuration was determined to be *R* by comparison of its optical rotation with the reported one.[24] The enantiomeric excess (ee) was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OJ, hexane:2-propanol=99:1, flow rate=0.6 mL/min): t_R=17.9 min (*R*-isomer); t_R=20.4 min (*S*-isomer).

1,2-Diphenylpropan-1-one (3'a): $[\alpha]_D^{22}$ +67.4° (*c*0.356, $CHCl_3$) for the product of 35% ee. The absolute configuration was determined to be *S* by comparison of its optical rotation with the reported one.[25] The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD, hexane:2-propanol=100:1, flow rate=0.5 mL/min, the sample was dissolved in a mixture of hexane:Et_2O=10:1, no separation was observed if the sample was dissolved only in hexane): t_R=15.9 min (*S*-isomer); t_R=18.8 min (*R*-isomer).

2-Phenylhexan-3-one (3'b): $[\alpha]_D^{22}$ –96.4° (*c*0.165,toluene) for the product of 30% ee. The absolute configuration was determined to be *R* by comparison of its optical rotation with the reported one.[26] The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OB', hexane, flow rate=1.0 mL/min): t_R=13.5 min (*S*-isomer); t_R=19.7 min (*R*-isomer).

2-Phenyl δ-valerolactone (3'c):[10] $[\alpha]_D^{22}$ +32.6° (*c*0.424, $CHCl_3$) for the product of 72% ee. The absolute configuration was determined to be *R* by comparison of the optical rotation of 2-phenyl-1,5-pentanediol from **3'c** with the reported one.[27] The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OB', hexane:2-propanol=8:2, flow rate=1.0 mL/min): t_R=29.9 min (*R*-isomer); t_R=34.0 min (*S*-isomer).

2-Methyl-1-tetralone (3'd): $[\alpha]_D^{16}$ –17.0° (*c*0.335, dioxane) for the product of 32% ee; CD (*c*0.031, MeOH) λext 308 nm, Δε -0.24 for the product of 48% ee. The absolute configuration was determined to be *S* by comparison of its optical rotation with the reported one.[28] The ee was determined by HPLC analysis using a chiral column (DAICEL CHIRALCEL OD-H, hexane:2-propanol=100:1, flow rate=1.0 mL/min): t_R=7.6 min (*R*-isomer); t_R=8.6 min (*S*-isomer).

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