Asymmetric Hydrosilylation of Ketones Using *Trans*-Chelating Chiral Peralkylbisphosphine Ligands Bearing Primary Alkyl Substituents on Phosphorus Atoms

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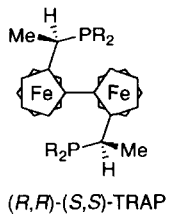
Asymmetric hydrosilylation of simple ketones with diphenylsilane proceeded at −40 °C in the presence of a rhodium complex (0.001—0.01 molar amount) coordinated with a trans-chelating chiral bisphosphine ligand bearing linear alkyl substituents on the phosphorus atoms, (*R*,*R*)-(*S*,*S*)-Et-, Pr-, or BuTRAP, giving the corresponding optically active (*S*)-secondary alcohols with up to 97% ee. The asymmetric hydrosilylation using TRAP ligands with bulkier *P*-substituents resulted in much lower enantioselectivities. The EtTRAP–rhodium catalyst was also effective for asymmetric hydrosilylation of keto esters with a coordination site for a rhodium atom (up to 98% ee). Optically active symmetrical diols were obtained with up to 99% ee from the corresponding diketones via the asymmetric reduction using 2.5 molar amounts of diphenylsilane.

Catalytic asymmetric hydrosilylation of ketones is one of the asymmetric reactions which has been intensively studied.[1] Some chiral nitrogen-based ligands have been utilized for the asymmetric hydrosilylation to give optically active secondary alcohols with over 90% ee,[2—4] but chiral bisphosphine ligands,[5—7] commonly used, had not achieved high enantioselectivity except for ketonic substrates bearing a secondary coordinating functional group.[8,9]

Recently, we designed and synthesized a novel type of chiral bisphosphines, (*S*,*S*)-2,2″-bis[(*R*)-1-(dialkylphosphino)-ethyl]-1,1″-biferrocenes [abbreviated to TRAP] (Chart 1).[10] The new chiral bisphosphines chelate to a transition metal atom in a trans-manner. Herein, we wish to describe that TRAPs are effective for asymmetric hydrosilylation of ketones, to give the corresponding secondary alcohols with up to 99% ee.[11,12] This is the first example of highly enantioselective hydrosilylation of simple ketones using a chiral bisphosphine ligand.[7] The TRAP ligands with linear alkyl groups on the phosphorus atoms, alkylTRAP,[10c] were superior to those with rigid and bulky *P*-substituents. Most chiral phosphine ligands in asymmetric catalysis have bulky and conformationally rigid substituents on the phosphorus atoms in order to transmit effectively the chiral information of the ligands to the reaction site.[13] To the best of our knowledge, EtDIOP is the only one exception,[14] but the ligand which bears flexible *P*-substituents has been ineffective for catalytic asymmetric synthesis, recording 37% ee at most.[15]



(*R*,*R*)-(*S*,*S*)-TRAP

R = Me (MeTRAP)
R = Et (EtTRAP)
R = Pr (PrTRAP)
R = Bu (BuTRAP)
R = *i*-Bu (*i*-BuTRAP)
R = *i*-Pr (*i*-PrTRAP)
R = Ph (PhTRAP)
R = 2-furyl (FurTRAP)

Chart 1. Structure of TRAP ligands.

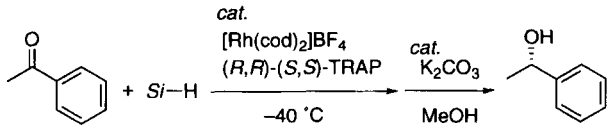
Results and Discussion

Asymmetric Hydrosilylation of Simple Ketones. Hydrosilylation of acetophenone (**1a**) was carried out at −40 °C in THF with 1.5 molar amounts of hydrosilane in the presence of 0.01 molar amount of a cationic rhodium complex prepared in situ from $[Rh(cod)_2]BF_4$ and a variety of (*R*,*R*)-(*S*,*S*)-TRAPs (Eq. 1). Results are summarized in Table 1. The substituents on the phosphorus atoms of TRAP affected significantly both enantioselectivity and catalytic activity. The chiral bisphosphines bearing linear alkyl *P*-substituents, Et-, Pr-, and BuTRAP, provided high enantioselectivity (Entries 1—3). The hydrosilylation of **1a** with diphenylsilane using (*R*,*R*)-(*S*,*S*)-Bu- or PrTRAP, followed by methanolysis of the resulting silyl ether, gave (*S*)-1-phenylethanol (**2a**) with 92% ee in high yield. Rhodium complexes involving TRAP ligands with β-branched and α-branched alkyl group on phosphorus showed low catalytic activity to give nearly racemic **2a** (Entries 4 and 5). Use of TRAP ligands with rigid and large *P*-aromatic substituents (PhTRAP, FurTRAP) decreased the stereoselectivity (Entries 6 and 7). Unexpectedly, TRAP ligands having flexible and small *P*-linear alkyl substituents showed higher enantioselectivity in the present asymmetric hydrosilylation than Ph- and FurTRAP ligands did.

Table 1. Asymmetric Hydrosilylation of Acetophenone (**1a**) Catalyzed by TRAP–Rhodium Complex[a)]

Entry	Ligand[b)]	Hydrosilane	Solvent	Time/h	Yield[c)]/%	ee[d)]/%	Confign.[e)]
1	EtTRAP	Ph_2SiH_2	THF	24	90	85	*S*
2	PrTRAP	Ph_2SiH_2	THF	5	89	92	*S*
3	BuTRAP	Ph_2SiH_2	THF	11	88	92	*S*
4	*i*-BuTRAP	Ph_2SiH_2	THF	142	83	1	*S*
5	*i*-PrTRAP	Ph_2SiH_2	THF	78	78	1	*R*
6	PhTRAP	Ph_2SiH_2	THF	9	85	15	*S*
7	FurTRAP	Ph_2SiH_2	THF	24	24	11	*S*
8[f)]	BuTRAP	Ph_2SiH_2	THF	30	82	63	*S*
9	BuTRAP	$PhMeSiH_2$	THF	5	83	56	*S*
10	BuTRAP	α-NpPhSiH$_2$[g)]	THF	24	—[h)]	—	—
11	BuTRAP	$PhSiH_3$	THF	48	20	0	—
12	BuTRAP	Ph_2SiH_2	DME	21	96	90	*S*
13	BuTRAP	Ph_2SiH_2	CH_2Cl_2	168	81	91	*S*
14	BuTRAP	Ph_2SiH_2	Toluene	4	86	90	*S*
15[i)]	BuTRAP	Ph_2SiH_2	THF	50	95	89	*S*

a) All reactions were carried out at −40 °C. The molar ratio of **1a** : hydrosilane : $[Rh(cod)_2]BF_4$: TRAP was 100 : 150 : 1.0 : 1.1 unless otherwise noted. b) (*R*,*R*)-(*S*,*S*)-TRAPs were used. c) Isolated yield. d) Determined by GLC analysis with Chiraldex G-TA. e) Assigned by specific rotation of **2a**. f) $[RhCl(cod)]_2$ was used. g) α-Np = 1-naphthyl. h) No reaction took place. i) The reaction was carried out in a 55% solution of **1a** in THF with 0.001 molar amount of the chiral catalyst.

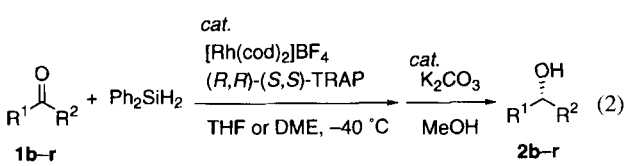


(1)

The neutral chloro-rhodium complex generated in situ by mixing $[RhCl(cod)]_2$ and BuTRAP was less effective than the cationic one (Entry 8). The decrease in the reactivity might be caused by occupation of two coordination sites by the chloro ligand and the trans-spanning biferrocene backbone of BuTRAP, because hydrosilylation catalyzed by a rhodium complex may need three vacant coordination sites on the metal center.

Besides *P*-substituents of TRAP, *Si*-substituents on hydrosilane played an important role in the enantioface-selection of ketone. Use of methylphenylsilane gave (*S*)-**2a** with 56% ee (Entry 9). 1-Naphthylphenylsilane did not react with **1a** at all (Entry 10). The bulky 1-naphthyl group might encumber the oxidative addition of the silicon–hydrogen bond to the congested BuTRAP–rhodium(I) complex. The hydrosilylation of acetophenone with phenylsilane did not lead to completion, giving racemic **2a** in only 20% yield (Entry 11). This may be due to a competing decomposition of phenylsilane in the presence of the rhodium complex. Use of solvents other than THF hardly affected enantioselectivity, but the reaction in dichloromethane proceeded very slowly (Entries 12—14). Decrease in the amount of the BuTRAP–rhodium catalyst did not cause significant loss of the enantioselectivity; (*S*)-**2a** with 89% ee was obtained in 95% yield (Entry 15).

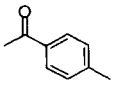
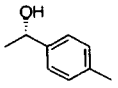
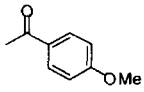
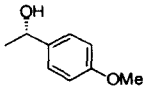
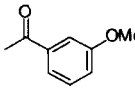
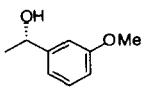
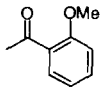
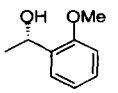
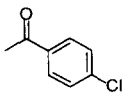
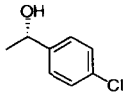
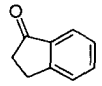
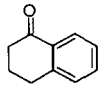
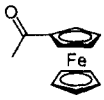
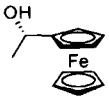
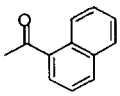
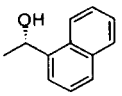
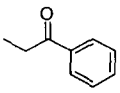
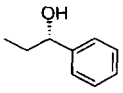
Other alkyl aryl ketones **1b—k** were subjected to the asymmetric hydrosilylation catalyzed by the BuTRAP–rhodium catalyst (Eq. 2). Results are summarized in Table 2. Acetophenone derivatives **1b—f** were reduced to the corresponding secondary alcohols **2b—f** with 79—91% ee by the BuTRAP–rhodium complex (Entries 1—5). Both electron-donating and -withdrawing substituents on the aromatic ring caused a decrease in enantioselectivity, but the position of the functional group hardly affected the selectivity. Cyclic alkyl aryl ketones **1g**, **1h**, and methyl ketones bearing ferrocenyl (**1i**) or 1-naphthyl (**1j**) group were converted to the corresponding secondary alcohols with high enantiomeric excesses of over 80% through the asymmetric hydrosilylation (Entries 6—9). The hydrosilylation of **1i** followed by methanolysis of the resulting silyl ether furnished (*S*)-ferrocenylethanol (**2i**) with 97% ee in 84% yield. Unfortunately, the reaction of propiophenone (**1k**) proceeded much more slowly than that of **1a**, giving (*S*)-**2k** with 62% ee at −10 °C (Entry 10). The ethyl substituent of **1k** might be too large for the coordination onto the congested BuTRAP–rhodium complex.



(2)

The alkylTRAP–rhodium catalysts were also effective for asymmetric hydrosilylation of aliphatic ketones (Table 3). In contrast to the hydrosilylation of alkyl aryl ketones, EtTRAP was more effective for the reaction of alkyl methyl ketones than BuTRAP was (Entries 1—8). Tertiary and secondary alkyl methyl ketones **1l** and **1m** were reduced with 96% and 81% ee, respectively (Entries 1 and 3). Hydrosilylation of linear 2-alkanone **1n**, which was one of challenging substrates for highly enantioselective reduction,[16] gave (*S*)-**2n** with 70% ee by using MeTRAP (Entry 5). Compared with the result of **1n**, the bulky phenyl group on γ-carbon of **1o** did not affect stereoselectivity significantly, but **1p** having a phenyl group at the β-position gave **2p** with higher enan-

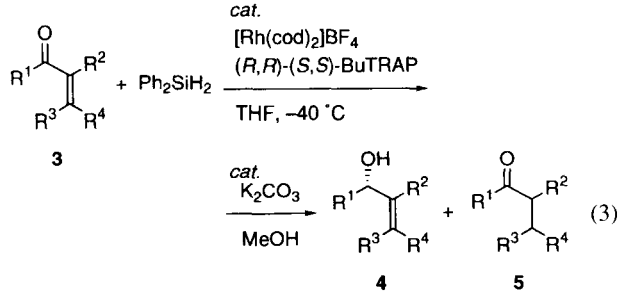
Table 2. Asymmetric Hydrosilylation of Alkyl Aryl Ketones[a]

Entry	Substrate 1		Time/h	Product 2		Yield[b]/%	ee[c]/%	Config.[d]
1		1b	5		2b	90	91	*S*
2		1c	7		2c	88	86	*S*
3		1d	6		2d	87	85	*S*
4[e]		1e	6		2e	79	84	*S*
5		1f	13		2f	88	79	*S*
6		1g	3		2g	87	87	*S*
7		1h	4		2h	83	84	*S*
8		1i	11		2i	84	97[f]	*S*
9		1j	9		2j	76	82	*S*
10[g]		1k	48		2k	73	62	*S*

a) The reactions were carried out in THF at −40 °C unless otherwise noted. The molar ratio of **1** : Ph_2SiH_2 : [Rh(cod)$_2$]BF_4 : (*R*,*R*)-(*S*,*S*)-BuTRAP was 100 : 150 : 1.0 : 1.1. b) Isolated yield. c) Determined by HPLC analysis with CHIRALCEL OB-H. d) Assigned by specific rotation of **2**. e) In DME. f) Determined by HPLC analysis of its *N*-(3,5-dinitrophenyl)carbamate derivative with SUMICHIRAL OA-4100. g) At −10 °C.

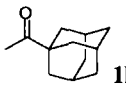
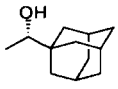
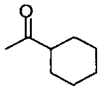
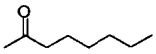
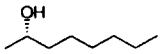
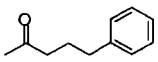
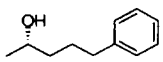
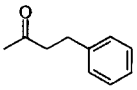
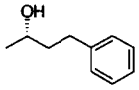
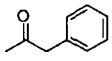
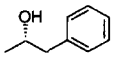
tiomeric excess (Entries 9 and 10). However, the asymmetric hydrosilylation of **1q** gave only 32% ee of (*S*)-**2q**. The low enantiomeric excess might result from the enolizable α-protons between the carbonyl and the phenyl group (Entry 11).[8] Optically active cyclic aliphatic alcohol **2r** was also obtained with high enantiomeric excess (Entry 12).

The hydrosilylation of α,β-unsaturated ketones **3** with diphenylsilane catalyzed by the BuTRAP–rhodium complex gave the corresponding allyl alcohols **4** along with a trace amount of 1,4-addition product **5**, as shown in Table 4 (Eq. 3).[17] α-Branched substrates **3a** and **3b** were reduced to afford (*S*)-**4a** and (*S*)-**4b** with 95% and 87% ees, respectively (Entries 1 and 2). The reaction of benzylideneacetone (**3c**) gave (*R*)-**4c** of 34% ee, suggesting that BuTRAP achieves the enantioface-selection of **3c** by recognizing the vinyl group as a smaller group than the methyl group (Entry 3).



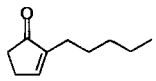
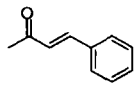
(3)

Table 3. Asymmetric Hydrosilylation of Dialkyl Ketones[a)]

Entry	Substrate **1**	Ligand[b)]	Time/h	Product **2**	Yield[c)]/%	ee/%	Confign.[d)]
1[e)]	 **1l**	EtTRAP	10	 **2l**	78	96[f)]	*S*[g)]
2[e)]	**1l**	BuTRAP	48	**2l**	92	91[f)]	*S*[g)]
3	 **1m**	EtTRAP	24	 **2m**	76	81[h)]	*S*
4	**1m**	BuTRAP	10	**2m**	62	80[h)]	*S*
5[i)]	 **1n**	MeTRAP	24	 **2n**	75	70[h)]	*S*
6[i)]	**1n**	EtTRAP	24	**2n**	88	65[h)]	*S*
7[i)]	**1n**	PrTRAP	24	**2n**	78	60[h)]	*S*
8[i)]	**1n**	BuTRAP	24	**2n**	81	55[h)]	*S*
9	 **1o**	BuTRAP	20	 **2o**	93	60[j)]	*S*[k)]
10	 **1p**	BuTRAP	30	 **2p**	93	70[l)]	*S*
11	 **1q**	BuTRAP	24	 **2q**	84	32[m)]	*S*
12[e)]	 **1r**	BuTRAP	26	 **2r**	70	88[m)]	*S*

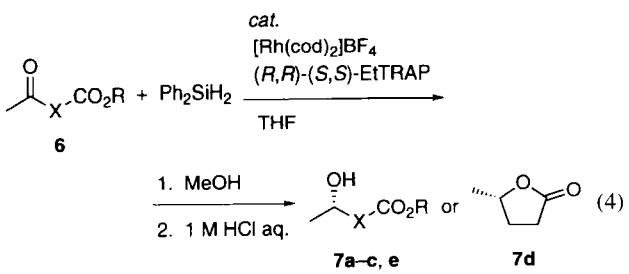
a) The reactions were carried out in DME at −40 °C unless otherwise noted. The molar ratio of **1** : Ph_2SiH_2 : [Rh-(cod)$_2$]BF_4 : TRAP was 100 : 150 : 1.0 : 1.1. b) (*R*,*R*)-(*S*,*S*)-TRAPs were used. c) Isolated yield. d) Assigned by specific rotation of **2** unless otherwise noted. e) In THF. f) Determined by HPLC analysis of its *N*-(3,5-dinitrophenyl)carbamate derivative with SUMICHIRAL OA-4100. g) Assigned by specific rotation of its acetate derivative. h) Determined by HPLC analysis of their *N*-(3,5-dinitrophenyl)carbamate derivatives with SUMICHIRAL OA-4500. i) At −30 °C. j) Determined by HPLC analysis with CHIRALCEL OJ. k) See text. l) Determined by HPLC analysis with CHIRALCEL OD-H. m) Determined by GLC analysis of its trifluoroacetate derivative with Chiraldex G-TA.

Table 4. Asymmetric Hydrosilylation of α,β-Unsaturated Ketones (**3**)[a)]

Entry	Substrate **3**	Time/h	**4** : **5**[b)]	Yield (**4**)[c)]/%	ee (**4**)/%	Confign. (**4**)
1	 **3a**	12	> 99 : 1	71	95[d)]	*S*[e)]
2	 **3b**	3	97 : 3	85	87[f)]	*S*[g)]
3	 **3c**	4	97 : 3	79	34[h)]	*R*[e)]

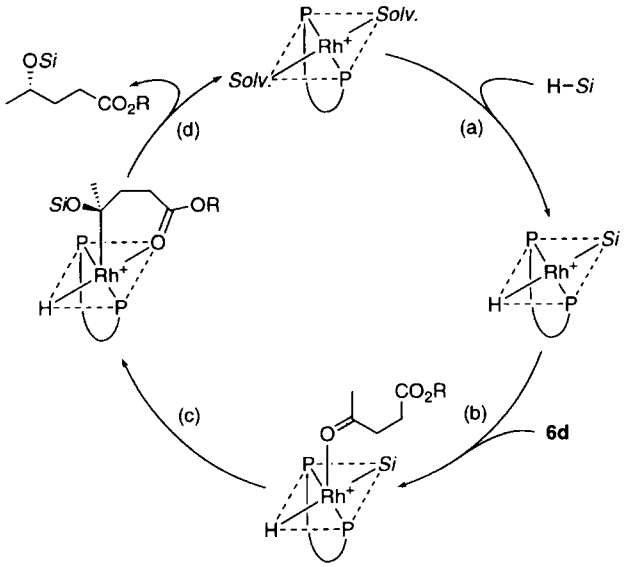
a) All reactions were carried out in THF at −40 °C. The molar ratio of **3** : Ph_2SiH_2 : [Rh(cod)$_2$]-BF_4 : (*R*,*R*)-(*S*,*S*)-BuTRAP was 100 : 150 : 1.0 : 1.1. b) Determined by GLC analysis of crude product. c) Isolated yield. d) Determined by GLC analysis with Chiraldex G-TA. e) Assigned by specific rotation. f) Determined by HPLC analysis of its *N*-(3,5-dinitrophenyl)carbamate derivative with SUMICHIRAL OA-4500. g) See text. h) Determined by HPLC analysis with CHIRALCEL OD-H.

Asymmetric Hydrosilylation of Keto Esters. In some asymmetric reductions of functional ketones, such as keto esters and hydroxy ketones, a chelate coordination of such a substrate to a metal atom may be essential for high enantioselectivity.[8,18] To investigate the chelate effect on the hydrosilylation catalyzed by alkylTRAP–rhodium complex, we have examined asymmetric hydrosilylation of keto esters **6** which may provide a secondary coordination site to the rhodium atom (Eq. 4).



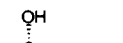
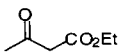
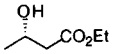
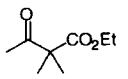
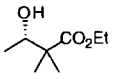
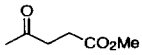
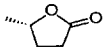
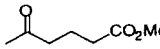
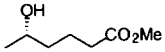
Results obtained with EtTRAP are summarized in Table 5. Ethyl pyruvate (**6a**) was found to be less reactive than simple ketones, giving (*S*)-**7a** with 80% ee at 0 °C (Entry 1). The low reactivity may be due to the weak binding of the ketone carbonyl group to a rhodium atom, which can be caused by the electron-withdrawing effect of the ethoxycarbonyl group. The reaction of ethyl acetoacetate (**6b**) proceeded at −30 °C, giving the corresponding secondary alcohol **7b** with only 32% ee (Entry 2). The very low enantioselectivity may suggest that the hydrosilylation was accompanied by transfer hydrogenation of the silyl enol ether of **6b**, which was formed by dehydrogenative coupling of its enol with the hydrosilane.[8] Actually, the reaction of β-keto ester **6c**, which has no α-acidic hydrogen atom, gave (*S*)-**7c** with 98% ee (Entry 3). High enantioselectivity was also obtained for the reaction of γ-keto ester **6d** (88% ee as lactone **7d**), while δ-keto ester **6e** gave the product **7e** in moderate selectivity (Entries 4 and 5). BuTRAP was less effective than EtTRAP except for **6a** (**6a**: 80% ee, **6b**: 16% ee, **6d**: 81% ee, **6e**: 60% ee). Based on the hydrosilylation with **1n**, these results suggest that the coordination of the methoxycarbonyl group of **6d** to the rhodium atom may play an important role in the enantioface-selection of the ketone.

One likely mechanism for the asymmetric hydrosilylation of **6d** is shown in Scheme 1. This involves: (a) oxidative addition of the hydrosilane to the TRAP–rhodium(I) species; (b) coordination of the ketone carbonyl group to the hydrido(silyl)rhodium(III) complex; (c) insertion of the car-



Scheme 1. A presumable mechanism for hydrosilylation of **6d**.

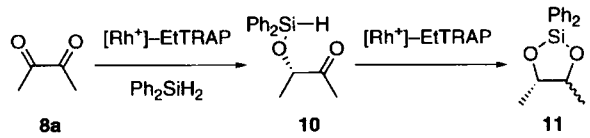
Table 5. Asymmetric Hydrosilylation of Keto Esters (**3**)[a]

Entry	Substrate **6**		Time/h	Product **7**		Yield[b]/%	ee/%	Config.[c]
1[d]		**6a**	4		**7a**	60	80[e]	*S*
2		**6b**	14		**7b**	43	32[e]	*S*
3[f]		**6c**	24		**7c**	80	98[g]	*S*
4		**6d**	31		**7d**	74	88[e]	*S*
5		**6e**	25		**7e**	74	69[h]	—[i]

a) The reactions were carried out in THF at −30 °C. The molar ratio of **6** : Ph_2SiH_2 : $[Rh(cod)_2]$ BF_4 : (*R,R*)-(*S,S*)-EtTRAP was 100 : 150 : 1.0 : 1.1 unless otherwise noted. b) Isolated yield. c) Assigned by specific rotation unless otherwise noted. d) At 0 °C. e) Determined by HPLC analysis with CHIRALCEL OB-H. f) The molar ratio of **6c** : Ph_2SiH_2 : $[Rh(cod)_2]BF_4$: EtTRAP was 200 : 300 : 1.0 : 1.1. g) Determined by HPLC analysis with CHIRALCEL AS. h) Determined by HPLC analysis of its *N*-(3,5-dinitrophenyl)carbamate derivative with SUMICHIRAL OA-4400. i) Not determined.

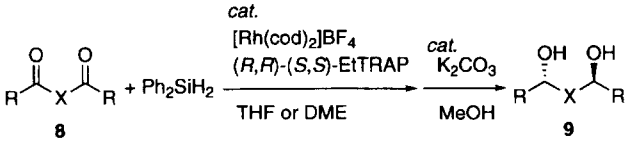
bon–oxygen double bond into the silicon–rhodium bond to form a diastereomeric (1-siloxyalkyl)rhodium intermediate, where the alkoxycarbonyl group coordinates to the rhodium atom; and then (d) reductive elimination to form the optically active silyl ether and the rhodium(I) species. Since the enantioselectivities for α-keto ester **6a** and δ-keto ester **6e** are comparable to those of simple methyl ketones, such a secondary interaction seems to be less important for these substrates.

Asymmetric Hydrosilylation of Symmetrical Diketones. The asymmetric hydrosilylation of diketones catalyzed by the EtTRAP–rhodium complex was applicable to an enantioselective synthesis of some symmetrical diols **9** (Eq. 5). Results are shown in Table 6. The asymmetric hydrosilylation of 1,2-diketone **8a** with 2.5 molar amounts of diphenylsilane afforded the optically active diol (2*S*,3*S*)-**9a** not only in high enantioselectivity but also in high diastereoselectivity (ratio of *dl* to *meso* isomer) (Entry 1). Both of the carbonyl groups were reduced completely with 1.5 molar amounts of diphenylsilane, but the resulting diol had only low enantiomeric excess and diastereomeric excess (Entry 2). The findings suggest that intramolecular hydrosilylation of the siloxy ketone **10** formed initially competes with intermolecular reaction (Scheme 2). However, the former, which might lead to the decrease in the stereoselectivity, may have been suppressed by the use of over 2.5 molar amounts of hydrosilane (Entry 3). Hydrosilylation of acetylacetone (**8b**), which has α-acidic hydrogens, gave a mixture of (2*R*,4*R*)-



Scheme 2. Intramolecular hydrosilylation pathway.

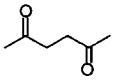
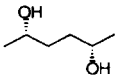
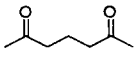
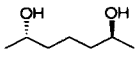
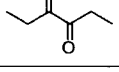
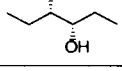
9b of 35% ee and *meso*-**9b** (42 : 58) (Entry 4).[19] However, high enantio- and diastereoselectivities were attained in the reduction of 1,3-diketone **8c** which lacks an active hydrogen atom (Entry 5). The asymmetric hydrosilylations of 1,4-diketone **8d** and 1,5-diketone **8e** also proceeded with high enantioselectivities, while their diastereoselectivities were moderate (Entries 6 and 7). 3,4-Hexanedione (**8f**) afforded the corresponding diol in moderate stereoselectivity (Entry 8).



(5)

BuTRAP provided lower stereoselectivity than EtTRAP in the asymmetric hydrosilylation of diketones, giving **9a**, **9d**, and **9e** with 94% ee (*dl*/*meso* = 81/19), 90% ee (*dl*/*meso* = 68/32), and 76% ee (*dl*/*meso* = 62/38), respectively. To our surprise, FurTRAP–rhodium, which presented a low stereoselectivity in the hydrosilylation of **1a** (Table 1, Entry 7), was effective for the hydrosilylation of **8a** to give **9a** of 91%

Table 6. Asymmetric Hydrosilylation of Symmetrical Diketones (**8**)[a]

Entry	Substrate **8**	Solvent	Temp/°C	Time/h	Product **9**	*dl* : *meso*[b]	Yield[c]/%	ee/%	Config.[d]
1	 **8a**	DME	0	30	 **9a**	90 : 10	69	95[e]	(2*S*,3*S*)
2[f]	**8a**	DME	0	43	**9a**	72 : 28	84	83[e]	(2*S*,3*S*)
3[g]	**8a**	DME	0	26	**9a**	90 : 10	94	96[e]	(2*S*,3*S*)
4[h]	 **8b**	THF	−30	75	 **9b**	42 : 58	45	35[i]	(2*R*,4*R*)
5	 **8c**	THF	−30	58	 **9c**	96 : 4	58	99[e]	(2*S*,4*S*)[j]
6	 **8d**	DME	−30	30	 **9d**	75 : 25	97	97[k]	(2*S*,5*S*)
7	 **8e**	THF	−30	94	 **9e**	69 : 31	75	89[k]	(2*S*,6*S*)[l]
8	 **8f**	DME	0	55	 **9f**	77 : 23	63	70[e]	(3*S*,4*S*)[m]

a) The molar ratio of **8** : Ph_2SiH_2 : [Rh(cod)$_2$] BF_4 : (*R*,*R*)-(*S*,*S*)-EtTRAP was 100 : 250 : 1.0 : 1.1 unless otherwise noted. b) Determined by GLC analysis of crude product. c) Isolated yield of a mixture of both diastereomers. d) Assigned by specific rotation unless otherwise noted. e) Determined by HPLC analysis of their bis[*N*-(3,5-dinitrophenyl)carbamate] derivatives with SUMICHIRAL OA-4000. f) 1.5 molar amounts of Ph_2SiH_2 were used. g) 4.0 molar amounts of Ph_2SiH_2 were used. h) (*R*,*R*)-(*S*,*S*)-BuTRAP was used. i) Determined by GLC analysis of its bis(trifluoroacetate) derivative with Chiraldex G-TA. j) See text. k) Determined by HPLC analysis of their bis[*N*-(3,5-dinitrophenyl)carbamate] derivatives with SUMICHIRAL OA-4100. l) Estimated by similarity to **9d** of the order of retention time in the chiral HPLC analysis. m) Estimated by similarity to **9a** of the order of retention time in the chiral HPLC analysis.

ee with 86 : 14 of diastereoselectivity. In contrast, PhTRAP showed only a very low stereoselectivity (29% ee, *dl*/*meso* = 49/51).

The enantioselective reduction of diketones involves successive stereoselective reductions of two carbonyl groups. Of mechanistic interest is whether the chirality of the catalyst and/or substrate (initially produced siloxy ketone) controls stereo-selection at the second hydrosilylation in the present asymmetric hydrosilylation of **8**. Both the diastereo- and the enantioselectivities can be calculated as shown in Scheme 3, if the chirality of the initially produced siloxy ketone has no influence on the stereo-selection at the second hydrosilylation. The ratio of *dl* and *meso* isomers and the enantiomeric excess of *dl*-diol are represented by Eqs. 6 and 7, respectively. In the calculation, the enantioselectivities X and Y for the first and second hydrosilylations may be approximated by those of the hydrosilylations of the corresponding keto esters and simple ketones, respectively. The approximation is based on the assumption that, in the first hydrosilylation of diketone, another carbonyl group may coordinate to a rhodium atom like the alkoxycarbonyl group in the hydrosilylation of keto esters, while the siloxy group initially formed has little ability to coordinate onto rhodium in the second hydrosilylation. The stereoselectivities with **8a**, and **8c**—**e** thus calculated are in good agreement with the observed diastereo- and enantioselectivities (Table 7). Consequently, we conclude that the stereoselectivity at the second hydrosilylation is not controlled by the chirality of the siloxy ketone but by that of the catalyst.

$$dl/meso = \frac{1+XY}{1-XY} \quad (6)$$

$$\text{ee} = \frac{X+Y}{1+XY} \quad (7)$$

Assignment of Absolute Configuration. Most of the absolute configurations of the alcoholic products obtained here were assigned by the signs of their specific rotations.

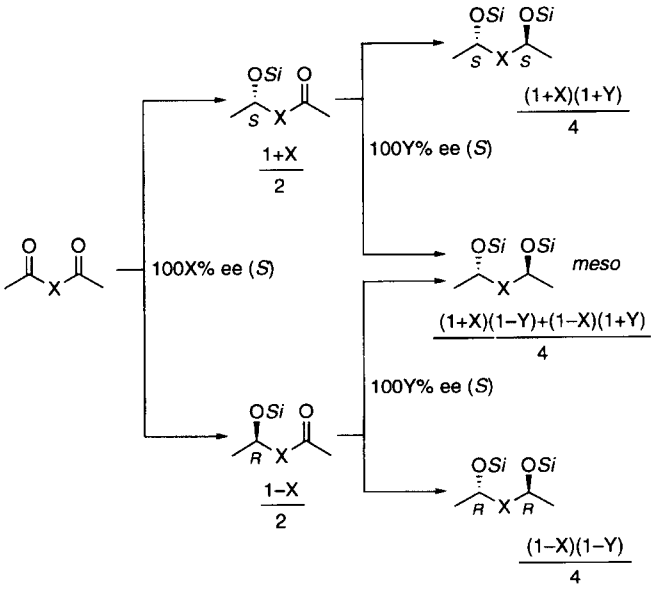
Table 7. Calculated Stereoselectivities in Asymmetric Hydrosilylation of **8**[a]

Entry	Substrate **8**	X[b]	Y[c]	*dl* : *meso*	ee/%
1	**8a**	0.80	0.81	82 : 18	97.7
2	**8c**	0.98	0.96	97 : 3	> 99.9
3	**8d**	0.88	0.65	79 : 21	97.3
4	**8e**	0.69	0.65	72 : 28	92.5

a) The stereoselectivities were calculated according to Eqs. 6 and 7. b) Enantioselectivities X for the first hydrosilylation were estimated with the selectivity of the corresponding reaction of **6** (**8a**: Entry 1, **8c**: Entry 3, **8d**: Entry 4, **8e**: Entry 5 in Table 5). c) Enantioselectivities Y for the second hydrosilylation were estimated with the selectivity of the corresponding reaction of **1** (**8a**: Entry 3, **8c**: Entry 1, **8d**, **e**: Entry 6 in Table 3).

The configurations of **2o** and **4b** were determined by ^{1}H NMR studies of their (*R*)-2-methoxy(phenyl)acetates according to the method established by Trost.[20] Representative results of the ^{1}H NMR analyses are shown in Fig. 1. In both cases, proton resonances belonging to the higher priority group of the major diastereomer appeared in lower magnetic field than those of the minor isomer, indicating the absolute configurations of **2o** and **4b** to be *S*.

The absolute configuration of **9c** was determined by comparison in chiral HPLC analysis with data from authentic (2*S*,3*S*)-**9c**. The authentic sample was synthesized from (*S*)-**7c** obtained from the present asymmetric hydrosilylation by the following reactions (Scheme 4): (*S*)-**7c** was treated with sodium hydride and benzyl bromide in the presence of tetrabutylammonium iodide catalyst to give benzyl ether **12**. Reduction of the ethoxycarbonyl group with lithium tetrahydridoaluminate, followed by Swern oxidation of the resulting alcohol, gave aldehyde **13**. Addition of methylmagnesium bromide to **13** gave a mixture of (2*S*,3*S*)- and *meso*-**14** (1 : 1). Deprotection of the benzyl group with hydrogenation catalyzed by palladium on carbon gave a mixture of (2*S*,3*S*)-



Scheme 3. Successive reductions in asymmetric hydrosilylation of diketones.

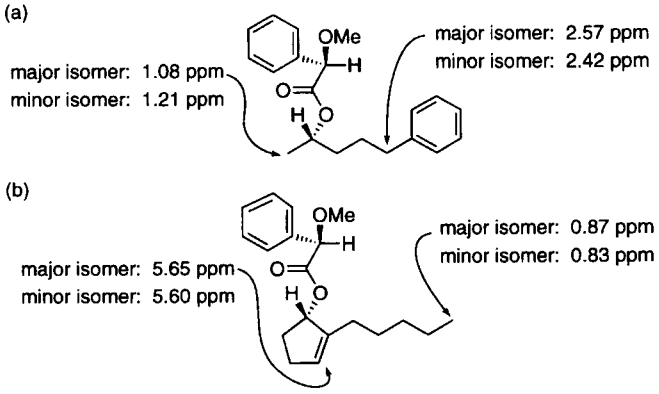
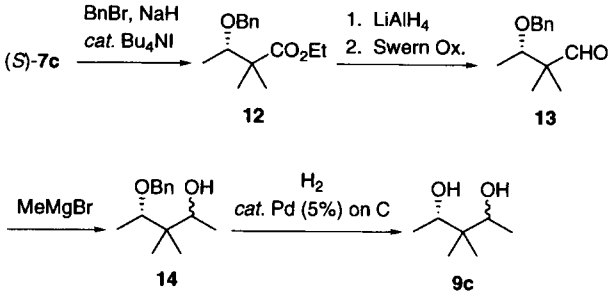


Fig. 1. Representative results of the ^{1}H NMR analyses of (*R*)-2-methoxy(phenyl)acetates of (a) **2o** and (b) **4b**.



Scheme 4. Conversion of (*S*)-**7c** into **9c**.

9c and *meso*-**9c**. The retention time of the bis[*N*-(3,5-dinitrophenyl)carbamate] derivative of the authentic (2*S*,3*S*)-**9c** in chiral HPLC analysis with SUMICHIRAL OA-4000 revealed the absolute configuration of **9c** obtained by the asymmetric hydrosilylation of **8c** to be (2*S*,3*S*).

Conclusion

Trans-chelating peralkylbisphosphines, (*R*,*R*)-(*S*,*S*)-Et-, Pr-, and BuTRAP were the first effective chiral phosphine ligands for asymmetric hydrosilylation of ketones catalyzed by rhodium complex. The hydrosilylation was applicable to asymmetric reductions of various types of ketonic substrates, providing the corresponding chiral secondary alcohols with high enantiomeric excesses. The TRAP ligands bearing flexible *P*-substituents were superior to those with rigid and bulky substituents such as phenyl group. The flexibility would be crucial for a high degree of enantioface-selection of carbonyl compounds.

Experimental

General. Preparative thin-layer chromatographies (PTLC) were performed with silica gel 60 PF_{254} (Merck). Medium-pressure liquid chromatographies (MPLC) were performed with a C.I.G. pre-packed column CPS-223L-1 (Kusano). Flash column chromatographies were performed with silica gel 60 (230—400 mesh, Merck).

Materials. Tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), and toluene were distilled from sodium–benzophenone ketyl under nitrogen. Dichloromethane was distilled from CaH_2. $[Rh(cod)_2]BF_4$,[21] 5-phenyl-2-pentanone (**1o**),[22] 2,2-dimethylcyclohexanone (**1q**),[23] ethyl 2,2-dimethyl-3-oxobutanoate (**6c**),[24] methyl 5-oxohexanoate (**6e**),[25] 3,3-dimethyl-2,4-pentanedione (**8c**),[26] and 2,6-heptanedione (**8e**)[27] were prepared according to the literature procedures. Diphenylsilane was purchased (Kanto) and purified by distillation before use.

General Procedure of Asymmetric Hydrosilylation of Ketones. A mixture of $[Rh(cod)_2]BF_4$ (4.1 mg, 10 μmol) and (*R*,*R*)-(*S*,*S*)-TRAP (11 μmol) in THF or DME (1 ml) was stirred at room temperature for 10 min in argon atmosphere. A liquid ketone (1.0 mmol) was added to the solution of the catalyst precursor at −40 °C. In the case of a solid substrate, the solution of the catalyst precursor was added to the ketone (1.0 mmol) at −40 °C. Diphenylsilane (276 mg, 1.5 mmol) was added to the solution; then the mixture was stirred at −40 °C. After completion of the reaction, a solution of K_2CO_3 (1 mg) in MeOH (1 ml) was added to the mixture. After stirring over 4 h at room temperature, the mixture was evaporated, and the residue was purified by PTLC (silica gel, hexane/EtOAc) unless otherwise noted.

1-Phenylethanol (2a). $[\alpha]_D^{21}$ −47.0 (*c* 1.48, CH_2Cl_2) for Entry 3 in Table 1, lit,[28] $[\alpha]_D^{21}$ −52.5 (*c* 2.27, CH_2Cl_2) for (*S*)-**2a**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.48 (d, *J* = 6.4 Hz, 3H), 1.98 (br, 1H) 4.87 (q, *J* = 6.4 Hz, 1H), 7.19—7.41 (m, 5H).

1-(4-Methylphenyl)ethanol (2b). $[\alpha]_D^{25}$ −50.7 (*c* 1.01, $CHCl_3$), lit,[29] $[\alpha]_D^{25}$ +51.6 (*c* 1.0, $CHCl_3$) for 93.8% ee of (*R*)-**2b**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.47 (d, *J* = 6.5 Hz, 3H), 1.88 (br, 1H), 2.34 (s, 3H), 4.86 (q, *J* = 6.5 Hz, 1H), 7.09—7.21 (m, 2H), 7.21—7.31 (m, 2H).

1-(4-Methoxyphenyl)ethanol (2c). $[\alpha]_D^{20}$ −35.8 (*c* 1.00, toluene), lit,[30] $[\alpha]_D$ +45.2 (neat, 1 dm) for (*R*)-**2c**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.44 (d, *J* = 6.4 Hz, 3H), 2.23 (br, 1H), 3.78 (s, 3H), 4.81 (q, *J* = 6.4 Hz, 1H), 6.80—6.89 (m, 2H), 7.21—7.31 (m, 2H).

1-(3-Methoxyphenyl)ethanol (2d). $[\alpha]_D^{20}$ −61.0 (*c* 1.25, MeOH), lit,[31] $[\alpha]_D$ +35 (*c* 1, MeOH) for 97% ee of (*R*)-**2d**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.46 (d, *J* = 6.5 Hz, 3H), 2.17 (br, 1H), 3.79 (s, 3H), 4.84 (q, *J* = 6.5 Hz, 1H), 6.75—6.83 (m, 1H), 6.89—6.95 (m, 2H), 7.20—7.29 (m, 1H).

1-(2-Methoxyphenyl)ethanol (2e). $[\alpha]_D^{20}$ −53.3 (*c* 1.18, toluene), lit,[32] $[\alpha]_D$ −59 (*c* 1.18, toluene) for (*S*)-**2e**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.49 (d, *J* = 6.5 Hz, 3H), 2.75 (br, 1H), 3.84 (s, 3H), 5.08 (q, *J* = 6.5 Hz, 1H), 6.83—7.00 (m, 2H), 7.20—7.37 (m, 2H).

1-(4-Chlorophenyl)ethanol (2f). $[\alpha]_D^{21}$ −40.8 (*c* 1.96, Et_2O), lit,[33] $[\alpha]_D^{21}$ +49.9 (*c* 2, Et_2O) for (*R*)-**2f**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.44 (d, *J* = 6.5 Hz, 3H), 2.24 (br, 1H), 4.83 (q, *J* = 6.5 Hz, 1H), 7.19—7.35 (m, 4H).

1-Indanol (2g). $[\alpha]_D^{22}$ +25.1 (*c* 3.02, $CHCl_3$), lit,[36] $[\alpha]_D^{22}$ +34 (*c* 1.895, $CHCl_3$) for (*S*)-**2i**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS)

δ = 1.79 (br, 1H), 1.94 (dddd, J = 5.3, 6.6, 8.5, and 13.2 Hz, 1H), 2.49 (dddd, J = 4.9, 6.8, 8.1, and 13.2 Hz, 1H), 2.82 (ddd, J = 6.6, 8.1, and 16.0 Hz, 1H), 3.06 (ddd, J = 4.9, 8.5, and 16.0 Hz, 1H), 5.24 (br t, 1H), 7.14—7.31 (m, 3H), 7.31—7.48 (m, 1H).

1-Tetralol (2h). $[\alpha]_D^{17}$ +27.9 (c 2.46, $CHCl_3$), lit,[37] $[\alpha]_D^{17}$ +32.65 (c 2.5, $CHCl_3$) for (*S*)-**2h**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.63—2.09 (m, 5H), 2.58—2.91 (m, 2H), 4.75 (dd, J = 4.0, 4.8 Hz, 1H), 7.01—7.28 (m, 3H), 7.33—7.48 (m, 1H).

1-Ferrocenylethanol (2i). $[\alpha]_D^{25}$ +31.5 (c 1.01, C_6H_6), lit,[35] $[\alpha]_D^{25}$ −30.5 (c 1.1, C_6H_6) for (*R*)-**2h**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.44 (d, J = 6.3 Hz, 3H), 1.86 (br, 1H), 4.13—4.27 (m, 4H), 4.20 (s, 5H), 4.46—4.62 (m, 1H).

1-(1-Naphthyl)ethanol (2j). $[\alpha]_D^{25}$ −69.3 (c 0.99, Et_2O), lit,[34] $[\alpha]_D^{25}$ +82.1 (c 1.0, Et_2O) for (*R*)-**2g**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.67 (d, J = 6.5 Hz, 3H), 1.94 (br, 1H), 5.68 (q, J = 6.5 Hz, 1H), 7.40—7.60 (m, 3H), 7.62—7.93 (m, 3H), 8.05—8.18 (m, 1H).

1-Phenyl-1-propanol (2k). $[\alpha]_D^{20}$ −30.7 (c 5.08, $CHCl_3$), lit,[38] $[\alpha]_D^{20}$ −45.45 (c 5.15, $CHCl_3$) for (*S*)-**2k**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.91 (t, J = 7.4 Hz, 3H), 1.61—1.91 (m, 2H), 1.95 (br, 1H), 4.58 (t, J = 6.6 Hz, ^{1}H), 7.20—7.42 (m, 5H).

1-(1-Adamantyl)ethanol (2l). Isolated by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O): ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.10 (d, J = 6.5 Hz, 3H), 1.28 (d, J = 5.1 Hz, 1H), 1.42—1.80 (m, 12H), 1.93—2.05 (m, 3H), 3.29 (dq, J = 5.1 and 6.5 Hz, 1H).

1-(1-Adamantyl)ethyl Acetate. Acetic anhydride (21 µl, 0.22 mmol), pyridine (24 µl, 0.31 mmol), and 4-(dimethylamino)pyridine (6 mg, 0.05 mmol) were added to a solution of 1-(1-adamantyl)-ethanol (36 mg, 0.20 mmol) prepared in Entry 2 of Table 3. After stirring for 30 min at room temperature, the mixture was diluted with 1 M HCl aq (1 M = 1 mol dm^{-3}) and then extracted with diethyl ether. The organic layer was washed with 1 M HCl aq, washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O) to give 35.3 mg (79%) of 1-(1-adamantyl)ethyl acetate: $[\alpha]_D^{25}$ −18.2 (c 0.56, CCl_4), lit,[16b] $[\alpha]_D^{25}$ +18.1 (c 3.77, CCl_4) for (*R*)-1-(1-adamantyl)ethyl acetate; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.10 (d, J = 6.5 Hz, 3H), 1.40—1.81 (m, 12H), 1.91—2.05 (m, 3H), 2.05 (s, 3H), 4.53 (q, J = 6.5 Hz, 1H).

1-Cyclohexylethanol (2m). Isolated by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O): $[\alpha]_D^{25}$ +5.84 (c 3.10, Et_2O) for Entry 4 in Table 3, lit,[39] $[\alpha]_D$ +8.43 (c 9.14, Et_2O) for (*S*)-**2m**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.81—1.37 (m, 6H), 1.15 (d, J = 6.3 Hz, 3H), 1.53—1.92 (m, 6H), 3.54 (quintet, J = 6.3 Hz, 1H).

2-Octanol (2n). Isolated by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O): $[\alpha]_D^{25}$ +5.69 (c 4.89, EtOH) for Entry 8 in Table 3, lit,[40] $[\alpha]_D$ +8.43 (c 9.14, EtOH) for (*S*)-**2n**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.80—0.98 (m, 3H), 1.19 (d, J = 6.1 Hz, 3H), 1.14—1.53 (m, 11H), 3.80 (sextet, J = 6.1 Hz, 1H).

5-Phenyl-2-pentanol (2o). $[\alpha]_D^{25}$ +4.02 (c 1.17, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.17 (d, J = 6.2 Hz, 3H), 1.33—1.88 (m, 5H), 2.63 (t, J = 7.5 Hz, 2H), 3.80 (sextet, J = 6.2 Hz, 1H), 7.10—7.41 (m, 5H).

4-Phenyl-2-butanol (2p). $[\alpha]_D^{25}$ +12.3 (c 6.05, $CHCl_3$), lit,[41] $[\alpha]_D^{18.5}$ +13.74 (neat) for (*S*)-**2p**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.22 (d, J = 6.2 Hz, 3H), 1.57 (br, 1H), 1.65—1.88 (m, 2H), 2.57—2.85 (m, 2H), 3.81 (sextet, J = 6.2 Hz, 1H), 7.10—7.41 (m, 5H).

1-Phenyl-2-propanol (2q). $[\alpha]_D^{20}$ +13.7 (c 2.33, C_6H_6), lit,[41] $[\alpha]_D^{20}$ +41.8 (c 5.26, C_6H_6) for (*S*)-**2q**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.25 (d, J = 6.1 Hz, 3H), 1.68 (br, 1H), 2.69 (dd, J = 7.8 and 13.4 Hz, 1H), 2.81 (dd, J = 5.0 and 13.4 Hz, 1H), 3.94—4.12 (m, 1H), 7.11—7.39 (m, 5H).

2,2-Dimethylcyclohexanol (2r). Isolated by bulb-to-bulb distillation: Bp 100 °C (bath temp)/17 mmHg (1 mmHg = 133.322 Pa); $[\alpha]_D^{20}$ +3.62 (c 1.57, EtOH), $[\alpha]_D^{20}$ +0.72 (c 3.02, CH_2Cl_2), lit,[42] $[\alpha]_D^{20}$ −3.43 (neat) for 64% ee of (*R*)-**2r**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.88 (s, 3H), 0.97 (s, 3H), 1.03—1.56 (m, 6H), 1.59—1.80 (m, 3H), 3.30 (dd, J = 5.9 and 9.6 Hz, 1H).

General Procedure of Asymmetric Hydrosilylation of α,β-Unsaturated Ketones (3). A mixture of $[Rh(cod)_2]BF_4$ (4.1 mg, 10 µmol) and (*R,R*)-(*S,S*)-BuTRAP (7.9 mg, 11 µmol) in THF (1 ml) was stirred at room temperature for 10 min in argon atmosphere. A ketone (1.0 mmol) and diphenylsilane (276 mg, 1.5 mmol) were added to the solution of the catalyst precursor at −40 °C, then the mixture was stirred at −40 °C. After completion of the reaction, the mixture was passed through a short column of Florisil (Et_2O) and evaporated. A solution of K_2CO_3 (1 mg) in MeOH (1 ml) was added to the residue. After stirring over 4 h at room temperature, the mixture was evaporated, and the residue was purified by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O).

1-(1-Cyclohexenyl)ethanol (4a). $[\alpha]_D^{20}$ −10.0 (c 4.24, $CHCl_3$), lit,[43] $[\alpha]_D^{20}$ −9.8 (c 4.25, $CHCl_3$) for 78% ee of (*S*)-**4a**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.26 (d, J = 6.5 Hz, 3H), 1.42—1.79 (m, 5H), 1.84—2.19 (m, 4H), 4.17 (q, J = 6.5 Hz, 1H), 5.62—5.73 (m, 1H).

2-Pentyl-2-cyclopentenol (4b). $[\alpha]_D^{20}$ −25.3 (c 1.05, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.89 (t, J = 6.6 Hz, 3H), 1.18−1.97 (m, 8H), 1.97—2.54 (m, 5H), 4.53—4.72 (m, 1H), 5.46—5.59 (m, 1H).

(*E*)-4-Phenyl-3-buten-2-ol (4c). $[\alpha]_D^{20}$ +11.5 (c 5.07, $CHCl_3$), lit,[44] $[\alpha]_D^{20}$ +24.7 (c 5.000, $CHCl_3$) for (*R*)-**4c**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.36 (d, J = 6.3 Hz, 3H), 1.81 (br, 1H), 4.47 (double quintet, J = 1.1 and 6.3 Hz, 1H), 6.25 (dd, J = 6.3 and 16.0 Hz, 1H), 6.56 (dd, J = 1.1 and 16.0 Hz, 1H), 7.13—7.45 (m, 5H).

General Procedure of Asymmetric Hydrosilylation of Keto Esters (6). A mixture of $[Rh(cod)_2]BF_4$ (4.1 mg, 10 µmol) and (*R,R*)-(*S,S*)-EtTRAP (6.6 mg, 11 µmol) in THF (1 ml) was stirred at room temperature for 10 min in argon atmosphere. A keto ester (1.0 mmol) and diphenylsilane (276 mg, 1.5 mmol) were added to the solution of the catalyst precursor at −30 °C; then the mixture was stirred. After completion of the reaction, MeOH (1 ml) and 1 M HCl aq (4 ml) were added to the mixture. After stirring over 1 h at 0 °C, the water layer was saturated with NaCl, and extracted five times with Et_2O. The organic layer was washed once with brine, dried over $MgSO_4$, and evaporated. The residue was purified by bulb-to-bulb distillation unless otherwise noted.

Ethyl Lactate (7a). Bp 80 °C (bath temp)/105 mmHg; $[\alpha]_D^{20}$ −0.39 (c 1.29, $CHCl_3$), lit,[45] $[\alpha]_D^{14}$ −10.0 (neat) for (*S*)-**7a**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 1.30 (t, J = 7.2 Hz, 3H), 1.42 (d, J = 6.9 Hz, 3H), 2.90 (br, 1H), 4.25 (q, J = 7.2 Hz, 2H), 4.27 (q, J = 6.9 Hz, 1H).

Ethyl 3-Hydroxybutanoate (7b). Bp 100 °C (bath temp)/100 mmHg; $[\alpha]_D^{20}$ +6.98 (c 1.26, $CHCl_3$), lit,[46] $[\alpha]_D^{20}$ +41.3 (c 1, $CHCl_3$) for (*S*)-**7b**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.23 (d, J = 6.3 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H), 2.32—2.59 (m, 2H), 3.05 (br, 1H), 4.11—4.30 (m, 3H).

Ethyl 3-Hydroxy-2,2-dimethylbutanoate (7c). Bp 100 °C (bath temp)/15 mmHg; $[\alpha]_D^{22}$ +6.98 (c 1.26, $CHCl_3$), lit,[24] $[\alpha]_D^{22}$ +3.43 (neat) for 83.7% ee of (*S*)-**7c**; ^{1}H NMR (200 MHz, $CDCl_3$,

TMS) δ = 1.15 (d, J = 6.4 Hz, 3H), 1.17 (s, 3H), 1.18 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H), 2.71 (br, 1H), 3.86 (q, J = 6.4 Hz, 1H), 4.17 (q, J = 7.1 Hz, 2H).

γ-Valerolactone (7d). Isolated by MPLC (pentane/Et_2O) after passing through a short column of silica gel (Et_2O); $[\alpha]_D^{20}$ −30.6 (c 0.82, CH_2Cl_2), lit,[47] $[\alpha]_D^{23}$ +30.1 (c 0.85, CH_2Cl_2) for (*R*)-**7d**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.42 (d, J = 6.2 Hz, 3H), 1.73—1.93 (m, 1H), 2.28—2.62 (m, 3H), 4.65 (double quintet, J = 6.2 and 7.9 Hz, 1H).

Methyl 5-Hydroxyhexanoate (7e). Isolated by MPLC (hexane/EtOAc) after passing through a short column of silica gel (Et_2O); $[\alpha]_D^{20}$ −12.3 (c 1.00, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.20 (d, J = 6.2 Hz, 3H), 1.37—1.92 (m, 4H), 1.78 (br, 1H), 2.35 (t, J = 7.3 Hz, 2H), 3.68 (s, 3H), 3.80 (sextet, J = 6.2 Hz, 1H).

General Procedure of Asymmetric Hydrosilylation of Diketones (8). A mixture of $[Rh(cod)_2]BF_4$ (4.1 mg, 10 μmol) and (*R*,*R*)-(*S*,*S*)-EtTRAP (6.6 mg, 11 μmol) in THF or DME (1 ml) was stirred at room temperature for 10 min in argon atmosphere. A diketone (1.0 mmol) and diphenylsilane (461 mg, 2.5 mmol) were added to the solution of the catalyst precursor at −30 °C; then the mixture was stirred. After completion of the reaction, MeOH (2 ml) and K_2CO_3 (ca. 50 mg) were added to the mixture. After stirring over 10 h at room temperature, the mixture was evaporated. The residue was purified by MPLC (hexane/EtOAc) after passing through a short column of silica gel (EtOAc).

2,3-Butanediol (9a). $[\alpha]_D^{20}$ +12.3 (c 1.49, $CHCl_3$) for mixture with *meso*-diol, lit,[48] $[\alpha]_D^{20}$ +12.85 (neat) for (2*S*,3*S*)-**9a**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.17 (d, J = 5.9 Hz, 6H), 2.79 (br, 2H), 3.44—3.60 (m, 2H).

2,4-Pentanediol (9b). $[\alpha]_D^{20}$ −7.00 (c 1.20, EtOH) for mixture with *meso*-diol, lit,[49] $[\alpha]_D^{20}$ −21.4 (c 10.5, EtOH) for (2*R*,3*R*)-**9b**.

3,3-Dimethyl-2,4-pentanediol (9c). $[\alpha]_D^{20}$ +3.26 (c 1.07, $CHCl_3$) for mixture with *meso*-diol; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.87 (s, 6H), 1.17 (d, J = 6.4 Hz, 6H), 3.47 (br, 2H), 3.82 (q, J = 6.4 Hz, 2H).

2,5-Hexanediol (9d). $[\alpha]_D^{20}$ +23.0 (c 1.88, $CHCl_3$) for mixture with *meso*-diol, lit,[50] $[\alpha]_D^{20}$ +39.4 (c 1.88, $CHCl_3$) for (2*S*,3*S*)-**9d**; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.21 (d, J = 6.2 Hz, 6H), 1.42—1.73 (m, 4H), 2.56 (br, 2H), 3.73—3.94 (br, 2H).

2,6-Heptanediol (9e). $[\alpha]_D^{20}$ +17.9 (c 1.01, $CHCl_3$) for mixture with *meso*-diol; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.19 (d, J = 6.2 Hz, 6H), 1.31—1.60 (m, 6H), 2.71 (br, 2H), 3.80 (q, J = 6.1 Hz, 2H).

3,4-Hexanediol (9f). ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 0.98 (t, J = 7.4 Hz, 6H), 1.31—1.70 (m, 4H), 2.69 (br, 2H), 3.29—3.41 (m, 2H).

General Procedure of Preparation of (*R*)-2-Methoxy(phenyl)-acetate Derivative. To a solution of (*R*)-2-methoxy(phenyl)acetic acid (10 mg, 60 μmol) in CH_2Cl_2 (0.2 ml) were added oxalyl chloride (8.7 μl, 100 μmol) and a catalytic amount of DMF (1 drop) at 0 °C. After stirring for 30 min at room temperature, the solvent and excess of oxalyl chloride were removed in vacuo. To the residue were added a solution of **2** (50 μmol) in CH_2Cl_2 (0.4 ml) and pyridine (20 μl, 250 μmol) at room temperature. After stirring for 1 h, the mixture was diluted with 8.5% H_3PO_4 aq, and extracted once with Et_2O. The organic layer was washed once with 8.5% H_3PO_4 aq, then once with brine; it was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc), giving the 2-methoxy(phenyl)acetate as a mixture of the two diastereomers.

Ethyl (*S*)-3-Benzyloxy-2,2-dimethylbutanoate (12). Sodium hydride (15 mg, 0.61 mmol) was added to a solution of 98% ee of (*S*)-**7c** (80 mg, 0.5 mmol) in THF at 0 °C. After stirring for 10 min, benzyl bromide (120 μl, 1.0 mmol) and tetrabutylammonium iodide (1.7 mg, 5 μmol) were added to the solution at room temperature. After stirring for 5 h, the mixture was diluted with saturated NH_4Cl aq, extracted three times with Et_2O, washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified with flash column chromatography of silica gel (hexane/EtOAc), giving 42 mg (33%) of **12**: ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ = 1.12 (s, 3H), 1.13 (d, J = 6.3 Hz, 3H), 1.210 (t, J = 7.2 Hz, 3H), 1.213 (s, 3H), 3.82 (q, J = 6.3 Hz, 1H), 4.10 (q, J = 7.2 Hz, 1H), 4.11 (q, J = 7.2 Hz, 1H), 4.41 (d, J = 11.8 Hz, 1H), 4.61 (d, J = 11.8 Hz, 1H), 7.05—7.45 (m, 5H).

(2*S*,4*S*)-4-Benzyloxy-3,3-dimethyl-2-pentanol (14). To a solution of **12** (31 mg, 0.12 mmol) in Et_2O (0.6 ml) was added lithium tetrahydridoaluminate (6.0 mg, 0.16 mmol) at −78 °C. The mixture was stirred at 0 °C for 1.5 h, diluted with saturated NH_4Cl aq, filtered, and extracted three times with Et_2O. The organic layer was washed with saturated NH_4Cl aq, dried over $MgSO_4$, and evaporated. A solution of dimethyl sulfoxide (19 μl, 0.27 mmol) in CH_2Cl_2 (0.06 ml) and a solution of the residue prepared above in CH_2Cl_2 (0.1 ml) were added to a solution of oxalyl chloride (12 μl, 0.14 mmol) in CH_2Cl_2 (0.3 ml) at −60 °C. After stirring for 15 min, triethylamine (82 μl, 0.59 mmol) was added to the mixture. After stirring for an additional 15 min at room temperature, the mixture was diluted with water and then extracted twice with CH_2Cl_2. The organic layer was washed with brine, dried over $MgSO_4$, and evaporated. To a solution of the residue (crude **13**) in Et_2O (0.5 ml) was added 2.19 M methylmagnesium bromide solution in Et_2O (0.1 ml, 0.22 mmol) at −78 °C. After stirring at 0 °C for 1.5 h, saturated NH_4Cl aq was added to the mixture. The mixture was extracted twice with Et_2O, washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified with PTLC (silica gel, hexane/EtOAc), giving 14.6 mg (55%) of a mixture of (2*S*,4*S*)- and *meso*-**14**.

(2*S*,4*S*)-3,3-Dimethyl-2,4-pentanediol ((2*S*,4*S*)-9c). A solution of **14** (14.6 mg, 66 μmol) in MeOH (1.0 ml) was added to a mixture of 5% palladium on carbon (3.7 mg) and $[Pd(\pi\text{-allyl})Cl]_2$ (0.4 mg, 1 μmol). The suspension was stirred at 70 °C under 100 kg cm^{-2} of hydrogen pressure for 48 h. The mixture was filtered to remove catalyst, and then evaporated. The residue was purified by column chromatography of silica gel (EtOAc), giving 0.8 mg (9%) of a mixture of (2*S*,4*S*)- and *meso*-**9c**.

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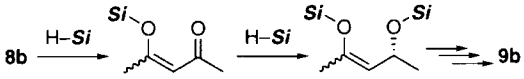

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