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Insight into the Rh-catalyzed cyclization of dissymmetrically racemic (±)-3,4-disubstituted 4-pentenal: regio-, diastereo-, enantioselectivity, and kinetic resolution

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Abstract—Rh-Catalyzed cyclization was applied for the kinetic resolution of dissymmetrical (±)-3-(1-methylvinyl)-4-phenylpent-4-enal. The cyclization by a chiral neutral Rh[(*S*)-BINAP]Cl afforded a mixture of 3,4-*cis*-4-methylcyclopentanone (>95% ee, 19% yield), 3,4-*trans*-4-methylcyclopentanone, and 3,4-*cis*-4-phenylcyclopentanone (>95% ee, 21% yield). The cyclization by a cationic Rh[(*R*)-BINAP]-ClO_4 afforded a mixture of 3,4-*trans*-4-methylcyclopentanone (>95% ee, 36% yield), 3,4-*cis*-4-methyl-, and 3,4-*trans*-4-phenylcyclopentanone, accompanied with recovery of the starting material (−)-4-pentenal (54% ee, 34% yield), and by a cationic Rh[(*S*)-BINAP]ClO_4 afforded the corresponding enantiomers. The course of the cyclization and the stereochemistry of products are discussed based on the plausible acyl–hydride rhodium intermediates.

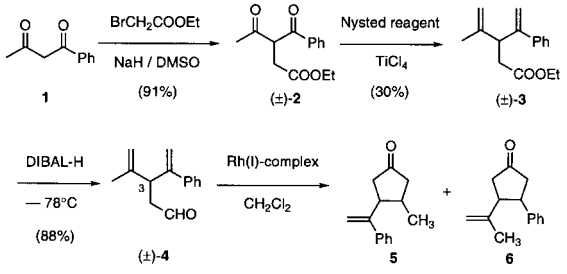
1. Introduction

Asymmetric cyclization of 4-pentenals by Rh-complexes was discovered independently by Bosnich[1] and us.[2] We reported recently that Rh-catalyzed cyclization could be applied to the symmetrical 3,4-disubstituted 4-pentenals for the enantio- and diastereoselective reaction,[3] and also to the symmetrical 3,3,4-trisubstituted 4-pentenals for the construction of a chiral quaternary carbon.[4] In the case of the symmetrical diene–aldehyde, very high enantiomeric excess (>95% ee) and diastereomeric excess (>95% de) of products were attained by using a neutral Rh[(*R*)- or (*S*)-BINAP]Cl and a cationic Rh[(*R*)- or (*S*)-BINAP]-ClO_4.[3b,5] Here we report the Rh-catalyzed cyclization of dissymmetrically racemic diene–aldehyde (±)-**4**, as a part of our ongoing research of Rh-catalyzed intramolecular hydroacylation. In the case that racemic 4-pentenal (±)-**4** is used as a substrate for the Rh-catalyzed cyclization, four types of selectivity, that is to say, regioselectivity, diastereoselectivity, enantioselectivity, and kinetic resolution of 4-pentenal might exist in the cyclization.

2. Results and discussion

2.1. Preparation of 4-pentenals

Benzoylacetone **1** was efficiently converted to ester **2** by alkylation with ethyl bromoacetate in 91% yield. The 1,3-dicarbonyl function in **2** was converted to diene **3** in 30% yield by treatment with the Nysted reagent {cyclodibromo-di-μ-methylene[μ-(tetrahydrofuran)]trizinc}[6] and $TiCl_4$. The 4-pentenal (±)-**4** was prepared from the diene **3** in 88% yield by reduction with DIBAL-H at −78°C, as shown in Scheme 1.



Scheme 1.

2.2. Rh-catalyzed cyclization

The results of Rh-catalyzed cyclization are summarized in Table 1. The cyclization by an achiral $Rh(PPh_3)_3Cl$ afforded a mixture of *cis*-**5** and *cis*-**6** in the ratio of 55 to 37 in 92% yield, but no *trans*-products were given. Unfortunately, these two constitutional isomers could not be separated by column chromatography on silica gel. Therefore, the ratio of isomers was determined by the intensity of the olefin proton peaks at δ 5.38 (br s) and 5.00 (m) of *cis*-**5** and 4.75 (m) and 4.54 (m) of *cis*-**6** in the ^1H NMR spectrum (Table 2). Moreover, the methyl proton signals appeared at δ 0.70 (d,

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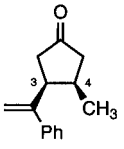
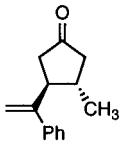
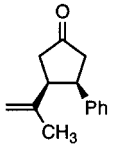
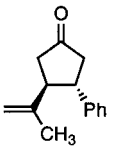
Table 1. Asymmetric cyclization of dissymmetrical 3,4-disubstituted 4-pentenal (±)-**4**

Entry	Rh-complex (equiv.)	Reaction time (h)	Yields (%)				Recovery (%)
			 *cis*–**5**	 *trans*-**5**	 *cis*-**6**	 *trans*-**6**	
1	$Rh(PPh_3)_3Cl$ (0.30)	24	55	0	37	0	0
2	Rh[(−)-DIOP]Cl (0.50)	5	43 (36% ee)	12	34 (64% ee)	0	0
3	Rh[(*S*)-BINAP]Cl (0.50)	72	19 (>95% ee)	1	21 (>95% ee)	0	11[a,b]
4	Rh[(*R*)-BINAP]ClO_4 (0.10)[c]	4	7	36 (>95% ee)	0	3	34[d]
5	Rh[(*S*)-BINAP]ClO_4 (0.10)	4	5	42 (>95% ee)	0	3	43[e]

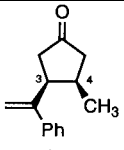
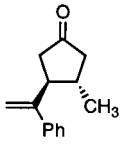
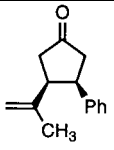
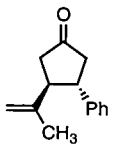
[a] Acyl-hydride Rh-complex seemed to be formed and the yield of recovery was low.
[b] $[\alpha]_D=-1.08$ (*c* 0.31, $CHCl_3$).
[c] Rh[(*R*)- or (*S*)-BINAP]ClO_4 was prepared in situ from Rh[(NBD)BINAP]ClO_4 by hydrogenation.
[d] $[\alpha]_D=-12.6$ (*c* 1.0, $CHCl_3$).

J=7.6 Hz) in *cis*-**5**, whereas they appeared at δ 1.38 (br s) in *cis*-**6**. The stereochemistry of the products was determined unambiguously to be *cis*-**5** and *cis*-**6** by the NOESY ^1H–^1H NMR spectrum, respectively. Correlation between the methine proton signal at δ 3.57 (m, 0.6H) of the C(3)-position and the methine signal at δ 2.50 (m, 0.6H) of the C(4)-position in *cis*-**5** was observed; also, correlation between the methine signal at δ 3.77 (br q, *J*=7.0 Hz, 0.4H) of C(3)-position and at δ 3.21 (br q, *J*=7.0 Hz, 0.4H) of the C(4)-position in *cis*-**6** was observed. The outcome of these stereochemistries was consistent with the previous results,[2,3b] namely, that the cyclization by the $Rh(PPh_3)_3Cl$ afforded 3,4-*cis*-products.

The cyclization by the chiral neutral Rh-complexes, such as Rh[(−)-DIOP]Cl,[5] Rh[(*S*)-BINAP]Cl afforded a mixture of *cis*-**5**, *trans*-**5**, and *cis*-**6**, but not *trans*-**6**, as shown in entries 2 and 3 in Table 1. The isomers of the products could not be separated by column chromatography on silica gel. The ratio of products was determined by the intensity of the olefin proton signals in the ^1H NMR spectra (Table 2). The *cis*-products **5** and **6** were obtained dominantly by the neutral Rh-complexes. The enantiomeric excess of *cis*-**5** and *cis*-**6** was determined by the ^1H NMR spectra after conversion to the corresponding (*R*,*R*)-2,3-butanediol acetals. The ^1H NMR spectrum of (*R*,*R*)-2,3-butanediol acetal derived from (±)-*cis*-**5** showed the olefin proton signals at δ 5.30 (br s) and 5.29 (br s) in the ratio of 1 to 1, while that from *cis*-**5** cyclized by Rh[(−)-DIOP]Cl showed the signals at δ 5.30 (br s) and 5.29 (br s) in the ratio of 68 to 32, and that cyclized by the Rh[(*S*)-BINAP]Cl only indicated the signal at δ 5.30 (br s). Also, the ^1H NMR spectrum of (*R*,*R*)-2,3-butanediol acetal derived from (±)-*cis*-**6** showed the olefin signals at δ 4.64 (br s, 0.5H×2) and δ 4.60, 4.57 (br s, each 0.5H) in the ratio of 1 to 1, but that of **6** cyclized by Rh[(−)-DIOP]Cl showed the same signals in the ratio of 82 to 18, and that of *cis*-**6** cyclized by the Rh[(*S*)-BINAP]Cl only indicated the signal at δ 4.64 (br s).

The cyclization by the cationic Rh[(*R*)- or (*S*)-BINAP]ClO_4 afforded a mixture of *cis*-**5**, *trans*-**5**, and *trans*-**6**, but not *cis*-**6**, as shown in entries 4 and 5. The ratio of products was determined by the olefin signals (Table 2). The dominant stereoisomer was 3,4-*trans*-product **5**, which was in accord with the previous results[3] that the cyclization by the cationic Rh[BINAP]ClO_4 afforded 3,4-*trans*-products. The relative stereochemistry of the major product was unambiguously determined to be *trans*-**5** by the NOESY ^1H–^1H NMR spectrum. Correlation between the methine proton signal at δ 2.89 (m, 0.78H) of the C(3)-position and the methyl proton signals at δ 1.15 (d, *J*=7.6 Hz, 2.34H) of the C(4)-position was observed. The enantiomeric excess of *trans*-**5** was determined to be >95% ee by the ^1H NMR spectra after conversion of *trans*-**5** into the corresponding (*R*,*R*)-2,3-butanediol acetal. In entries 4 and 5, the starting material **4** was recovered, and the specific rotation showed $[\alpha]_D^{31}=-12.6$ (*c* 1.0, $CHCl_3$, entry 4) and $[\alpha]^{27}_D=+12.7$ (*c* 1.6, $CHCl_3$, entry 5), respectively. The ^1H NMR spectra

Table 2. Chemical shifts of cyclopentanones **5** and **6** in the ^1H NMR spectra

Compound	 *cis*--**5**	 *trans*-**5**	 *cis*-**6**	 *trans*-**6**
Olefinic-H	5.38 (br s) 5.00 (m)	5.30 (m) 5.16 (m)	4.75 (m) 4.54 (m)	4.75 (m) 4.70 (m)
Methyl-H	0.70 (d, *J*=7.6 Hz)	1.15 (d, *J*=7.6 Hz)	1.38 (br s)	1.69 (br s)

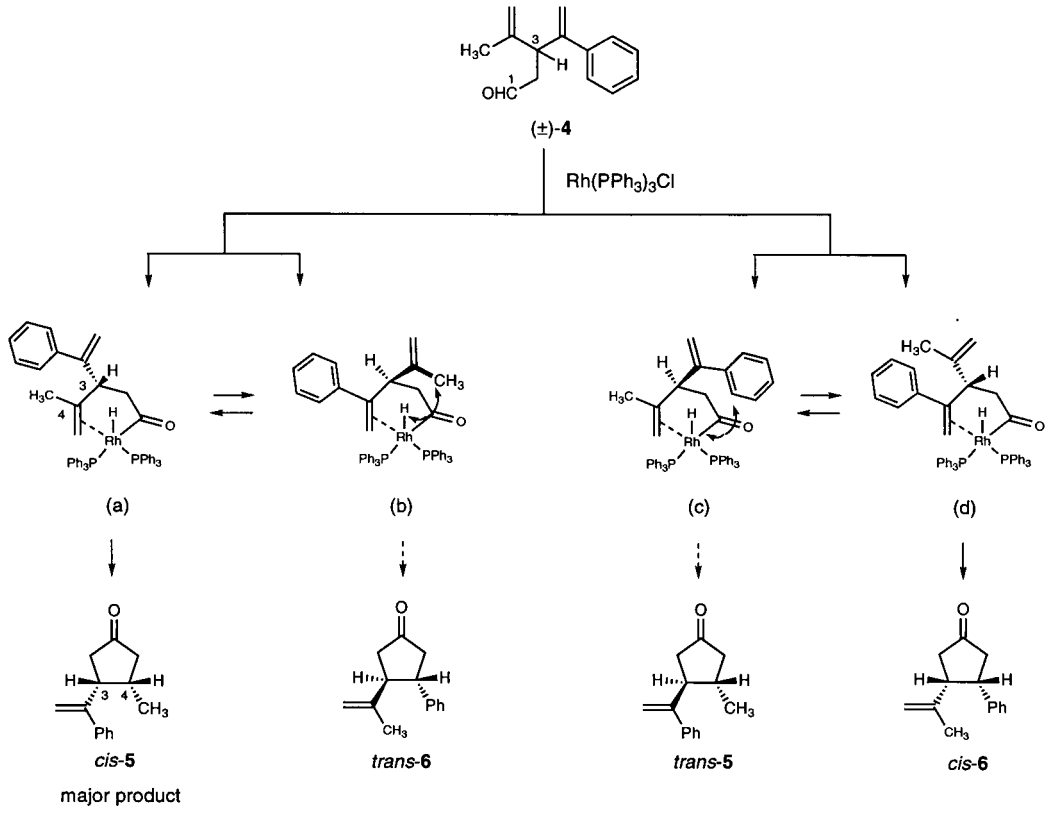


Figure 1. Plausible acyl–hydride intermediates for $Rh(PPh_3)_3Cl$-catalyzed cyclization.

of the (+)-MTPA ester derived from (±)-**4** via the corresponding primary alcohol, showed the olefin signals at δ 4.76 (m) and 4.74 (m) in the ratio of 1 to 1, whereas that derived from (−)-**4** (entry 4) showed the signals in a different ratio, and the enantiomeric excess of the recovered (−)-**4** was determined to be 54% ee (entry 4).

2.3. Plausible mechanism for Rh-catalyzed cyclization

The mechanism for regioselection could not be clearly explained. The difference in the electrostatic state and the bulkiness between the phenyl and methyl substituents may affect the course of cyclization.

The outcome of diastereoselectivity was in accord with the previous results, that is to say, the cyclization by the neutral $Rh(PPh_3)_3Cl$ or Rh[BINAP]Cl complex afforded 3,4-*cis*-cyclopentanone, and that by the cationic $Rh[BINAP]ClO_4$ afforded 3,4-*trans*-cyclopentanone. These results may be explained by the putative acyl–hydride rhodium intermediates. We have already reported that the cyclization by the neutral Rh-complex afforded *cis*-products by way of the stable intermediate, in which no unfavorable steric factors exist; on the other hand, the cyclization by the cationic $Rh[BINAP]ClO_4$ afforded *trans*-products by way of the least stable intermediate of the putative acyl–hydride intermediates because the rate of reductive elimination from such intermediates might be faster than that of other intermediates.[3b,7]

The cyclization of (±)-**4** by the achiral $Rh(PPh_3)_3Cl$ afforded a mixture of *cis*-**5** and *cis*-**6** by way of the intermediates (a, d), in which no steric repulsions exist. The intermediates (b, c) which generate *trans*-products, seem to be less stable due to the steric repulsions as indicated by arrows in Fig. 1.

Fig. 2 shows the plausible acyl–hydride Rh-intermediates with the (*S*)-BINAP ligand. Ellipsoids represent the phenyl groups at phosphorus in the BINAP ligand, and imply hindered regions. We assumed that two pseudo-axial phenyl groups relative to the rhodium–phosphorus plane formed the hindered regions at the vertical, and these regions would strongly affect the stereoselection. Two pseudo-equatorial phenyl groups may also form the hindered regions at the horizontal, but these regions would exert only minimal effect on the stereoselection. Also, we assumed that the stereoselection by the neutral Rh[BINAP]Cl is governed by the thermodynamically preferred intermediate, and that by the cationic $Rh[BINAP]ClO_4$ is determined by the rate of reductive elimination from the acyl–hydride intermediate.[1,3,7] Taking these assumptions into consideration, the cyclization by the neutral Rh[(*S*)-BINAP]Cl could be explained by the thermodynamically favorable intermediates. Four intermediates (f, g, i, l) of the eight acyl–hydride intermediates (e–l) would produce 3,4-*cis*-products, and the intermediates (g, i) seem to be more favorable than the intermediates (f, l) because no steric repulsion exists in the intermediates (g, i). The intermediate (g) from (3*S*)-**4** generates (3*R*,4*S*)-*cis*-**6**, and the intermediate (i) from (3*R*)-**4** gives (3*R*,4*S*)-*cis*-**5**. Consequently, both enantiomers (3*S*)- and (3*R*)-4-pentenals **4** could be used for the cyclization by the neutral Rh[(*S*)-BINAP]Cl. The results that the cyclization by the Rh[(S)-BINAP]Cl

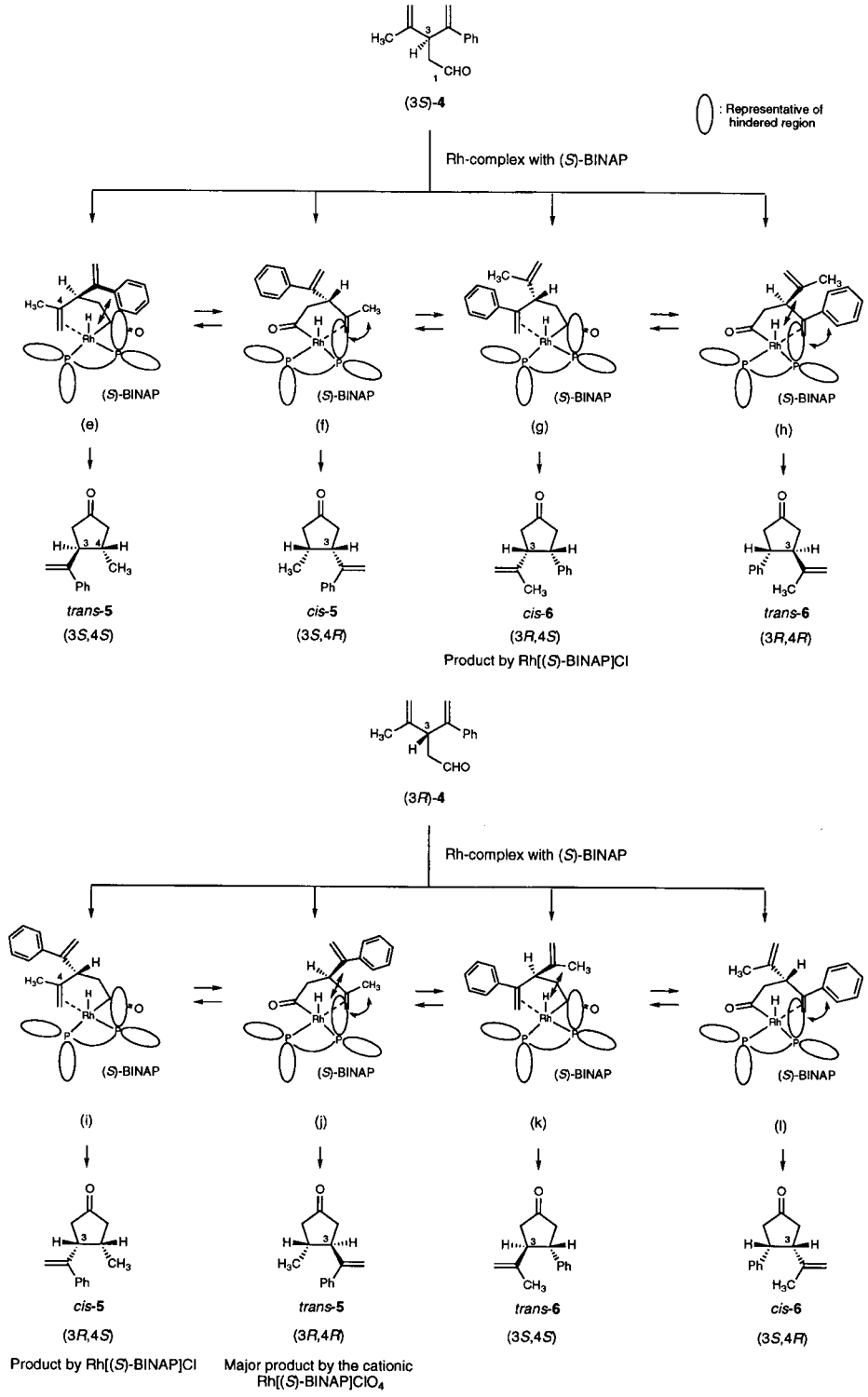


Figure 2. Plausible acyl–hydride intermediates for the chiral Rh-catalyzed cyclization.

afforded *cis*-**5** (>95% ee) and *cis*-**6** (>95% ee) and the recovered material **4** (entry 3) showed $[\alpha]^{27}_{D}=-1.08°$, which meant the recovered **4** was almost a racemate, accord with the plausible mechanism.

The cyclization by the cationic Rh[(*S*)-BINAP]ClO_4 affords 3,4-*trans*-products, which could be explained by the rate of reductive elimination, and the rate of reductive elimination from the unfavorable intermediates seems to be faster than that from the favorable intermediates. Four intermediates (e, h, j, k) would produce 3,4-*trans*-products. The rate of reductive elimination from the sterically unfavorable intermediates (h, j), in which two steric repulsions exist, might be faster than that from the intermediates (e, k), in which one steric repulsion exists. The intermediate (h) from (3*S*)-**4** generates (3*R*,4*R*)-*trans*-**6**, and the intermediate (j) from

(3*R*)-**4** gives (3*R*,4*R*)-*trans*-**5**. In fact, the cyclization of (±)-**4** by the cationic Rh[(*S*)-BINAP]ClO_4 afforded *trans*-**5** (>95% ee) as a major product, but not *trans*-**6** in moderate yield. The olefin bearing phenyl substituent seems to be less reactive than the olefin bearing an alkyl substituent in the Rh-catalyzed cyclization.[2b,d,3b] The absolute configuration of *trans*-**5** cyclized by Rh[(*S*)-BINAP]ClO_4 might be 3*R*,4*R*, and that of the recovered (+)-**4**, which showed $[\alpha]^{27}_D$=+12.7, might be 3*S*.[8]

3. Conclusions

Rh-Catalyzed cyclization was applied for the kinetic resolution of racemic 3,4-disubstituted 4-pentenal (±)-**4**. The cyclization by the achiral Rh(PPh_3)$_3$Cl afforded the cyclopentanones *cis*-**5** (55%) and *cis*-**6** (37%), stereoselectively. The cyclizations by the chiral Rh-complex proceeded enantiospecifically to produce the optically active cyclopentanones, that is to say, the cyclization of (±)-**4** by the neutral Rh[(*S*)-BINAP]Cl afforded *cis*-**5** (>95% ee, 19% yield) and *cis*-**6** (>95% ee, 21% yield), and that by the cationic Rh[(*S*)- or (*R*)-BINAP]ClO_4 afforded *trans*-**5** (>95% ee, 36–42% yields), accompanied with recovery of the optically active starting material **4**. The strategy using the chiral Rh-complexes for the kinetic resolution would be a practical and useful method to prepare optically active cyclopentanones.

4. Experimental

4.1. General methods

Anhydrous THF was purchased from Kanto Chemical Co., and used as received. Benzene and CH_2Cl_2 were distilled from P_2O_5. (*R*)- and (*S*)-BINAP were purchased from Kanto Chemical Co. Inc. ^{1}H NMR spectra were determined at 270 or 500 MHz. Infrared spectra were recorded on a JASCO A-100 spectrometer. EIMS, FABMS, and HRMS spectra were taken on a JEOL JMS 610H or SX102 spectrometer. General procedures used for syntheses followed those of the previous reports.[3,4]

4.1.1. Ethyl 3-oxo-3-(phenylcarbonyl)pentanoate (2). A solution of benzoylacetone (25.0 g, 154 mmol) in DMSO (100 mL) was added dropwise to a stirred suspension of NaH (60% in oil, 6.78 g, 170 mmol) in DMSO (150 mL) at room temperature, and stirred for 30 min. The mixture was cooled to 0°C, and ethyl bromoacetate (18.9 mL, 170 mmol) was added dropwise. The whole was warmed to room temperature, and stirred overnight, and then diluted with saturated aqueous NH_4Cl, extracted with ether, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel (20% EtOAc in hexane) to give **2** (34.8 g, 91%) as a colorless oil: IR (neat) 1720, 1680, 1600 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.01–8.05 (m, 2H), 7.49–7.67 (m, 3H), 5.01 (t, *J*=6.9 Hz, 1H), 4.14 (q, *J*=7.3 Hz, 2H), 3.04 (dd, *J*=6.9, 17.1 Hz, 1H), 2.96 (dd, *J*=6.9, 17.1 Hz, 1H), 2.18 (s, 3H), 1.23 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 201.8, 195.8, 171.2, 136.3, 133.8, 128.9, 128.7, 61.0, 57.7, 33.0, 29.0, 14.0; FAB(+)HRMS calcd for $C_{14}H_{17}O_4$ (M^++1) 249.1127, found 249.1129.

4.1.2. Ethyl 4-methyl-3-(1-phenylvinyl)pent-4-enoate (3). A solution of **2** (10.0 g, 40.3 mmol) in THF (50 mL) was added dropwise to the vigorous stirred suspension of Nysted reagent[5] (20% suspension in THF, 202 g, 88.7 mmol) in THF (50 mL) at −78°C, and stirred for 15 min. Then, $TiCl_4$ (9.7 mL, 88.5 mmol) was added slowly to the stirred mixture at −78°C, and then the whole was warmed to room temperature, and stirred for 2 h. The mixture was diluted with water, and extracted with ether. The etheral extract was washed with 5% aqueous $NaHCO_3$, brine, and dried over $MgSO_4$. After removal of the solvent, the oily residue was purified by column chromatography on silica gel (10% EtOAc in hexane) to give **3** (2.9 g, 30%) as a colorless oil: IR (neat) 1730, 1620 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.25–7.42 (m, 5H), 5.32 (br s, 1H), 5.10 (br s, 1H), 4.85 (m, 1H), 4.82 (br s, 1H), 4.09 (q, *J*=7.3 Hz, 2H), 3.81 (t, *J*=7.9 Hz, 1H), 2.64 (d, *J*=7.9 Hz, 2H), 1.71 (br s, 3H), 1.21 (t, *J*=7.3 Hz, 3H); FABMS *m*/*z* 245 (M^++1).

4.1.3. 3-(1-Methylvinyl)-4-phenylpent-4-enal (4). A solution of DIBAL-H in hexane (0.95 M, 4.0 mL, 3.77 mmol) was added dropwise to a stirred solution of **3** (765 mg, 3.14 mmol) in toluene (7 mL) at −78°C, and the solution was stirred for 1 h. The reaction was quenched with MeOH (3 mL), and the whole was diluted with cold 1N HCl (30 mL), extracted with EtOAc, washed with 5% aqueous $NaHCO_3$, brine, and dried over $MgSO_4$. Removal of the solvent afforded an oily residue, which was purified by column chromatography on silica gel (10% EtOAc in hexane) to give **4** (550 mg, 88%) as a colorless oil: IR (neat) 1730, 1630 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 9.71 (t, *J*=2.3 Hz, 1H), 7.27–7.40 (m, 5H), 5.37 (br s, 1H), 5.10 (br s, 1H), 4.91 (m, 1H), 4.82 (br s, 1H), 3.85 (t, *J*=7.6 Hz, 1H), 2.71 (dd, *J*=7.6, 2.3 Hz, 2H), 1.74 (br s, 3H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 201.6, 148.9, 144.6, 141.5, 128.3, 127.6, 126.7, 114.2, 113.1, 46.1, 46.0, 20.8; FAB(+)HRMS calcd for $C_{14}H_{17}O_1$ (M^++1) 201.1279, found 201.1275.

4.1.4. Cyclization by the achiral Rh(PPh_3)$_3$Cl. A solution of **4** (100 mg, 0.50 mmol) and Rh(PPh_3)$_3$Cl (139 mg, 0.15 mmol) in CH_2Cl_2 (16 mL) was stirred for 24 h under Ar atmosphere. After removal of the solvent, the residue was purified by column chromatography on silica gel (10% EtOAc in hexane) to leave a mixture of *cis*-**5** and *cis*-**6** (92.3 mg, 92%, *cis*-**5**/*cis*-**6**=6/4) as a colorless oil: IR (neat) 1740 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10–7.43 (m, 5H), 5.38 (br s, 0.6H), 5.00 (m, 0.6H), 4.75 (m, 0.4H), 4.54 (m, 0.4H), 3.77 (br q, *J*=7.0 Hz, 0.4H), 3.57 (m, 0.6H), 3.21 (br q, *J*=7.0 Hz, 0.4H), 2.35–2.79 (m, 4H), 2.10 (m, 0.6H), 1.38 (br s, 1.2H), 0.70 (d, *J*=7.6 Hz, 1.8H); EIMS *m*/*z* 200 (M^+, 40), 170 (24), 156 (70), 130 (100), 115 (59), 77 (43); HRMS calcd for $C_{14}H_{16}O_1$ (M^+) 200.1201, found 200.1201.

4.1.5. Cyclization by the neutral Rh[(−)-DIOP]Cl. A mixture of [Rh(cyclooctene)Cl]$_2$ (90 mg, 0.12 mmol) and bisphosphine (−)-DIOP (125 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 1 h, then a solution of **4** (100 mg, 0.50 mmol) in CH_2Cl_2 (2 mL) was added dropwise to the stirred solution. After being stirred at room

temperature for 5 h, the solution was concentrated in vacuo to leave the residue, which was dissolved in ether (20 mL), and the precipitated Rh-complex was filtered off. Removal of the solvent gave the residue, which was purified by column chromatography on silica gel to afford a mixture of *cis*-**5**, *trans*-**5**, and *cis*-**6** (89 mg, 89%, *cis*-**5**/*trans*-**5**/*cis*-**6**=43/12/34) as a colorless oil.

4.1.6. Cyclization by the neutral Rh[(*S*)-BINAP]Cl. The cyclization by the neutral Rh[(*S*)-BINAP]Cl afforded a mixture of *cis*-**5**, *trans*-**5**, and *cis*-**6** (41%, *cis*-**5**/*trans*-**5**/*cis*-**6**=19/1/21) as a colorless oil. The starting material **4** was recovered in 11% yield. The specific rotation of recovered **4**: $[\alpha]^{27}_{D}=-1.08$ (*c* 0.31, $CHCl_3$).

4.1.7. Cyclization by the cationic Rh[(*R*)-BINAP]ClO_4. A solution of [Rh(NBD)(*R*)-BINAP]ClO_4 (34 mg, 0.038 mmol) in CH_2Cl_2 (5 mL) was stirred under H_2 atmosphere at room temperature for 2 h. Then, Ar gas was bubbled into the solution for 15 min. This bright red solution of [Rh(*R*)-BINAP]ClO_4 was used for the cyclization without isolation. A solution of **4** (150 mg, 0.75 mmol) in CH_2Cl_2 (5 mL) was added dropwise to the stirred solution of [Rh(*R*)-BINAP]-ClO_4 under an Ar atmosphere. After being stirred at room temperature for 4 h, the solution was concentrated in vacuo to leave a residue. The residue was dissolved in ether (20 mL), and the precipitated Rh-complex was filtered off. After removal of ether, the residue was purified by column chromatography on silica gel. The fraction eluted with 15% EtOAc in hexane afforded a mixture of **5** and **6** (69 mg, 46%, *cis*-**5**/*trans*-**5**/*trans*-**6**=7/36/3) as a colorless oil and eluted with 9% EtOAc in hexane gave recovered **4** (51 mg, 34%): Recovered material **4**: $[\alpha]_{D}^{31}=-12.6$ (*c* 1.00, $CHCl_3$). A mixture of **5** and *trans*-**6**: IR (neat) 1740 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.25–7.45 (m, 5H), 5.38 (br s, 0.15H), 5.30 (m, 0.78H), 5.16 (m, 0.78H), 5.00 (m, 0.15H), 4.75 (m, 0.07H), 4.70 (m, 0.07H), 3.67 (m, 0.15H), 2.89 (m, 0.78H), 2.10–2.65 (m, 4.29H), 1.83 (m, 0.78H), 1.69 (br s, 0.21H), 1.15 (d, *J*=7.6 Hz, 2.34H), 0.70 (d, *J*=7.6 Hz, 0.45H); HRMS calcd for $C_{14}H_{16}O_1$ (M^+) 200.1201, found 200.1204.

4.1.8. Cyclization by the cationic Rh[(*S*)-BINAP]ClO_4. The cyclization by the cationic Rh[(*S*)-BINAP]ClO_4 afforded a mixture of **5** and **6** (50%, *cis*-**5**/*trans*-**5**/*trans*-**6**=5/42/3). The starting material **4** was recovered in 43% yield.

4.1.9. (*R*,*R*)-2,3-Butanediol acetals of 5 and 6. A mixture of cyclopentanone **5,6** (15 mg, 75 mmol), (*R*,*R*)-butanediol (20 mg, 0.22 mmol), and *p*-TsOH–H_2O (5 mg) in benzene (20 mL) was refluxed for 3 h, fixed with Dean–Stark apparatus. After being cooled to room temperature, the solution was washed with 5% aqueous $NaHCO_3$, brine, and dried over $MgSO_4$. After removal of the solvent, the residue was briefly purified by column chromatography on silica gel to give the crude acetal.

4.1.10. Determination of enantiomeric excess of *cis*-5. The 500 MHz ^1H NMR spectrum of the (*R*,*R*)-2,3-butanediol acetal of (±)-*cis*-**5** cyclized by the $Rh(PPh_3)_3Cl$ showed the olefin proton signals at δ 5.30 (br s) and 5.29 (br s) in the ratio of 1 to 1, while those derived from *cis*-**5** cyclized by Rh[(−)-DIOP]Cl showed the olefin signals at δ 5.30 (br s) and 5.29 (br s) in the ratio of 68 to 32. Therefore, the enantiomeric excess of *cis*-**5** cyclized by Rh[(−)-DIOP]Cl (entry 2 in Table 1) was determined to be 36% ee. The olefin proton signal of the (*R*,*R*)-butanediol acetal of *cis*-**5** cyclized by the neutral Rh[(*S*)-BINAP]Cl, was observed only at δ 5.30 (br s) in the ^1H NMR spectrum.

4.1.11. Determination of enantiomeric excess of *cis*-6. The 500 MHz ^1H NMR spectrum of the (*R*,*R*)-2,3-butanediol acetal of (±)-*cis*-**6** showed the olefin proton signals at δ 4.64 (br s) and δ 4.60, 4.57 (each, br s) in the ratio of 1 to 1, while those from *cis*-**6** cyclized by Rh[(−)-DIOP]Cl showed the olefin signals at δ 4.64 (br s) and δ 4.60, 4.57 (each, br s) in the ratio of 82 to 18, and those from *cis*-**6** cyclized by the Rh[(*S*)-BINAP]Cl showed the signal at δ 4.64 (br s), only.

4.1.12. Determination of enantiomeric excess of *trans*-5. The 500 MHz ^1H NMR spectrum of the (*R*,*R*)-2,3-butanediol acetal derived from *trans*-**5** cyclized by the cationic Rh[(*R*)-BINAP]ClO_4 showed the methine proton signals at δ 2.58 (dt, *J*=7.8, 11.4 Hz), while those cyclized by Rh[(*S*)-BINAP]ClO_4 showed the signals at δ 2.65 (dt, *J*=7.8, 11.4 Hz). Therefore, the enantiomeric excess of *trans*-**5** (entry 5 and 6) was determined to be >95% ee.

4.1.13. Determination of enantiomeric excess of the recovered starting material (4). $LiAlH_4$ (4 mg, 0.10 mmol) was added portionwise to a stirred solution of **4** (10 mg, 0.05 mmol) in THF (4 mL) at 0°C, and stirred at room temperature for 3 h. The reaction was quenched with diluted HCl, and then the whole was evaporated in vacuo. The residue was dissolved in pyridine (5 mL) and four drops of (+)-MTPACl was added. The solution was diluted with brine, extracted with EtOAc, and dried over $MgSO_4$. After removal of the solvent, the residue was briefly purified by column chromatography on silica gel. The ^1H NMR spectrum of (+)-MTPA ester derived from racemic (±)-**4** showed the olefin proton signal at δ 4.76 (m) and 4.74 (m) in the ratio of 1 and 1, while those derived from the recovered (−)-**4** showed the signal at δ 4.76 (m) and 4.74 (m) in the ratio of 23 and 77.

References

1. (a) Barnhart, R. W.; Wang, X.; Noheda, P.; Bergens, S. H.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1994**, *116*, 1821–1830. (b) Barnhart, R. W.; McMorran, D. A.; Bosnich, B. *Chem. Commun.* **1997**, 589–590. (c) Bosnich, B. *Acc. Chem. Res.* **1998**, *31*, 667–674.
2. (a) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, *13*, 1287–1290. (b) Taura, Y.; Tanaka, M.; Wu, X.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron* **1991**, *47*, 4879–4888. (c) Sakai, K. *J. Synth. Org. Chem. (Japan)* **1993**, *51*, 733–743. (d) Fujio, M.; Tanaka, M.; Wu, X. M.; Funakoshi, K.; Sakai, K.; Suemune, H. *Chem. Lett.* **1998**, 881–882.
3. (a) Wu, X.-M.; Funakoshi, K.; Sakai, K. *Tetrahedron Lett.* **1992**, *33*, 6331–6334. (b) Tanaka, M.; Imai, M.; Fujio, M.; Sakamoto, E.; Takahashi, M.; Eto-Kato, Y.; Wu, X.-M.; Funakoshi, K.; Sakai, K.; Suemune, H. *J. Org. Chem.* **2000**, *65*, 5806–5816.

4. (a) Takahashi, M.; Tanaka, M.; Sakamoto, E.; Imai, M.; Funakoshi, K.; Sakai, K.; Suemune, H. *Chem. Pharm. Bull.* **2000**, *48*, 1822–1825. (b) Takahashi, M.; Tanaka, M.; Sakamoto, E.; Imai, M.; Matsui, A.; Funakoshi, K.; Sakai, K.; Suemune, H. *Tetrahedron Lett.* **2000**, *41*, 7879–7883.
5. Abbreviations: BINAP: 2,2(-Bis(diphenylphosphino)-1,1-(-binaphthyl; (+)-DIOP: (4*S*,5*S*)-(+)-4,5-Bis(diphenylphosphinomethyl)-2,3-dimethyl-1,3-dioxolane.
6. Nysted reagent is commercially available from Aldrich Co.: Matsubara, S.; Sugihara, M.; Utimoto, K. *Synlett* **1998**, 313–315.
7. Morrison, J. D. *Asymmetric Synthesis*, Vol. 5; Academic: New York, 1985 (pp 46–66).
8. The absolute configuration of *trans*-**5** and (+)-**4** was assumed based on the plausible intermediates and the previous results of Rh-catalyzed cyclizations.