Application of Rh-Catalyzed Cyclization to the Formation of a Chiral Quaternary Carbon

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Rh-Catalyzed cyclization was applied to the formation of a chiral quaternary carbon. It has become clear that the Rh-complex can discriminate between isopropenyl and 2-isopentenyl (or isopentyl) substituents, and the cyclization afforded 3,3,4-trisubstituted cyclopentanones with a chiral quaternary carbon in a stereoselective manner. The cyclization of 4-pentenals 6a, b by an achiral neutral $Rh(PPh_3)_3Cl$ afforded 3,3,4-*cis*-trisubstituted cyclopentanones (±)-7a, b in 86—96%, and the cyclization by a cationic Rh[(*R*)-BINAP]ClO_4 afforded 3,3,4-*trans*-trisubstituted cyclopentanones (−)-8a, b of 82—86% ee in 88—98% yields. The mechanism of stereoselection by Rh-complexes is also discussed.

Key words Rhodium-catalyzed cyclization; quaternary carbon; cyclopentanone; enantioselective; diastereoselective

Catalytic asymmetric process to produce a chiral quaternary carbon is especially fascinating to organic chemists because both the formaion of the chiral quaternary carbons and the catalytic asymmetric reactions using transition metals are interesting.[1] Recently, we reported that cyclization using Rh-complex[2] could be applicable for the concurrent induction of two chiral centers from symmetrical 4-pentenals[3] and, furthermore, the reaction could be used to produce a chiral quaternary carbon.[4] Here, we wish to report the Rh-catalyzed cyclization of 4-pentenal[5] bearing a quaternary carbon, which is composed of diisopropenyl, formylmethyl, and 2-isopentenyl (or isopentyl) groups. For enantio- and diastereoselective cyclization, the Rh-complex and BINAP ligand need to discriminate between isopropenyl and 2-isopentenyl substituents. The structure of these two substituents seems to be very similar. When the substituent at the quaternary carbon is a 2-isopentenyl group, the substrate **6a** is a 5-pentenal as well as a 4-pentenal.[6]

Results and Discussion

Preparation of 4-Pentenals Acetylacetone **1** was converted into ester **2** by alkylation with methyl bromoacetate in 92% yield. The ester **2** was again alkylated with 2-isopentenyl bromide to afford β-keto ester **3a** bearing a quaternary carbon in 71% yield. Olefination of the 1,3-dicarbonyl function in **3a** with Nysted reagent[7] gave diene **4a** in 74% yield. Moreover, hydrogenation of the olefin fuction in **3a**, followed by olefination, afforded diene **4b** in 60% overall yield. The dienes **4a, b** were converted into the corresponding aldehydes **6a, b** by reduction with $LiAlH_4$ and subsequent oxidation with PCC (**6a**: 73% from **4a**, and **6b**: 62% from **4b**), respectively (Chart 1).

Rh-Catalyzed Cyclization The results of cyclization by Rh-complexes are summarized in Table 1. The cyclization of **6a** by an achiral $Rh(PPh_3)_3Cl$ afforded 3,3,4-*cis*-trisubstituted cyclopentanone **7a** in 96% yield, as a major product. The ratio of *cis* and *trans* was determined to be 91 (*cis*-**7a**) to 9 (*trans*-**8a**), based on the ratio of methyl proton signals at δ: 1.07 (3H, d, J=6.9 Hz) and δ: 0.89 (3H, d, J=6.9 Hz) in the ^{1}H-NMR spectrum. The relative configuration of **7a** was unambiguously determined to be 3,4-*cis* from the NOESY ^{1}H–^{1}H-NMR spectrum. A correlation between the methyl proton signals δ: 0.89 (3H, d) at the C(4)-position and the methyl signals δ: 1.74 (3H, br s) of the isopropenyl group was observed. Cyclization by a neutral Rh[(*R*)-BINAP]Cl was unsuccessful, due to the low catalytic activity of the neutral Rh[(*R*)-BINAP]Cl. The cyclization by a cationic Rh[(*R*)-BINAP]ClO_4 proceeded smoothly to produce *trans*-(−)-**8a** in 98% yield. In the NOESY ^{1}H–^{1}H-NMR spectrum of **8a**, a correlation between the methylene signals δ: 2.10 (1H, dd) and 2.32 (1H, dd) of the 2-isopentenyl group and the methyl signals δ: 1.07 (3H, d) at the C(4)-position was observed. The ratio of diastereomers was 2 (*cis*-**7a**) to 98 (*trans*-**8a**). The reaction required only 5 mol% of Rh-complex, and the starting material **6a** disappeared after 2 h at room temperature. The cyclization of **6a** by the cationic Rh[(*S*)-BINAP]-ClO_4 afforded an enantiomer; (+)-**8a** in 96% yield. The cyclization of **6b** by the Rh-complex gave similar results to those of **6a**. The selectivity of *cis* and *trans* was a little lower

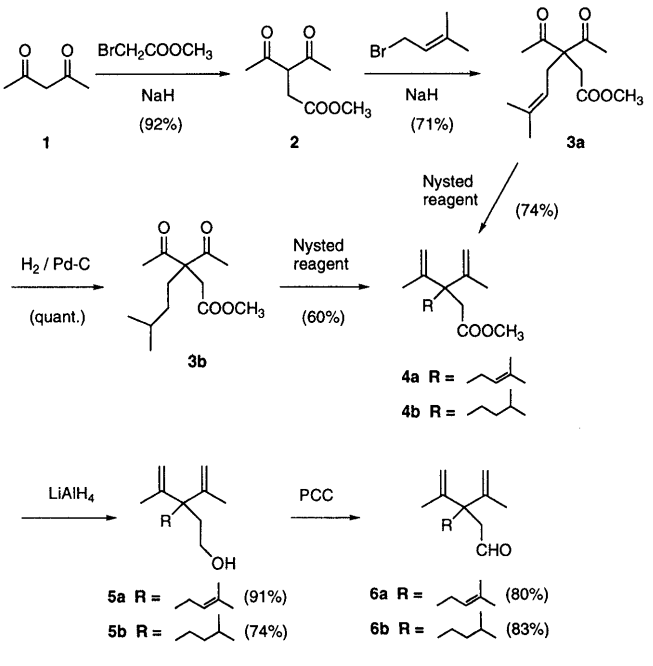

Chart 1

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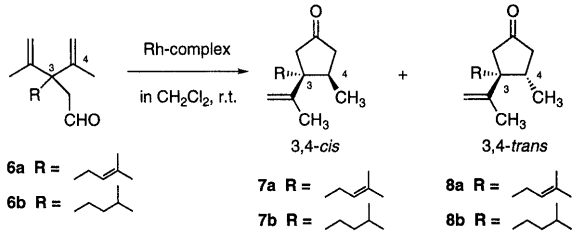
Table 1. Formation of a Quaternary Carbon Using Rh-Cyclization



Entry	Substrate	Rh-complex (eq)	Reaction time (h)	Isolated yield (%)[a]	*cis*/*trans*	Opt. purity of major product (% ee)	$[\alpha]_D$
1	**6a**	$Rh(PPh_3)_3Cl$ (0.5)	24	96	91/9	—	—
2	**6a**	Rh[(*R*)-BINAP]ClO_4 (0.05)	2	98	2/98	86	−16.2
3	**6a**	Rh[(*S*)-BINAP]ClO_4 (0.05)	2	96	2/98	82	+16.2
4	**6b**	$Rh(PPh_3)_3Cl$ (0.5)	24	86	88/12	—	—
5	**6b**	Rh[(*R*)-BINAP]ClO_4 (0.05)	2	88	4/96	85	−81.9
6	**6b**	Rh[(*S*)-BINAP]ClO_4 (0.05)	2	90	3/97	86	+83.1

a) Products **7** and **8** were obtained as inseparable mixtures of *cis* and *trans*.

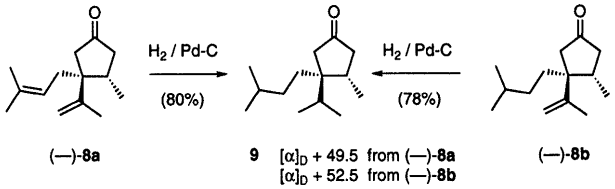


Chart 2

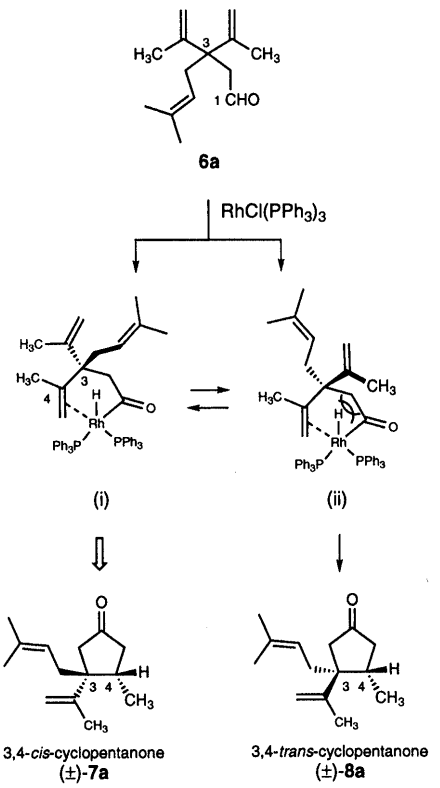


Fig. 1. Plausible Acyl–Hydride Rhodium Intermediate for the $Rh(PPh_3)_3Cl$-Catalyzed Cyclization

than that of **6a**, both with the $Rh(PPh_3)_3Cl$ and the cationic Rh[BINAP]ClO_4, as shown by entries 4—6 in Table 1.

The enantiomeric excess of (−)-**8a**, **b** and (+)-**8a**, **b** was determined by the ^{1}H-NMR spectra, after conversion of the ketone into (*R*,*R*)-2,3-butanediol acetal. For example, the (*R*,*R*)-2,3-butanediol acetal derived from (−)-**8a** showed olefinic proton signals at δ: 4.77 (br s) and 4.74 (br s) in the ratio of 2 to 28, while that of (+)-**8a** showed δ: 4.77 (br s) and 4.74 (br s) in the ratio of 30 to 3 in the ^{1}H-NMR spectra. The ^{13}C-NMR spectra of the (*R*,*R*)-2,3-butanediol acetals derived from (−)- and (+)-**8b** also supported the enantiomeric excess. The hydrogenation of (−)-**8a**, which was cyclized by the cationic Rh[(*R*)-BINAP]ClO_4 gave cyclopentanone **9** in 80% yield, and the hydrogenation of (−)-**8b** also afforded the same product **9** in 78% yield. The specific rotation of **9** prepared from (−)-**8a** showed $[\alpha]_D^{26}$ +49.5°, and that of **9** from (−)-**8b** also showed $[\alpha]_D^{28}$ +52.5°, as shown in Chart 2. This result means that no difference of enantioselection exists between the cyclization of **6a** and **6b**.

Plausible Mechanism for Stereoselection The stereoselectivity in the Rh-catalyzed cyclization could be explained by the plausible acyl–hydride intermediates.[3,4] The cyclization of **6** by $Rh(PPh_3)_3Cl$ afforded 3,3,4-*cis*-trisubstituted cyclopentanone (±)-**7**. The *cis*-product **7** would be obtained by cyclization through a favorable intermediate (i). Considering the plausible acyl–hydride intermediates, the intermediate (ii), which would produce 3,3,4-*trans*-trisubstituted cyclopentanone **8**, seems to be less stable than intermediate (i) because the unfavorable steric repulsion between the isopropenyl group and the Rh metal would be stronger than that between the 2-isopentenyl group and the Rh metal (Fig. 1).

Cyclization by the cationic Rh[(*R*)-BINAP]ClO_4 afforded 3,3,4-*trans*-trisubstituted cyclopentanone (−)-**8**. To produce the 3,3,4-*trans*-trisubstituted cyclopentanone **8**, the reaction needs to proceed not by way of the favorable intermediate (iv), but by the unfavorable intermediate (iii) where the repulsion between the isopropenyl group and the Rh metal exists. We have already reported that cyclization by the cationic Rh-complex proceeded by way of the unfavorable acyl–hydride intermediate to give the 3,3,4-*trans*-trisubstituted cyclopentanone. The cyclization of **6a**, **b** by the cationic Rh[(*R*)-BINAP]ClO_4 seems to proceed by way of the unfavorable intermediate (iii) where two repulsions exist. One is the repulsion between the methyl group at the C(4)-position

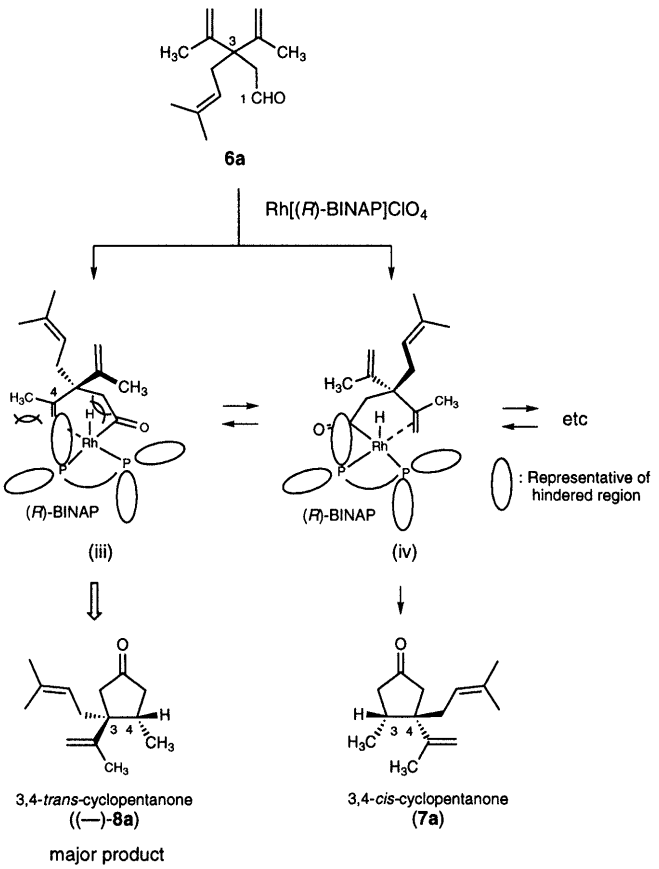


Fig. 2. Plausible Acyl–Hydride Rhodium Intermediate for the Cationic Rh-Catalyzed Cyclization

and the (*R*)-BINAP ligand, and the other is between the isopropenyl function and the Rh metal. Cyclization by way of intermediate (iii) would afford (3*S*,4*S*)-(−)-**8a**, as shown in Fig. 2.

Conclusion

The Rh-catalyzed cyclization was used to obtain cyclopentanones with a chiral quaternary carbon. It has become clear that the neutral $Rh(PPh_3)_3Cl$ could discriminate between 2-isopentenyl and isopropenyl substituents, and the cyclization afforded (±)-3,3,4-*cis*-trisubstituted cyclopentanones **7a, b**, stereoselectively. Also, it has been shown that the cationic Rh[(*R*)-BINAP]ClO_4 could discriminate between similar substituents, such as 2-isopentenyl and isopropenyl, and cyclization gives the optically active (−)-3,3,4-*trans*-trisubstituted cyclopentanones **8a, b** in a diastereo- and enantioselective manner.

Experimental

General Methods THF was purchased from Kanto Chemical Co., and used without distillation. 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 60, 270 or 500 MHz. Infrared spectra were recorded on a JASCO A-100 spectrometer. EI-MS, FAB-MS, and HRMS spectra were obtained on a JEOL JMS 610H, DX300, or SX102 spectrometer. General procedures used for syntheses followed those in previous reports.[2—4]

3-Methoxycarbonylmethyl-2,4-pentanedione (2) A solution of acetylacetone (5.00 g, 50 mmol) in THF (20 ml) was added to a stirred suspension of NaH (2.40 g, 60%) in THF (60 ml) at 0 °C, and the whole was stirred at room temperature for 10 min. Methyl bromoacetate (9.18 g, 60 mmol) in THF (20 ml) was added to the solution at 0 °C, and stirred overnight at room temperature. The solution was diluted with brine, extracted with ether, washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel (30% EtOAc in hexane) to give **2** (7.90 g, 92%) as a colorless oil: IR (neat) cm^{-1}: 1730, 1600. ^{1}H-NMR (60 MHz, $CDCl_3$) δ: 4.13 (1H, t, J=7 Hz), 3.72 (3H, s), 2.89 (2H, d, J=7 Hz), 2.22 (6H, s). EI-MS *m/z*: 172 (M^+).

Methyl 3,3-Diacetyl-6-methyl-5-heptenoate (3a) Compound **3a** was prepared from **2** in a similar manner to that described for the preparation of **2**: 71% yield; a colorless oil; IR (neat) cm^{-1}: 1735, 1700. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.78 (1H, tm, J=7.6 Hz), 3.65 (3H, s), 2.98 (2H, s), 2.76 (2H, br d, J=7.6 Hz), 2.16 (6H, s), 1.68 (3H, br s), 1.58 (3H, s). FAB-MS *m/z*: 241 (M^++H).

Methyl 3,3-Diacetyl-6-methylheptanoate (3b) A suspension of **3a** (1.00 g, 4.2 mmol) and Pd-C (10%, 1.00 g) in MeOH (50 ml) and THF (10 ml) was stirred under an H_2 atmosphere for 2 h. The Pd catalyst was filtered off, and the solution was evaporated *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 10% EtOAc in hexane afforded **3b** (1.00 g, quant.) as a colorless oil: IR (neat) cm^{-1}: 1720, 1700. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 3.64 (3H, s), 2.96 (2H, s), 2.14 (6H, s), 1.98 (2H, m), 1.51 (1H, m), 0.93 (2H, m), 0.87 (6H, d, J=6.6 Hz). FAB-MS *m/z*: 243 (M^++H).

Methyl 3,3-Diisopropenyl-6-methyl-5-heptenoate (4a) A solution of **3a** (6.00 g, 25 mmol) in THF (100 ml) was added dropwise to a vigorously stirred suspension of Nysted reagent (20% suspension in THF, 148 g) in THF (100 ml) at −78 °C, and stirred for 15 min. Then, $TiCl_4$ (5.6 ml) was added dropwise to the stirred mixture at −78 °C, and then the whole was warmed to room temperature, and stirred for a further 30 min. The mixture was diluted with water, and extracted with EtOAc. The 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 (1% EtOAc in hexane) to give **4a** (4.40 g, 74%) as a colorless oil: IR (neat) cm^{-1}: 1735, 1635. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.96 (2H, s), 4.95 (1H, m), 4.79 (2H, s), 3.58 (3H, s), 2.58 (2H, s), 2.48 (2H, br d, J=6.9 Hz), 1.70 (3H, br s), 1.66 (3H, br s), 1.62 (6H, br s). FAB(+)HRMS *m/z*: 237.1851 (Calcd for $C_{15}H_{25}O_2$ (M^++H): 237.1854).

Methyl 3,3-Diisopropenyl-6-methylheptanoate (4b) Compound **4b** was prepared from **3b** in a similar manner to that described for the preparation of **4a**: 60% yield; a colorless oil; IR (neat) cm^{-1}: 1740, 1635. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.95 (2H, m), 4.77 (2H, br s), 3.59 (3H, s), 2.61 (2H, s), 1.68 (2H, m), 1.60 (6H, br s), 1.52 (1H, m), 1.05 (2H, m), 0.90 (6H, d, J=6.9 Hz). FAB(+)HRMS *m/z*: 239.2006 (Calcd for $C_{15}H_{27}O_2$ (M^++H): 239.2011).

3,3-Diisopropenyl-6-methyl-5-hepten-1-ol (5a) A solution of **4a** (5.90 g, 25 mmol) in ether (50 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (950 mg, 25 mmol) in ether (150 ml) at room temperature, and stirred for 5 h. The reaction was quenched with EtOAc and H_2O, then filtered through celite, and the filtrate dried over $MgSO_4$. Removal of the solvent afforded an oily residue, which was purified by column chromatography on silica gel (4% EtOAc in hexane) to give **5a** (4.70 g, 91%) as a colorless oil: IR (neat) cm^{-1}: 3320 (br), 1635. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.97 (2H, m), 4.94 (1H, m), 4.86 (2H, br s), 3.52 (2H, t, J=7.4 Hz), 2.25 (2H, br d, J=6.6 Hz), 1.83 (2H, t, J=7.4 Hz), 1.69 (3H, br s), 1.63 (3H, br s), 1.58 (6H, br s), 1.42 (1H, br). FAB-MS *m/z*: 231 (M^++Na), 207 (M^+−H).

3,3-Diisopropenyl-6-methyl-1-heptanol (5b) Compound **5b** was prepared from **4b** in a similar manner to that described for the preparation of **5a**: 74% yield; a colorless oil; IR (neat) cm^{-1}: 3320 (br), 1630. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.96 (2H, m), 4.85 (2H, br s), 3.54 (2H, t, J=7.4 Hz), 1.86 (2H, t, J=7.4 Hz), 1.57 (6H, br s), 1.41—1.60 (4H, m), 0.97 (2H, m), 0.89 (6H, d, J=6.6 Hz). EI-MS *m/z*: 210 (M^+, 3), 195 (44), 165 (24), 151 (22), 139 (100).

3,3-Diisopropenyl-6-methyl-5-heptenal (6a) A mixture of **5a** (1.04 g, 5.00 mmol), PCC (1.10 g, 5.10 mmol), and NaOAc (100 mg, 1.20 mmol) in CH_2Cl_2 (30 ml) was stirred at room temperature for 3 h. The mixture was diluted with ether, and filtered through florisil to remove chromate. The filtrate was concentrated *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 2% ether in pentane afforded **6a** (824 mg, 80%) as a colorless oil: IR (neat) cm^{-1}: 1720, 1635. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 9.59 (1H, t, J=3.0 Hz), 5.04 (2H, br s), 4.96 (1H, dm, J=7.0 Hz), 4.86 (2H, br s), 2.49 (2H, d, J=3.0 Hz), 2.41 (2H, br d, J=7.0 Hz), 1.70 (3H, br s), 1.63 (6H, br s), 1.62 (3H, br s). FAB(+)HRMS *m/z*: 207.1751 (Calcd for $C_{14}H_{23}O_1$ (M^++H): 207.1749.

3,3-Diisopropenyl-6-methylheptanal (6b) Compound **6b** was prepared from **5b** in a similar manner to that described for the preparation of **6a**: 83% yield; a colorless oil; IR (neat) cm^{-1}: 1720, 1630. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 9.58 (1H, t, J=3.0 Hz), 5.03 (2H, m), 4.84 (2H, br s), 2.54 (2H, d,

J=3.0 Hz), 1.65 (2H, m), 1.61 (6H, br s), 1.50 (1H, m), 1.01 (2H, m), 0.88 (6H, d, J=6.6 Hz). EI-MS m/z: 208 (M^+, 2), 193 (4), 190 (6), 175 (5), 168 (23), 151 (35), 137 (100). HRMS m/z: 208.1830 (Calcd for $C_{14}H_{24}O$ (M^+): 208.1827).

(3*RS*,4*SR*)-(±)-3-Isopropenyl-3-(3-methyl-2-butenyl)-4-methylcyclopetanone (7a) A solution of **6a** (103 mg, 0.50 mmol) in CH_2Cl_2 (2 ml) was added dropwise to a stirred solution of $Rh(PPh_3)_3Cl$ (231 mg, 0.25 mmol) in CH_2Cl_2 (3 ml), and the solution was stirred overnight at room temperature. Removal of the solvent afforded a residue, which was dissolved in ether (30 ml), and the precipitated Rh-complex was filtered off. After removal of ether, the oily residue was purified by column chromatography on silica gel to afford (±)-**7a** (99 mg, 96%, *cis*/*trans*=91/9) as a colorless oil: IR (neat) cm^{-1}: 1740, 1640. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.94 (1H, br s), 4.89 (1H, m), 4.61 (1H, br s), 2.62 (1H, dd, J=7.9, 18.8 Hz), 2.41 (1H, d, J=17.8 Hz), 2.20—2.32 (2H, m), 1.95—2.13 (3H, m), 1.74 (3H, br s), 1.67 (3H, br s), 1.54 (3H, br s), 0.89 (3H, d, J=6.9 Hz). ^{13}C-NMR (125.7 MHz, $CDCl_3$) δ: 218.9, 146.0, 134.0, 119.6, 112.7, 52.2, 45.1, 44.5, 37.5, 34.8, 25.9, 19.5, 18.0, 17.5. EI-MS m/z: 206 (M^+, 6), 163 (11), 150 (6), 138 (18), 123 (16), 109 (26), 95 (31), 69 (100). HRMS m/z: 206.1666 (Calcd for $C_{14}H_{22}O$ (M^+): 206.1671.

(3*RS*,4*SR*)-(±)-3-Isoamyl-3-isopropenyl-4-methylcyclopetanone (7b) Cyclization of **6b** by $Rh(PPh_3)_3Cl$ afforded **7b** in 86% yield (*cis*/*trans*=88/12): a colorless oil; IR (neat) cm^{-1}: 1745, 1640. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.92 (1H, br s), 4.61 (1H, br s), 2.58 (1H, dd, J=7.9, 19.0 Hz), 2.47 (1H, d, J=17.8 Hz), 2.25 (1H, m), 2.11 (1H, d, J=19.0 Hz), 1.98 (1H, dm, J=17.8 Hz), 1.71 (3H, br s), 1.60 (1H, m), 1.44 (1H, m), 1.24 (1H, m), 0.90—0.99 (2H, m), 9.93 (3H, d, J=6.6 Hz), 0.83—0.90 (6H, m). ^{13}C-NMR (125.7 MHz, $CDCl_3$) δ: 218.9, 146.1, 112.7, 51.8, 44.9, 44.5, 38.5, 34.4, 33.5, 28.4, 22.7, 22.4, 19.4, 17.5. EI-MS m/z: 208 (M^+, 2), 152 (4), 138 (21), 123 (23), 95 (16), 82 (100). HRMS m/z: 208.1827 (Calcd for $C_{14}H_{24}O$ (M^+): 208.1827).

(3*S*,4*S*)-(−)-3-Isopropenyl-3-(3-methyl-2-butenyl)-4-methylcyclopentanone (−)-(8a)[8] A solution of Rh[(NBD)(*R*)-BINAP]ClO_4 (23 mg, 0.025 mmol) in CH_2Cl_2 (4 ml) was stirred under an 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 **6a** (103 mg, 0.50 mmol) in CH_2Cl_2 (3 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 2 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 the solvent, the residue was purified by column chromatography on silica gel to give (−)-**8a** (101 mg, 98%, *cis*/*trans*=2/98) as a colorless oil: $[\alpha]_D^{30}$ −16.17° (c=1.45, $CHCl_3$). IR (neat) cm^{-1}: 1735, 1630. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.92—5.02 (2H, m), 4.74 (1H, br s), 2.50 (1H, dd, J=8.5, 19.0 Hz), 2.38—2.45 (2H, m), 2.31 (1H, dd, J=5.9, 15.2 Hz), 2.22 (1H, d, J=18.3 Hz), 2.07 (1H, dd, J=7.9, 15.2 Hz), 1.93 (1H, dd, J=6.5, 19.0 Hz), 1.77 (3H, br s), 1.67 (3H, br s), 1.58 (3H, br s), 1.07 (3H, d, J=6.9 Hz). ^{13}C-NMR (125.7 MHz, $CDCl_3$) δ: 218.6, 147.3, 133.4, 120.3, 112.5, 50.5, 47.6, 44.9, 36.6, 30.7, 25.9, 20.3, 18.0, 15.6. EI-MS m/z: 206 (M^+, 18), 163 (27), 137 (25), 123 (18), 109 (35), 95 (37), 69 (100). HRMS m/z: 206.1669 (Calcd for $C_{14}H_{22}O$ (M^+): 206.1671).

(3*R*,4*R*)-(+)-3-Isopropenyl-3-(3-methyl-2-butenyl)-4-methylcyclopentanone (+)-(8a) Cyclization of **6a** by Rh[(*S*)-BINAP]ClO_4 afforded (+)-**8a** in 96% yield (*cis*/*trans*=2/98). $[\alpha]_D^{26}$ +16.23° (c=1.13, $CHCl_3$).

Determination of Enantiomeric Excess of 8a The enantiomeric excesses of **8a** were determined from the ^{1}H-NMR spectra of the acetals derived from (*R*,*R*)-2,3-butandiol. A mixture of cyclopentanone **8a** (15 mg, 0.07 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 in a 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. The ^{1}H-NMR spectrum of the butanediol acetal of (−)-**8a** cyclized by Rh[(*R*)-BINAP]ClO_4 showed olefinic proton signals at δ 4.77 (br s) and 4.74 (br s) in the ratio of 2 to 28, while that from (+)-**8a** cyclized by Rh[(*S*)-BINAP]ClO_4 showed olefinic signals at δ 4.77 (br s) and 4.74 (br s) in the ratio of 30 to 3.

(3*S*,4*S*)-(−)-3-Isoamyl-3-isopropenyl-4-methylcyclopentanone (−)-(8b) Cyclization of **6b** by Rh[(*R*)-BINAP]ClO_4 afforded (−)-**8b** in 88% yield (*cis*/*trans*=4/96). $[\alpha]_D^{25}$ −81.92° (c=1.43, $CHCl_3$). IR (neat) cm^{-1}: 1745, 1635. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 4.92 (1H, br s), 4.68 (1H, br s), 2.45—2.55 (2H, m), 2.38 (1H, m), 2.16 (1H, dd, J=1.2, 18.3 Hz), 1.85 (1H, dm, J=18.3 Hz), 1.75 (3H, br s), 1.61 (1H, td, J=6.6, 15.2 Hz), 1.47 (1H, m), 1.32 (1H, td, J=6.6, 15.2 Hz), 1.04 (3H, d, J=6.9 Hz), 0.90—1.01 (2H, m), 0.88 (3H, d, J=6.6 Hz), 0.86 (3H, d, J=6.6 Hz). ^{13}C-NMR (125.7 MHz, $CDCl_3$) δ: 218.6, 147.5, 112.6, 50.4, 46.7, 45.0, 36.1, 34.1, 30.9, 28.6, 22.7, 22.5, 19.9, 16.2. EI-MS m/z: 208 (M^+, 3), 165 (3), 152 (6), 138 (22), 123 (28), 110 (9), 95 (14), 82 (100). HRMS m/z: 208.1835 (Calcd for $C_{14}H_{24}O$ (M^+): 208.1827).

(3*R*,4*R*)-(+)-3-Isoamyl-3-isopropenyl-4-methylcyclopentanone (+)-(8b) Cyclization of **6b** by Rh[(*S*)-BINAP]ClO_4 afforded (+)-**8b** in 90% yield (*cis*/*trans*=3/97). $[\alpha]_D^{25}$ +83.13° (c=1.15, $CHCl_3$).

Determination of Enantiomeric Excess of 8b The ^{1}H-NMR spectrum of the (*R*,*R*)-2,3-butanediol acetal of (−)-**8b** cyclized by Rh[(*R*)-BINAP]-ClO_4 showed olefinic proton signals at δ 4.78 (br s) and 4.76 (br s) in the ratio of 2 to 24, while that from (+)-**8b** cyclized by Rh[(*S*)-BINAP]ClO_4 showed olefinic signals at δ 4.78 (br s) and 4.76 (br s) in the ratio of 27 to 2. The enantiomeric excesses were also supported by the ^{13}C-NMR spectra. (*R*,*R*)-2,3-Butanediol acetal of (−)-**8b**: ^{13}C-NMR (125.7 MHz, $CDCl_3$, major peaks) δ: 148.9, 115.4, 110.9, 78.3, 78.0, 51.3, 47.1, 45.7, 39.7, 34.0, 29.2, 28.8, 22.8, 22.7, 20.8, 17.2, 17.1, 15.0. (*R*,*R*)-2,3-Butanediol acetal of (+)-**8b**: ^{13}C-NMR (125.7 MHz, $CDCl_3$, major peaks) δ: 148.8, 115.7, 111.1, 78.2, 77.9, 51.4, 46.8, 45.5, 39.2, 34.0, 30.4, 28.8, 22.7, 22.7, 20.6, 17.3, 17.2, 15.3.

(3*S*,4*S*)-3-Isoamyl-3-isopropyl-4-methylcyclopentanone (9) A suspension of (−)-**8a** (41.4 mg, 0.20 mmol) and 10% Pd-C (80 mg) in MeOH (6 ml) was stirred under an H_2 atmosphere for 2 h. The Pd catalyst was filtered off, and the filtrate was concentrated *in vacuo* to leave an oily residue, which was purified by column chromatography on silica gel. The fraction eluted with 2% EtOAc in hexane afforded **9** (34 mg, 80%) as a colorless oil: $[\alpha]_D^{26}$ +49.51° (c=1.15, $CHCl_3$). IR (neat) cm^{-1}: 1730. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.93—2.49 (4H, m), 1.81 (1H, m), 1.11—1.59 (4H, m), 1.07 (3H, d, J=6.9 Hz), 0.95—1.00 (2H, m), 0.87—0.94 (12H, m). EI-MS m/z: 210 (M^+, 10), 195 (6), 167 (18), 139 (19), 111 (19), 97 (31), 84 (40), 69 (100). HRMS m/z: 210.1980 (Calcd for $C_{14}H_{26}O$ (M^+): 210.1984). Compound (−)-**8b** was also converted into **9** (78%) in the similar conditions: $[\alpha]_D^{28}$ +52.52° (c=1.30, $CHCl_3$).

References and Notes

1) Corey E. J., Guzman-Perez A., *Angew. Chem. Int. Ed.*, **37**, 388—401 (1998).
2) *a*) Sakai K., Ide J., Oda O., Nakamura N., *Tetrahedron Lett.*, **13**, 1287—1290 (1972); *b*) Taura Y., Tanaka M., Wu X.-M., Funakoshi K., Sakai K., *Tetrahedron*, **47**, 4879—4888 (1991); *c*) K., *J. Sakai*, *Synth. Org. Chem.* (Jpn), **51**, 733—743 (1993); *d*) Fujio M., Tanaka M., Wu X. M., Funakoshi K., Sakai K., Suemune H., *Chem. Lett.*, **1998**, 881—882.
3) Wu X.-M., Funakoshi K., Sakai K., *Tetrahedron Lett.*, **34**, 5927—5930 (1993).
4) 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.*, 5806—5816 (2000).
5) *a*) Ducray P., Rousseau B., Mioskowski C., *J. Org. Chem.*, **64**, 3800—3801 (1999); *b*) Bosnich B., *Acc. Chem. Res.*, **31**, 667—674 (1998); *c*) Barnhart R. W., McMorran D. A., Bosnich B., *Chem. Commun.*, **1997**, 589—590.
6) Koga I., Funakoshi K., Matsuda A., Sakai K., *Tetrahedron Asym.*, **4**, 1857—1868 (1993).
7) Nysted reagent is commercially available from Aldrich Co.: Matsubara S., Sugihara M., Utimoto K., *Synlett*, **1998**, 313—315.
8) The absolute configuration of products was assumed based on the plausible intermediates and the previous results of Rh-catalyzed cyclizations.