# Stereochemistry in Palladium-Catalyzed Cyclization Forming a Vinyldihydrofuran via a π-Allylpalladium Intermediate

Tamio Hayashi,* Masaki Yamane, and Akira Ohno

*Department of Chemistry, Faculty of Science, Kyoto University, Sakyo, Kyoto 606-01, Japan*

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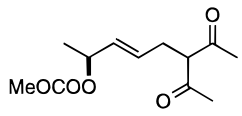
We have previously reported that the reaction of dimethyl (*Z*)-2-butenylene dicarbonate (**1**) with acetylacetone (**2a**) or methyl acetylacetate (**2b**) in the presence of a palladium catalyst coordinated with a chiral ferrocenylbisphosphine or ruthenocenylbisphosphine ligand forms optically active vinyldihydrofuran **3** in up to 86% ee[1,2] (Scheme 1). The cyclization proceeds successively through two π-allylpalladium(II) intermediates **4** and **6**. Thus, oxidative addition of dicarbonate **1** to a palladium(0) species forms the first π-allylpalladium intermediate **4**, which undergoes nucleophilic attack of the enolate anion of **2** to give the carbon−carbon bond formation product **5**. Cyclization by the intramolecular attack of enolate oxygen on the π-allyl takes place on the second π-allylpalladium intermediate **6**, which is formed by the oxidative addition of monocarbonate **5** to palladium(0).

The stereochemical pathway of the palladium-catalyzed allylic substitution reactions has been studied in reactions with several kinds of nucleophiles.[3,4] The oxidative addition forming π-allylpalladium usually proceeds with inversion of configuration at the stereogenic allylic carbon,[3−5] while the stereochemistry at the nucleophilic substitution of the π-allylpalladium is dependent upon the nature of the nucleophile.[3,6] Here we report that the intramolecular attack of enolate oxygen on the π-allylpalladium, which is the second nucleophilic attack forming **3** from **6** in Scheme 1, proceeds with inversion of configuration at the π-allyl carbon.

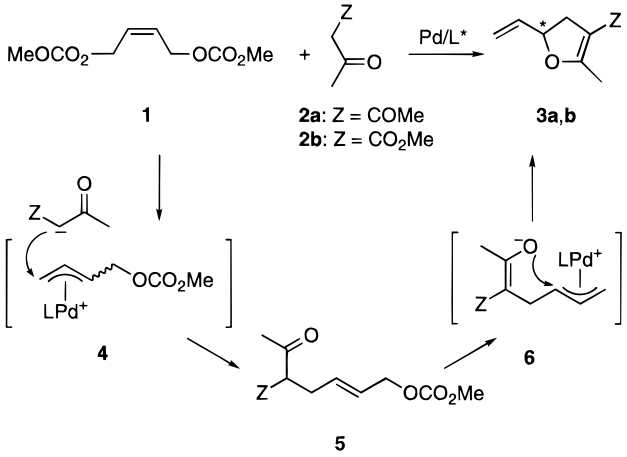
For the stereochemical studies on the intramolecular allylic substitution reaction, we have designed an enantiomeric system. Enantiomerically pure allylic monocarbonate (*S*)-**7**, which is similar to the intermediate **5a**



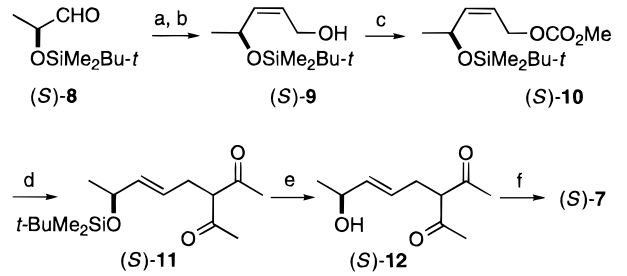

(*S*)-**7**

but has a stereogenic carbon center at the α-position, was used as a starting substrate. The π-allylpalladium intermediate formed from (*S*)-**7** should contain two different substituents at the 1 and 3 positions and hence does not undergo racemization under usual reaction conditions.[3,4]

**Scheme 1**




**Scheme 2**[a]




[a] (a) $Ph_3P{=}CHCO_2Me$, MeOH, 0 °C, 7.5 h; (b) DIBALH, $CH_2Cl_2$, rt, 14 h; (c) $ClCO_2Me$, pyridine, DMAP, THF, rt, 17 h; (d) $Pd_2(dba)_3{\cdot}CHCl_3$, dppf, acetylacetone, rt, 2.5 h; (e) 46% HF aq, MeCN, rt, 3.5 h; (f) $ClCO_2Me$, pyridine, DMAP, $CH_2Cl_2$, rt, 40 h.

The optically active allylic carbonate (*S*)-**7** was prepared from (*S*)-2-((*tert*-butyldimethylsilyl)oxy)propanal[7] (**8**) (>99% ee) by a sequence of reactions shown in Scheme 2. Thus, the Wittig olefination of aldehyde (*S*)-**8** with ((methoxycarbonyl)methylene)triphenylphosphorane followed by reduction of the ester with diisobutylaluminum hydride gave allylic alcohol (*S*)-**9**. Treatment of (*S*)-**9** with methyl chloroformate and pyridine followed by palladium-catalyzed allylic alkylation of the resulting carbonate (*S*)-**10** with acetylacetone gave alkylation product (*S*)-**11**, where the carbon−carbon double bond is *trans*. Silyl ether was converted into carbonate by deprotection of the silyl ether with hydrofluoric acid in acetonitrile followed by esterification with methyl chloroformate to give allylic monocarbonate (*S*)-**7**.

Allylic carbonate (*S*)-**7** was subjected to the palladium-catalyzed intramolecular substitution reaction (Scheme 3). Thus, (*S*)-**7** was treated with 2 mol % of a palladium(0) catalyst generated from tris(dibenzylideneacetone)dipalladium(0) and 1,1′-bis(diphenylphosphino)ferrocene (dppf)[8] in THF at 60 °C for 15 h. Evaporation of the solvent followed by silica gel column chromatography gave 98% yield of 2-(1-propenyl)-4-acetyl-5-methyl-2,3-dihydrofuran (**13**) which consists of (*E*)- and (*Z*)-isomers

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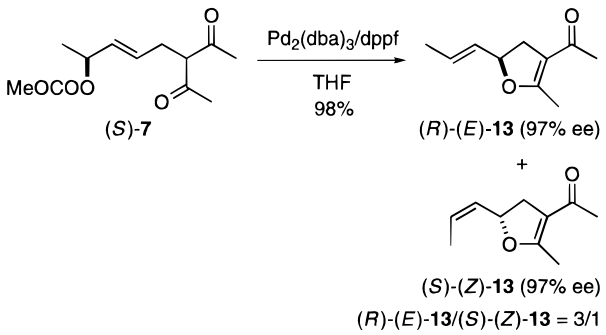
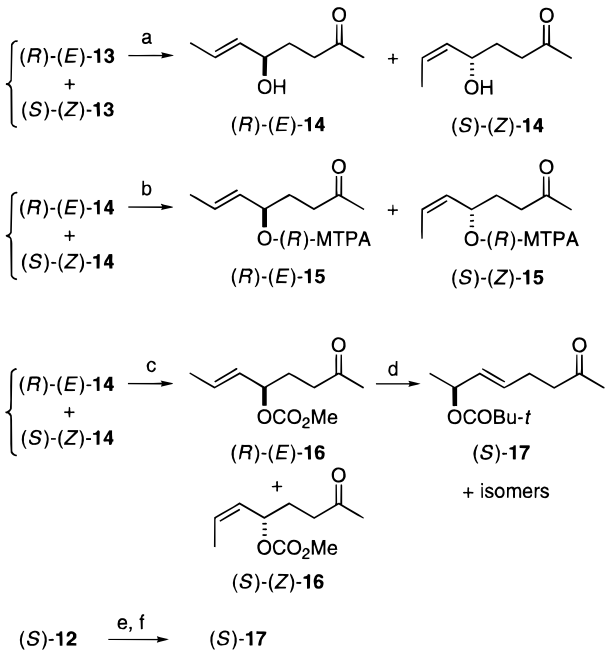
**Scheme 3**



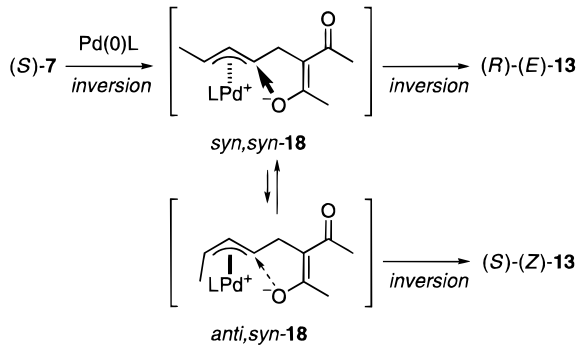

**Scheme 4**[a]




[a] (a) 50% KOH aq, MeOH, reflux, 2.5 h; (b) (*R*)-MTPA chloride, pyridine, DMAP, $CH_2Cl_2$, rt, 45 h; (c) $ClCO_2Me$, pyridine, DMAP, $CH_2Cl_2$, rt, 4 h; (d) $[PdCl(\pi\text{-}C_3H_5)]_2$, dppf, $Hex_4NBr$, $Me_3CCOONa$, THF, 60 °C, 1 h; (e) NaOMe, MeOH, reflux, 1.5 h; (f) $Me_3CCOCl$, pyridine, $CH_2Cl_2$, rt, 1.5 h.

in a ratio of 3 to 1. Both isomers, (*E*)-**13** and (*Z*)-**13**, were determined to have 97% enantiomeric purity by GLC analysis with a chiral stationary phase column. The absolute configurations of (*E*)-**13** and (*Z*)-**13** were assigned to be (*R*) and (*S*), respectively, by Mosher's method[9] using 2-methoxy-2-phenyl-2-(trifluoromethyl)-acetic acid (MTPA) esters. Thus, alkaline hydrolysis and deacetylation of (*E*)-**13** and (*Z*)-**13** by treatment with aqueous potassium hydroxide in methanol followed by esterification of the resulting allylic alcohols **14** with (*R*)-MTPA chloride gave (*R*)-(*E*)-**15** and (*S*)-(*Z*)-**15** (see Experimental Section). The absolute configurations of **13** were confirmed by converting them into (*S*)-7-((2,2-dimethylpropanoyl)oxy)-(*E*)-5-octen-2-one (**17**) ($[\alpha]^{20}_D$ = −19.0 (*c* 0.3, chloroform)) (Scheme 4). Thus, the alcohols **14** were esterified into methyl carbonate **16**, which was then subjected to allylic transposition with sodium pivalate catalyzed by palladium(0)[10] to give (−)-(*E*)-**17** together with a minor amount of its (*Z*)-isomer and regioisomers. The 1,3-rearrangement is known to proceed with net retention of configuration, the incoming nucleophile, pivalate in this case, attacking the $\pi$-allylpalladium intermediate from the same side as the leaving group.[10] The authentic sample of (*S*)-(−)-**17** ($[\alpha]^{20}_D$ = −22.2 (*c* 1.8, chloroform)) was obtained by deacetylation of (*S*)-**12** followed by pivalate ester formation. The enantiomeric purity (97% ee) of (*R*)-(*E*)-**13** and (*S*)-(*Z*)-**13** indicates that the palladium-catalyzed cyclization of (*S*)-**7** proceeded with high stereoselectivity. Almost the same stereochemical outcome was observed in cyclization catalyzed by a palladium complex coordinated with 1,2-bis(diphenylphosphino)butane (dppb), which gave (*R*)-(*E*)-**13** of 97% ee and (*S*)-(*Z*)-**13** of 97% ee in a ratio of 4 to 1 (80% yield).

**Scheme 5**




The stereochemical outcome observed here can be visualized by the mechanism shown in Scheme 5, where the $\pi$-allylpalladium intermediate *syn*,*syn*-**18**, formed by oxidative addition of allylic carbonate (*S*)-**7** to palladium(0) with inversion,[3−5] undergoes nucleophilic attack of enolate oxygen with inversion at the $\pi$-allyl carbon[11] to result in dihydrofuran (*R*)-(*E*)-**13** with net retention of configuration. Thus, the intramolecular attack of enolate oxygen on $\pi$-allylpalladium was demonstrated to take place from the side opposite to palladium. The isomerization of $\pi$-allylpalladium intermediate from *syn*,*syn*-**18** to *anti*,*syn*-**18** by the $\pi-\sigma-\pi$ mechanism, where palladium transfers from α-face to $\beta$-face, followed by nucleophilic attack of enolate oxygen from the side opposite to palladium gives (*S*)-(*Z*)-**13** as a minor product.

## Experimental Section

**(*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-(*Z*)-2-penten-1-ol (9).** To a solution of 8.04 g (44.6 mmol) of (*S*)-2-((*tert*-butyldimethylsilyl)oxy)propanal (**8**)[7] in 160 mL of methanol was added at 0 °C 22.4 g (66.9 mmol) of ((methoxycarbonyl)methylene)triphenylphosphorane, and the mixture was stirred at the same temperature for 7.5 h. Evaporation of the solvent followed by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave 10.7 g (43.9 mmol) of crude methyl (*S*)-4-((*tert*-butyldimethylsilyl)oxy)-(*Z*)-2-pentenoate, which was used for the subsequent reduction without further purification. $^1$H NMR ($CDCl_3$): $\delta$ 0.03 (s, 3 H), 0.05 (s, 3 H), 0.88 (s, 9 H), 1.25 (d, $J$ = 6.7 Hz, 3 H), 3.71 (s, 3 H), 5.44 (dqd, $J$ = 1.3, 6.7, 7.6 Hz, 1 H), 5.67 (dd, $J$ = 1.3, 11.9 Hz, 1 H), 6.22 (dd, $J$ = 7.6, 11.9 Hz, 1 H). To a dichloromethane (100 mL) solution of the methyl ester obtained above was added at 0 °C a solution of 129 mmol of diisobutylaluminum hydride in hexane (1.01 M, 128 mL). After

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the mixture was stirred at rt for 14 h, it was diluted with ether and the reaction was quenched with methanol. Filtration through a pad of Celite, evaporation of the solvent, and silica gel column chromatography (hexane/ethyl acetate = 1/1) gave 6.84 g (71%) of (*S*)-4-((*tert*-butyldimethylsilyl)oxy)-(*Z*)-2-penten-1-ol (**9**). $[\alpha]^{20}_D = +47.4$ (*c* 0.3, chloroform). $^1$H NMR: $\delta$ 0.06 (s, 3 H), 0.07 (s, 3 H), 0.88 (s, 9 H), 1.22 (d, $J$ = 6.3 Hz, 3 H), 1.83 (bs, 1 H), 4.09−4.31 (m, 2 H), 4.58 (quint, $J$ = 6.3 Hz, 1 H), 5.47−5.60 (m, 2 H). Anal. Calcd for $C_{11}H_{24}O_2Si$: C, 61.06; H, 11.18. Found: C, 61.00; H, 11.39.

**Methyl (*S*)-4-((*tert*-Butyldimethylsilyl)oxy)-(*Z*)-2-pentenyl Carbonate (10).** To a solution of 6.84 g (31.6 mmol) of (*S*)-**9** in 40 mL of THF were added successively at 0 °C 4.0 mL (49 mmol) of pyridine, a catalytic amount of DMAP, and 3.0 mL (39 mmol) of methyl chloroformate. The mixture was stirred at rt for 17 h. Saturated sodium bicarbonate solution was added, and it was extracted with ether. The organic phase was washed with aqueous cupric sulfate and water, dried over anhydrous sodium sulfate, and evaporated. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1) to give 6.56 g (76%) of methyl (*S*)-4-((*tert*-butyldimethylsilyl)-oxy)-(*Z*)-2-pentenyl carbonate (**10**). $^1$H NMR: $\delta$ 0.04 (s, 3 H), 0.05 (s, 3 H), 0.87 (s, 9 H), 1.21 (d, $J$ = 6.3 Hz, 3 H), 3.79 (s, 3 H), 4.60−4.78 (m, 2 H), 4.71 (dqd, $J$ = 1.3, 6.3, 6.9 Hz, 1 H), 5.45 (tdd, $J$ = 1.0, 6.9, 11.2 Hz, 1 H), 5.67 (dtd, $J$ = 1.3, 7.9, 11.2 Hz, 1 H). Anal. Calcd for $C_{13}H_{26}O_4Si$: C, 56.90; H, 9.55. Found: C, 57.11; H, 9.68.

**(*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-3-acetyl-(*E*)-5-octen-2-one (11).** A solution of 174 mg (0.168 mmol) of tris(dibenzylideneacetone)dipalladium·$CHCl_3$ and 223 mg (0.402 mmol) of 1,1′-bis(diphenylphosphino)ferrocene (dppf) in 20 mL of THF was kept stirring at rt for 20 min. To the resulting yellow solution were added 1.70 mL (16.5 mmol) of acetylacetone and 2.05 g (7.47 mmol) of (*S*)-**10**, and the mixture was stirred at rt for 2.5 h. Water was added, and the aqueous layer was extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to give 1.00 g (43%) of (*S*)-7-((*tert*-butyldimethylsilyl)oxy)-3-acetyl-(*E*)-5-octen-2-one (**11**). $[\alpha]^{20}_D = -13.9$ (*c* 0.29, chloroform). $^1$H NMR shows that **11** exists as keto and enol forms (keto/enol = 7/5) in $CDCl_3$. $^1$H NMR: $\delta$ 0.02 (s, $^7/_{12} \times 3$ H), 0.03 (s, $^5/_{12} \times 6$ H), 0.04 (s, $^7/_{12} \times 3$ H), 0.88 (s, $^5/_{12} \times 9$ H), 0.89 (s, $^7/_{12} \times 9$ H), 1.16 (d, $J$ = 6.5 Hz, $^5/_{12} \times 3$ H), 1.18 (d, $J$ = 6.5 Hz, $^7/_{12} \times 3$ H), 2.10 (s, $^7/_{12} \times 6$ H), 2.17 (s, $^5/_{12} \times 6$ H), 2.56 (t, $J$ = 7.3 Hz, $^7/_{12} \times 2$ H), 2.94 (d, $J$ = 5.0 Hz, $^5/_{12} \times 2$ H), 3.68 (t, $J$ = 7.5 Hz, $^7/_{12} \times 1$ H), 4.22 (quint, $J$ = 6.5 Hz, $^7/_{12} \times 1$ H), 4.28 (quint, $J$ = 6.5 Hz, $^5/_{12} \times 1$ H), 5.44 (dd, $J$ = 6.5, 15.0 Hz, $^7/_{12} \times 1$ H), 5.45 (dd, $J$ = 6.5, 15.0 Hz, $^5/_{12} \times 1$ H), 5.56 (td, $J$ = 5.0, 15.0 Hz, $^5/_{12} \times 1$ H), 5.57 (td, $J$ = 7.3, 15.0 Hz, $^7/_{12} \times 1$ H). Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13. Found: C, 64.00; H, 10.27.

**(*S*)-7-Hydroxy-3-acetyl-(*E*)-5-octen-2-one (12).** To 4 mL of an acetonitrile solution of 1.00 g (3.19 mmol) of (*S*)-**11** was added 0.41 mL of 46% hydrofluoric acid, and the mixture was stirred at rt for 3.5 h. Saturated sodium hydrocarbonate solution was added, and the aqueous layer was extracted with ether. The ether extracts were dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (hexane/ethyl acetate = 1/1) to give 550 mg (94%) of (*S*)-7-hydroxy-3-acetyl-(*E*)-5-octen-2-one (**12**). $[\alpha]^{20}_D = -21.8$ (*c* 0.2, chloroform). $^1$H NMR shows that **12** exists as keto and enol forms (keto/enol = 7/5) in $CDCl_3$. $^1$H NMR: $\delta$ 1.23 (d, $J$ = 6.0 Hz, $^9/_{14} \times 3$ H), 1.26 (d, $J$ = 6.0 Hz, $^5/_{14} \times 3$ H), 2.11 (s, $^5/_{14} \times 6$ H), 2.18 (s, $^9/_{14} \times 6$ H), 2.57 (t, $J$ = 7.0 Hz, $^9/_{14} \times 2$ H), 2.97 (d, $J$ = 5.5 Hz, $^5/_{14} \times 2$ H), 3.70 (t, $J$ = 7.0 Hz, $^9/_{14} \times 1$ H), 4.24 (m, $^9/_{14} \times 1$ H), 4.31 (m, $^5/_{14} \times 1$ H), 5.51 (td, $J$ = 5.5, 16.0 Hz, $^5/_{14} \times 1$ H), 5.52 (td, $J$ = 7.0, 16.0 Hz, $^9/_{14} \times 1$ H), 5.60 (dd, $J$ = 5.5, 16.0 Hz, $^9/_{14} \times 1$ H), 5.66 (dd, $J$ = 5.5, 16.0 Hz, $^5/_{14} \times 1$ H). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.01; H, 8.60.

**Methyl (*S*)-3-Acetyl-2-oxo-(*E*)-5-octen-7-yl Carbonate (7).** To a dichloromethane solution of 45.3 mg (0.246 mmol) of (*S*)-**12**, 0.065 mL (0.804 mmol) of pyridine, and 8.3 mg (0.068 mmol) of DMAP was added 0.047 mL (0.53 mmol) of methyl chloroformate at 0 °C, and the mixture was stirred at rt for 40 h. Saturated sodium hydrocarbonate solution was added, and the aqueous layer was extracted with chloroform. The chloroform extracts were washed with saturated cupric(II) sulfate solution and brine and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by preparative thin layer silica gel chromatography (hexane/ethyl acetate = 1/1) to give 50.6 mg (84%) of methyl (*S*)-3-acetyl-2-oxo-(*E*)-5-octen-7-yl carbonate (**7**). $[\alpha]^{20}_D = -59.3$ (*c* 0.70, chloroform). $^1$H NMR shows that **7** exists as keto and enol forms (keto/enol = 7/5) in $CDCl_3$. $^1$H NMR: $\delta$ 1.32 (d, $J$ = 6.9 Hz, $^1/_2 \times 3$ H), 1.35 (d, $J$ = 6.9 Hz, $^1/_2 \times 3$ H), 2.09 (s, $^1/_2 \times 6$ H), 2.17 (s, $^1/_2 \times 6$ H), 2.57 (t, $J$ = 6.6 Hz, $^1/_2 \times 2$ H), 2.98 (d, $J$ = 4.6 Hz, $^1/_2 \times 2$ H), 3.70 (t, $J$ = 7.4 Hz, $^1/_2 \times 1$ H), 3.76 (s, $^1/_2 \times 3$ H), 3.76 (s, $^1/_2 \times 3$ H), 5.11 (quint, $J$ = 6.9 Hz, $^1/_2 \times 1$ H), 5.19 (quint, $J$ = 6.9 Hz, $^1/_2 \times 1$ H), 5.46 (dd, $J$ = 15.5, 6.9 Hz, $^1/_2 \times 1$ H), 5.55 (dd, $J$ = 6.9, 15.5 Hz, $^1/_2 \times 1$ H), 5.63 (td, $J$ = 6.9, 15.5 Hz, $^1/_2 \times 1$ H), 5.76 (td, $J$ = 4.6, 15.5 Hz, $^1/_2 \times 1$ H). Anal. Calcd for $C_7H_{12}O_4$: C, 52.49; H, 7.55. Found: C, 52.53; H, 7.48.

**2-(1-Propenyl)-4-acetyl-5-methyl-2,3-dihydrofuran (13).** A solution of 7.0 mg (0.0068 mmol) of tris(dibenzylideneacetone)-dipalladium·$CHCl_3$ and 7.8 mg (0.014 mmol) of 1,1′-bis(diphenylphosphino)ferrocene (dppf) in 12 mL of THF was kept stirring at rt for 10 min. To the resulting yellow solution was added 153 mg (0.630 mmol) of (*S*)-**7**, and the mixture was stirred at 60 °C for 15 h. The catalyst was removed by short silica gel column chromatography (THF). Evaporation of the solvent followed by preparative thin layer silica gel chromatography (hexane/ethyl acetate = 3/1) gave 102 mg (98%) of 2-(1-propenyl)-4-acetyl-5-methyl-2,3-dihydrofuran (**13**) which consists of (*R*)−(*E*)- and (*S*)−(*Z*)-isomers in a ratio of 3 to 1 (for the determination of absolute configuration, see below). Specific rotation of the (*E*) and (*Z*) mixture: $[\alpha]^{20}_D = -82.6$ (*c* 0.4, chloroform). $^1$H NMR of (*E*)-**13**: $\delta$ 1.73 (dd, $J$ = 1.5, 6.5 Hz, 3 H), 2.19 (s, 3 H), 2.21 (t, $J$ = 1.5 Hz, 3 H), 2.71 (qdd, $J$ = 1.5, 8.0, 14.0 Hz, 1 H), 3.08 (qdd, $J$ = 1.5, 10.0, 14.0 Hz, 1 H), 4.99 (td, $J$ = 8.0, 10.0 Hz, 1 H), 5.58 (qdd, $J$ = 1.5, 8.0, 15.0 Hz, 1 H), 5.79 (qd, $J$ = 6.5, 15.0 Hz, 1 H). $^1$H NMR of (*Z*)-**13**: $\delta$ 1.74 (dd, $J$ = 2.0, 7.0 Hz, 3 H), 2.20 (s, 3 H), 2.22 (t, $J$ = 1.5 Hz, 3 H), 2.67 (qdd, $J$ = 1.5, 8.5, 14.0 Hz, 1 H), 3.13 (qdd, $J$ = 1.5, 10.0, 14.0 Hz, 1 H), 5.39 (ddd, $J$ = 8.5, 9.0, 10.0 Hz, 1 H), 5.58 (qdd, $J$ = 2.0, 9.0, 11.0 Hz, 1 H), 5.79 (qd, $J$ = 7.0, 11.0 Hz, 1 H). Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.46; H, 8.56. The enantiomeric purity of (*R*)-(*E*)-**13** and (*S*)-(*Z*)-**13** was determined to be 97% ee by GLC analysis with a chiral stationary phase column, CP Cyclodex $\beta$236M.

**5-Hydroxy-6-octen-2-one (14).** To a solution of 82.5 mg (0.502 mmol) of dihydrofuran **13** (*E*/*Z* = 3/1) obtained above in 2.5 mL of methanol was added 0.3 mL of 50% aqueous potassium hydroxide, and the mixture was stirred at reflux for 2.5 h. Water was added, and the aqueous layer was extracted with chloroform. The extracts were dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by preparative thin layer silica gel chromatography (hexane/ethyl acetate = 2/1) to give 59.8 mg (83%) of 5-hydroxy-6-octen-2-one (**14**) which is a mixture of (*R*)-(*E*)-**14** and (*S*)-(*Z*)-**14** in a ratio of 3 to 1. $^1$H NMR of (*E*)-**14**: $\delta$ 1.70 (dd, $J$ = 1.5, 6.5 Hz, 3 H), 1.79 (m, 2 H), 2.16 (s, 3 H), 2.55 (t, $J$ = 7.0 Hz, 2 H), 4.07 (m, 1 H), 5.47 (qdd, $J$ = 1.5, 7.0, 15.5 Hz, 1 H), 5.67 (dqd, $J$ = 1.0, 6.5, 15.5 Hz, 1 H). $^1$H NMR of (*Z*)-**14**: $\delta$ 1.67 (dd, $J$ = 1.5, 7.0 Hz, 3 H), 1.80 (m, 2H), 2.16 (s, 3 H), 2.56 (t, $J$ = 6.0 Hz, 2 H), 4.48 (m, 1 H), 5.39 (qdd, $J$ = 1.5, 8.5, 10.5 Hz, 1 H), 5.58 (dqd, $J$ = 1.0, 7.0, 10.5 Hz, 1 H). Anal. Calcd for $C_8H_{14}O_2$ C, 67.57; H, 9.92. Found: C, 67.38; H, 9.89.

**2-Oxo-6-octen-5-yl (*R*)-2-Methoxy-2-phenyl-2-(trifluoromethyl)acetate (MTPA Ester 15).** To a solution of 18.1 mg (0.127 mmol) of the mixture of (*R*)-(*E*)-**14** and (*S*)-(*Z*)-**14** (*E*/*Z* = 3/1) in 0.2 mL of dichloromethane, 0.03 mL (0.37 mmol) of pyridine, and 7.6 mg (0.063 mmol) of DMAP was added successively 0.70 mg (0.26 mmol) of (*R*)-MTPA chloride at 0 °C, and the mixture was stirred at rt for 45 h. Saturated sodium hydrocarbonate solution was added, and the aqueous layer was extracted with chloroform. The extracts were dried over anhydrous sodium sulfate and evaporated under reduced pressure. The MTPA esters (*R*)-(*E*)-**15** and (*S*)-(*Z*)-**15** (*E*/*Z* = 3/1) were obtained (45 mg, 99%) by preparative thin layer silica gel chromatography (hexane/ethyl acetate = 1/1). Comparison of $^1$H NMR specra of the MTPA esters **15** obtained from racemic alcohol **14** with the spectra of those from the optically active **14** obtained in the present studies showed that (*E*)-**15** and (*Z*)-**15** have (*R*) and (*S*) configurations, respectively. For the determi-

nation, the protons assigned to $CH_3CO-$ (s), $-COCH_2-$ (t), and $CH_3CH=$ (d) were used. Their chemical shifts for the enantiomers of (*E*)-**15** and (*Z*)-**15** are as follows. (*R*)-(*E*)-**15**: 2.04, 2.30, 1.72. (*S*)-(*E*)-**15**: 2.12, 2.44, 1.69. (*S*)-(*Z*)-**15**: 2.12, 2.46, 1.77. (*R*)-(*Z*)-**15**: 2.06, 2.32, 1.80.

**Methyl 2-Oxo-6-octen-5-yl Carbonate (16).** To a solution of 40.0 mg (0.28 mmol) of a mixture of (*R*)-(*E*)-**15** and (*S*)-(*Z*)-**15** (*E*/*Z* = 3/1) in 0.30 mL of dichloromethane were added 0.069 mL (0.85 mmol) of pyridine, 10 mg (0.80 mmol) of DMAP, and 0.054 mL (0.70 mmol) of methyl chloroformate at 0 °C. After the mixture was stirred at rt for 4 h, saturated sodium bicarbonate solution was added. The aqueous layer was extracted with chloroform. The extracts were washed with aqueous cupric sulfate and brine, dried over anhydrous sodium sulfate, and evaporated under reduced pressure. The carbonate **16** (29.7 mg, 52%) was obtained as a mixture of (*E*) and (*Z*) isomers (*E*/*Z* = 3/1) by silica gel column chromatography (hexane/ethyl acetate = 4/1). $^1$H NMR of (*R*)-(*E*)-**16**: $\delta$ 1.75 (dd, *J* = 1.5, 6.5 Hz, 3 H), 1.93 (q, *J* = 7.0 Hz, 2 H), 2.14 (s, 3 H), 2.49 (m, 2 H), 3.76 (s, 3 H), 5.02 (q, *J* = 7.0 Hz, 1 H), 5.41 (qdd, *J* = 1.5, 7.0, 14.0 Hz, 1 H), 5.79 (qd, *J* = 6.5, 14.0 Hz, 1 H). $^1$H NMR of (*S*)-(*Z*)-**16**: $\delta$ 1.74 (dd, *J* = 1.5, 7.0 Hz, 3 H), 1.96 (q, *J* = 7.0 Hz, 2 H), 2.15 (s, 3 H), 2.50 (m, 2 H), 3.76 (s, 3 H), 5.35 (qdd, *J* = 1.5, 9.0, 10.5 Hz, 1 H), 5.41 (q, *J* = 9.0 Hz, 1 H), 5.70 (qd, *J* = 7.0, 10.5 Hz, 1 H). Anal. Calcd for $C_{10}H_{16}O_4$: C, 59.99; H, 8.05. Found: C, 60.18; H, 8.17.

**(*S*)-7-((2,2-Dimethylpropanoyl)oxy)-(*E*)-5-octen-2-one (17). Method A (From 12).** To a solution of 99 mg (0.54 mmol) of (*S*)-**12** in 5.5 mL of methanol was added 13 mg (0.24 mmol) of sodium methoxide, and the mixture was heated to reflux for 1.5 h. Water was added, and the aqueous layer was extracted with ether. The extracts were dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure to give 46 mg (60%) of crude (*S*)-7-hydroxy-(*E*)-5-octen-2-one. $^1$H NMR: $\delta$ 1.25 (d, *J* = 6.3 Hz, 3 H), 1.69 (bs, 1 H), 2.15 (s, 3 H), 2.26−2.34 (m, 2 H), 2.53 (t, *J* = 7.3 Hz, 2 H), 4.26 (quint, *J* = 6.3 Hz, 1 H), 5.50−5.69 (m, 2 H). To the crude alcohol was added successively 1.2 mL of dichloromethane, 0.034 mL (0.42 mmol) of pyridine, and 0.043 mL (0.35 mmol) of pivaloyl chloride. After the mixture was stirred at rt for 1.5 h, it was evaporated under reduced pressure. Column chromatography on silica gel (hexane/ethyl acetate = 3/1) gave 71 mg (two steps, 58%) of (*S*)-7-(2,2-dimethylpropanoyl)-(*E*)-5-octen-2-one (**15**). $[\alpha]^{20}_D = -22.2$ (*c* 1.8, chloroform). $^1$H NMR: $\delta$ 1.18 (s, 9 H), 1.26 (d, *J* = 6.3 Hz, 3 H), 2.14 (s, 3 H), 2.30 (ddt, *J* = 2.3, 6.6, 7.3 Hz, 2 H), 2.51 (t, *J* = 7.3 Hz, 2 H), 5.27 (d quint, *J* = 0.7, 6.3 Hz, 1 H), 5.47 (tdd, *J* = 2.3, 6.3, 15.3 Hz, 1 H), 5.66 (dtd, *J* = 0.7, 6.6, 15.3 Hz, 1 H). Anal. Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.01; H, 9.97.

**Method B (From 16).** To a solution of 1.2 mg (0.0033 mmol) of $[PdCl(\pi\text{-}C_3H_5)]_2$, 3.7 mg (0.0067 mmol) of 1,1′-bis(diphenylphosphino)ferrocene, 76 mg (0.17 mmol) of tetrahexylammonium bromide, and 26.9 mg (0.13 mmol) of carbonate **16** in 2.0 mL of THF was added a solution of sodium pivalate (0.22 mmol) prepared from pivalic acid and sodium hydride in 2.0 mL of THF, and the mixture stirred at 60 °C for 1 h. The catalyst was removed by short silica gel column chromatography (THF). Evaporation of the solvent followed by medium-pressure silica gel chromatography (hexane/ethyl acetate = 4/1) gave 12.5 mg (41%) of (*S*)-7-(2,2-dimethylpropanoyl)-(*E*)-5-octen-2-one (**17**) ($[\alpha]^{20}_D = -19.0$ (*c* 0.3, chloroform)) and 8.7 mg (29%) of other isomers.

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