Asymmetric Hetero Diels−Alder Reaction Catalyzed by Chiral Cationic Palladium(II) and Platinum(II) Complexes

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The hetero Diels−Alder reaction of nonactivated conjugated dienes **1** with arylglyoxals **2** and glyoxylate esters **7** proceeded enantioselectively in the presence of a catalytic amount of cationic chiral BINAP−palladium or −platinum complexes and 3 Å molecular sieves (MS3A). The addition of MS3A effectively improved the enantioselectivity of the reaction. Excellent ee's were obtained from the reactions of 2,3-dimethyl-1,3-butadiene (**1a**) and 1,3-cyclohexadiene (**1d**) with dienophiles **2** and **7**. The square-planar structure of $[Pd(S\text{-BINAP})(PhCN)_2](PF_6)_2$ was determined by X-ray diffraction, and a chiral induction model involving the square-planar palladium complex coordinated with BINAP and a dienophile is proposed.

Introduction

The hetero Diels−Alder (DA) reaction of conjugated dienes with carbonyl compounds as dienophiles has been a fundamental reaction in organic chemistry.[1] The reaction between 1-methoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene (Danishefsky's diene) and aldehydes provides useful access to dihydropyranones, and several groups have reported an enantioselective catalytic version of this reaction.[2] In contrast, the reaction between nonactivated dienes and aldehydes gives dihydropyranes. In comparison with the reaction between Danishefsky's diene and aldehydes, there have been fewer reports on the asymmetric version of this reaction. Nakai and Mikami et al. first reported the asymmetric hetero DA reaction of isoprene, a nonactivated diene, with methyl glyoxylate catalyzed by a chiral BINOL-titanium complex.[3] Although the yield of the hetero DA product was rather low as a result of the predominant formation of the hetero ene product, enantioselectivity of the hetero DA product was very high. Jørgensen and co-workers reported the asymmetric hetero DA reaction of dienes with glyoxylate esters catalyzed by bisoxazoline-copper[4] and -zinc[5] complexes and BINOL-aluminum complexes,[6] which showed improved hetero DA selectivity and high enantioselectivity.

Recently, it has been recognized that certain transition metal complexes display considerable Lewis acidic character and can be used as catalysts instead of the typical Lewis acids. These complexes have a number of merits, i.e., stability to air and moisture, high turnover number, and a well-defined structure. Copper complexes with chiral oxazoline-based ligands,[4,7] η^5-cyclopentadienyl-,[2d] η^6-arene-,[8] and salen-ruthenium[9] complexes, η^5-pentamethylcyclopentadienyl rhodium complexes,[10] and DBFOX-nickel complexes[11] have been developed for use as transition-metal-based Lewis acid catalysts. Previously, we demonstrated that the hetero DA reaction of nonactivated simple dienes with aldehydes was catalyzed by cationic palladium(II) complexes, $[PdL_2(RCN)_2](BF_4)_2$, affording the corresponding 5,6-dihydro-2*H*-pyrans[12] and that a highly enantioselective DA reaction of dienes with *N*-acryloyloxazolidinone was achieved using a chiral BINAP complex, $[Pd(BINAP)(PhCN)_2](BF_4)_2$.[13] Cationic BINAP-palladium complexes have also been reported to

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Table 1. Hetero DA Reaction of 1a with 2a Catalyzed by Palladium Complexes with Various Chiral Phosphine Ligands[a]

entry	ligand (L*)	yield (%)[b]	ee (%)[c]
1	(*S*)-BINAP	69	58
2	(*S*)-TolBINAP	51	40
3	(*R*,*R*)-CHIRAPHOS	36	4
4	(−)-DIOP	35	12
5	(*S*)-(*R*)-BPPFOAc	33	1
6	(*S*)-(*R*)-BPPFA	26	1
7	(*S*)-(*R*)-BPPFOH	42	17

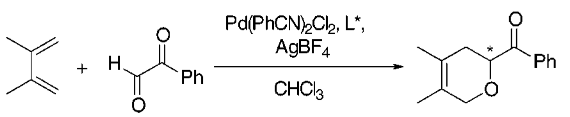
[a] Reaction conditions: **1a** (3.0 mmol), **2a** (2.0 mmol), $Pd(PhCN)_2Cl_2$ (0.04 mmol), ligand (0.04 mmol), $AgBF_4$ (0.1 mmol), 4 mL of $CHCl_3$, rt, 20 h, N_2 atmosphere. [b] Determined by GLC. [c] Determined by HPLC using Chiralpak AD, 5% *i*-PrOH in hexane.

catalyze the enantioselective addition of enol silyl ethers to aldehydes[14] and aldimines[15] with high enantioselectivity.

Herein, we report the highly enantioselective hetero DA reaction of nonactivated dienes with arylglyoxals and glyoxylate esters using cationic BINAP-palladium and -platinum complexes as a chiral catalyst. This is the first report of enantioselective cyclization of dienes with arylglyoxals yielding optically active 2-aroyl-3,6-dihydro-2*H*-pyranes.

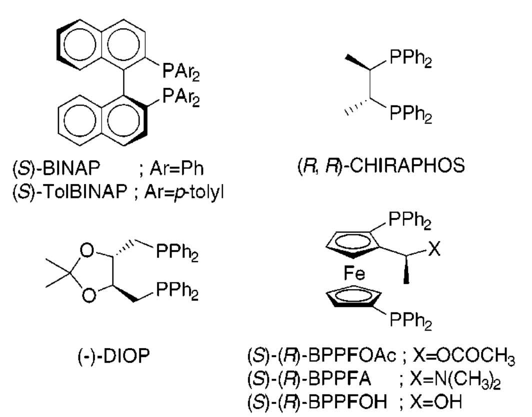
Results and Discussion

At first, a variety of chiral diphosphine ligands were tested for the cationic palladium-catalyzed hetero DA reaction of 2,3-dimethyl-1,3-butadiene (**1a**) with phenylglyoxal (**2a**) (eq 1, Table 1). The cationic complexes were



(1)

1a **2a** **3aa**



prepared in situ by mixing 2 mol % of $Pd(PhCN)_2Cl_2$, 1.0 equiv (for Pd) of the ligands, and 2.5 equiv (for Pd) of $AgBF_4$ prior to the reaction. The use of (*S*)-BINAP as the ligand of palladium gave product **3aa** in the highest yield, 69%, with the highest ee, 58% (entry 1). (*S*)-TolBINAP, which has *p*-tolyl groups attached to the phosphorus atoms instead of the phenyl groups found in (*S*)-BINAP,

Table 2. Hetero DA Reaction of 1a with 2a Catalyzed by Cationic BINAP-Palladium and -Platinum Complexes under Various Conditions[a]

entry	catalyst	additive	reaction (°C/h)	yield (%)[b]	ee (%)[c]
1	$Pd(PhCN)_2Cl_2$ (*S*)-BINAP, $AgBF_4$	none	rt/20	69	58
2	[Pd(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$	none	rt/20	54	79
3	[Pd(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$	MS3A	rt/20	67	96
4	[Pd(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$	MS3A	0/24	70	99
5	[Pt(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$	none	rt/20	54	93
6	[Pt(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$	MS3A	0/24	60	97

[a] Reaction conditions: **1a** (1.5 mmol), **2a** (1.0 mmol), catalyst (0.02 mmol), MS3A (50 mg if used), 2 mL of $CHCl_3$, N_2 atmosphere. [b] Determined by GLC. [c] Determined by HPLC using Chiralpak AD, 5% *i*-PrOH in hexane. (*R*)-Enantiomer was formed predominantly by use of (*S*)-BINAP.

gave **3aa** in lower yield and with a lower ee than (*S*)-BINAP (entry 2). Other chiral diphosphines such as (*R*,*R*)-CHIRAPHOS, (−)-DIOP, and the series of ferrocenyl phosphines gave modest yields but with very low ee's (entries 3−7).

The hetero DA reaction of **1a** with **2a** was carried out under various reaction conditions using the cationic palladium complex coordinated with (*S*)-BINAP and two benzonitriles, [Pd(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$, which was prepared separately. Results are summarized in Table 2. The *R*-enantiomer of **3aa** was formed predominantly by use of the (*S*)-BINAP complex (vide infra). The use of the isolated complex increased the ee of **3aa** to 79% from the 58% obtained by the reaction using the catalyst prepared in situ (entries 1 and 2). To further improve the enantioselectivity, the reaction was carried out in the presence of 3 Å molecular sieves (MS3A), which is known to frequently be effective in improving enantioselectivity in Lewis acid catalyzed DA and ene reactions.[3,16] MS3A is assumed to remove a trace amount of water and acidic impurities. The acidic impurities in the present reaction would be generated from the palladium complex and water and would catalyze the undesired nonenantioselective reaction path. We found that the ee of **3aa** reached 96% when the reaction was carried out in the presence of 50 mg of MS3A (entry 3). Similar enantioselectivity was shown in the control examination, in which **2a** and the palladium complex were mixed with MS3A, which was then filtered off before the addition of **1a**. Therefore, the presence of MS3A is not necessary to obtain the high enantioselectivity. The reaction at 0 °C in the presence of MS3A gave **3aa** in a good yield of 70% with the highest ee of 99% (entry 4). The cationic BINAP-platinum complex was found to also catalyze the enantioselective reaction of **1a** with **2a**. The reaction catalyzed by [Pt(*S*-BINAP)$(PhCN)_2$]$(BF_4)_2$ in the absence of MS3A gave a higher ee, 93% (entry 5), than that obtained by catalysis with the palladium complex under same reaction conditions (entry 2). The addition of MS3A and the adoption of lower reaction temperature also improved the yield and ee, affording **3aa** in 60% yield with an ee of 97% (entry 6).

The reactions of various dienes (**1a**−**e**) with arylglyoxals (**2a**−**d**) were carried out in the presence of 2 mol % of (*S*)-BINAP-palladium or -platinum complex and MS3A. Results are summarized in Table 3. Hetero ene products

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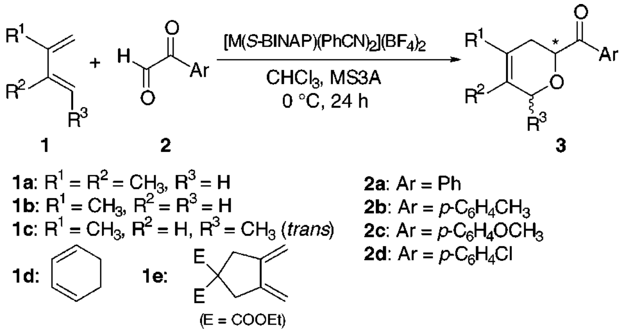
Table 3. Hetero DA Reaction of Dienes with Arylglyoxals Catalyzed by Cationic BINAP-Palladium and -Platinum Complexes[a]

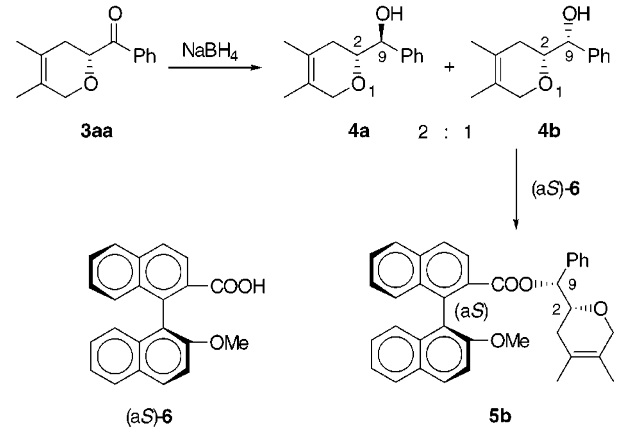


entry	1	2	M	3	yield (%)[b]	ee (%)[c]
1	**1a**	**2a**	Pd	**3aa**	67	99 (*R*)
2			Pt		60	97 (*R*)
3	**1a**	**2b**	Pd	**3ab**	50	94
4			Pt		50	93
5	**1a**	**2c**	Pd	**3ac**	64	98
6			Pt		65	98
7	**1a**	**2d**	Pd	**3ad**	57	97
8			Pt		44	96
9	**1b**	**2a**	Pd	**3ba**	21	33
10			Pt		55	91
11	**1c**	**2a**	Pd	**3ca**	46 (*cis*)	38
					20 (*trans*)	80
12			Pt		53 (*cis*)	1
					10 (*trans*)	50
13	**1d**	**2a**	Pd	**3da**	69	>99
14			Pt		74	>99
15	**1e**	**2a**	Pd	**3ea**	80	98[d]

[a] Reaction conditions: **1** (3.0 mmol), **2** (2.0 mmol), catalyst (0.04 mmol), MS3A (100 mg), 4 mL of $CHCl_3$, 0 °C, 24 h, N_2 atmosphere. [b] Isolated yield. [c] Determined by HPLC using Chiralpak AD, 5% *i*-PrOH in hexane. [d] Determined by HPLC using Chiralcel OD-H, 10% *i*-PrOH in hexane.

were not observed in the reaction with arylglyoxals. The reactions of **1a** with *p*-methyl-, *p*-methoxy-, and *p*-chloro-substituted phenylglyoxals (**2b**−**d**) catalyzed by both the palladium complex and the platinum complex also proceeded enantioselectively, affording **3ab**, **3ac**, and **3ad** in 44−65% isolated yields with 93−98% ee (entries 3−8). The considerable difference in the enantioselectivity observed in the reaction of isoprene (**1b**) and *trans*-2-methyl-1,3-pentadiene (**1c**) may arise from the structural differences between the palladium and the platinum complexes. The reaction of **1b** with **2a** catalyzed by the palladium complex gave **3ba** in low yield of 21% with low ee of 31% (entry 9), whereas **3ba** was isolated in 55% yield with a high ee of 91% when the platinum complex was used as catalyst (entry 10). The reaction of **1c** with **2a** catalyzed by the palladium or the platinum complex gave **3ca** as a *cis-trans* mixture of a similar ratio; however, the ee of the major *trans* form was 38% for the palladium complex and only 1% for the platinum complex (entries 11 and 12). 1,3-Cyclohexadiene (**1d**), a cyclic internal diene, reacted with **2a**, affording a good isolated yield of **3da** in almost optically pure form (>99% ee) by use of both the palladium and the platinum complexes (entries 13 and 14). In the case of **1d**, only the *endo* adduct was formed. This result indicates that the reaction proceeds via the concerted pericyclic mechanism according to the *endo* rule. If the reaction of *trans*-**1c** with **2a** also proceeds concertedly, only *trans*-**3ca** should be obtained. However, as mentioned above, the **3ca** obtained was actually a *cis-trans* mixture. Therefore, it can be assumed that another reaction pathway exists, such as stepwise addition via the zwitter ionic intermediate, as has been proposed in the cyclization of dienes with benzaldehyde.[12,17] Low enantioselectivity in the reaction of **1b** and **1c** may be interpreted in terms of differences in reaction pathways. Cyclic *diexo*-1,2-dimethylene substrate **1e** could also be applied to the highly enantioselective hetero DA reaction with **1a** to give **3ae** in 80% yield with 98% ee (entry 15).

Scheme 1



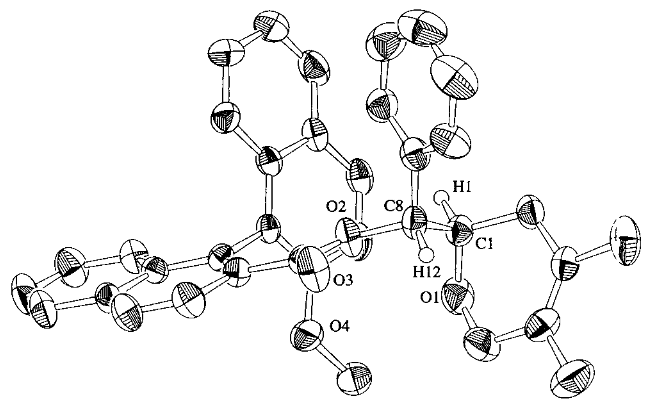


Figure 1. ORTEP view of (*aS*,*R*,*R*)-**5b**. Hydrogen atoms are only shown for asymmetric carbons. The ellipsoids are drawn at the 40% probability level.

To determine the absolute configuration of the major enantiomer **3aa** of 99% ee obtained from the asymmetric hetero DA reaction of **1a** with **2a** catalyzed by (*S*)-BINAP-palladium complex, it was reduced with $NaBH_4$ to a diastereomeric mixture of alcohols (**4a**, **4b**) and then converted to ester **5** with Miyano's chiral derivatizing agent, (a*S*)-2′-methoxy-1,1′-binaphthyl-2-carboxylic acid (**6**) (Scheme 1).[18] The ester **5b** derived from minor alcohol **4b** and (a*S*)-**6** gave a suitable crystal, which was subjected to X-ray crystal structure analysis. The absolute configuration of **5b** was designated as (a*S*,2*R*,9*R*), from which the absolute configuration of **3aa** formed in the asymmetric hetero DA reaction was determined to be *R* (Figure 1).

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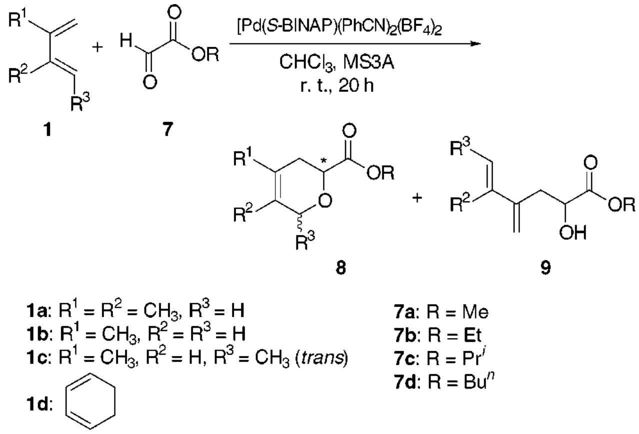
Table 4. Hetero DA Reaction of Dienes with Glyoxylate Esters Catalyzed by Cationic BINAP-Palladium Complexes[a]



			DA			ene		
entry	**1**	**7**	**8**	yield (%)[b]	ee (%)[c]	**9**	yield (%)[b]	ee (%)[c]
1	**1a**	**7a**	**8aa**	34	95 (*R*)	**9aa**	34	57
2	**1a**	**7b**	**8ab**	36	95 (*R*)	**9ab**	35	62
3	**1a**	**7c**	**8ac**	43	97 (*R*)	**9ac**	32	76
4	**1a**	**7d**	**8ad**	42	96 (*R*)	**9ad**	35	64
5	**1b**	**7b**	**8bb**	33	11[d]	**9bb**	31	3
6	**1c**	**7b**	**8cb**	42 (*cis*)	7[d]	**9cb**	13	21
				16 (*trans*)	23			
7	**1d**	**7b**	**8db**	77	98 (1*S*,3*R*,4*R*)			

[a] Reaction conditions: **1** (4.5 mmol), **6** (3.0 mmol), catalyst (0.06 mmol), MS3A (150 mg), 6 mL of $CHCl_3$, rt, 20 h, N_2 atmosphere. [b] Isolated yield. [c] Determined by GLC using Chrompak Chirasil-DEX CB, N_2. [d] Determined by GLC using Astec Chiraldex G-TA, N_2.

The cationic BINAP-palladium complex catalyzed hetero DA reaction of dienes (**1**) with glyoxylate esters (**7**) also proceeded enantioselectively. Results are summarized in Table 4. The reactions of the dienes suited for ene reaction (**1a**−**c**) with glyoxylate esters **7** gave almost the same amount of both hetero DA products **8** and ene products **9**. The ee's of the all-hetero DA products from **1a** with glyoxylate esters **7a**−**d** were excellent, whereas the ee's of the ene products were moderate to good (entries 1−4). A bulkier alkyl moiety in **7** improved the ee's of both the hetero DA product and the ene product and also the hetero DA selectivity. Thus the isopropyl ester **7c** gave **8ac** with 97% ee and **9ac** with 76% ee, and the hetero DA/ene ratio came to 1.34/1. Although the reaction of **1b** with **7b** gave products **8bb** and **9bb** in almost the same yield as the reaction of **1a** with **7b**, the ee's of both **8bb** and **9bb** were low (entry 5). The reaction of **1c** with **7b** gave a *cis*-*trans* mixture of **8cb** in 58% total yield with good hetero DA selectivity, but the ee of the major *trans* form was only 7% (entry 6). The reaction of cyclic diene **1d** with **7b** afforded selectively *endo* adduct **8db** in a good isolated yield of 77% with an excellent ee of 98%.

To gain structural information about the cationic palladium species coordinated with BINAP, the crystal structure of $[Pd(S\text{-BINAP})(PhCN)_2](PF_6)_2$ was determined by X-ray diffraction. As shown in Figure 2, the complex has a slightly distorted square-planar geometry, being coordinated with two phosphorus atoms of (*S*)-BINAP and two benzonitriles. The dihedral angle of the two naphthyl groups of the (*S*)-BINAP is 69.5(6)°, and the bite angle (P−Pd−P) is 90.76(5)°. As has been found

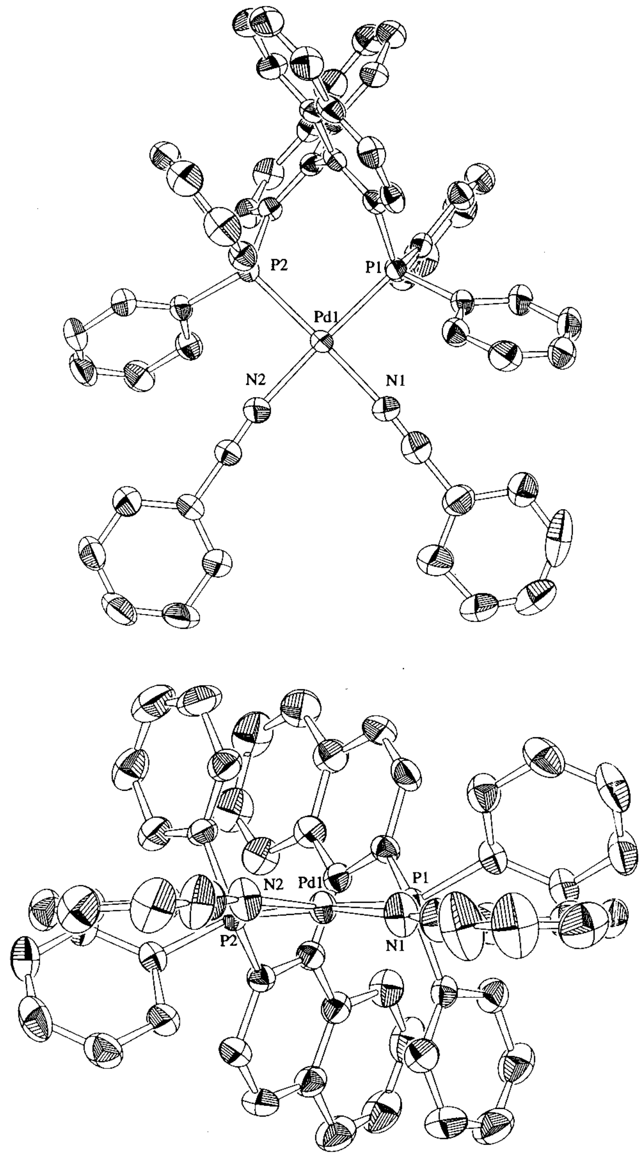


Figure 2. ORTEP view of $[Pd(S\text{-BINAP})(PhCN)_2](PF_6)_2$. Hydrogen atoms and PF_6 anions are omitted for clarity. The ellipsoids are drawn at the 40% probability level.

in other palladium-, rhodium-, and ruthenium-BINAP complexes,[19] two of the phenyl groups of (*S*)-BINAP are oriented axially and the other two phenyl groups equatorially with respect to the square-plane of the complex. The equatorial phenyl groups are extruded toward the coordination sites of the benzonitriles, and the two benzonitriles are situated below and above the P−Pd−P plane, respectively. This structural information shows that considerable steric hindrance exists between the equatorial phenyl groups and the coordinating benzonitriles.

A proposed chiral induction model is illustrated with phenylglyoxal (**2a**) and the palladium-(*S*)-BINAP complex in Figure 3. It is presumed that dicarbonyl compound **2a** would replace the benzonitriles and L_2 coordinates to the palladium-(*S*)-BINAP complex via the two carbonyl oxygen atoms, affording the square-planar complex as the intermediate. Because the attack on the *si* face of the

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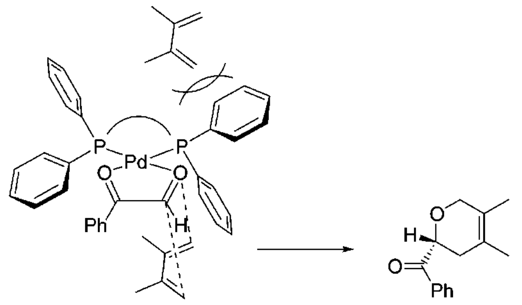

(*R*)-**3aa**

Figure 3. A proposed chiral induction model for the reaction of **1a** with **2a**.

formyl group in **2a** may be obstructed by the equatorial phenyl group of the (*S*)-BINAP, the attack of **1a** on the *re* face is favored to afford the observed (*R*)-cycloadduct **3aa**.

Experimental Section

General Methods. All reactions were carried out in Schlenk tubes using anhydrous solvents under N_2. $CHCl_3$ was dried over CaH_2, distilled, and stored over 4 Å molecular sieves. NMR spectra were recorded using $CDCl_3$ as the solvent. Elemental analyses were carried out in the Microanalytical Laboratory of the Institute for Chemical Reaction Science, Tohoku University. Spherical silica gel (100−210 μm, Kanto Chemical) was used for column chromatography. Enantiomer excess (ee) was determined by GLC or HPLC as described in the footnotes of the tables.

Materials. 2,3-Dimethyl-1,3-butadiene (**1a**), 2-methyl-1,3-butadiene (**1b**), and cyclohexa-1,3-diene (**1d**) were purchased from Tokyo Chemical Industry and used as received. *trans*-2-Methyl-1,3-pentadiene (**1c**) was purchased from Aldrich and used as received. 4,4-Diethoxycarbonyl-1,2-dimethylenecyclopentane (**1e**) was prepared as described in the literature[20] from 4,4-diethoxycarbonylhept-6-ene-1-yne. Phenylglyoxal (**2a**) was purchased from Tokyo Chemical Industry and distilled before use. Substituted phenylglyoxals (**2b**−**d**)[21] and glyoxylate esters (**7a**−**d**)[22] were prepared as described in the literature and distilled before use.

Preparation of Cationic Palladium and Platinum Complexes. A mixture of $PdCl_2$ (887 mg, 5.0 mmol) and acetonitrile (50 mL) was refluxed for about 1.5 h under N_2 until the suspension became clear, and the solution was filtered while hot to remove insoluble impurities. To the solution was added (*S*)-BINAP (3.11 g, 5.0 mmol), and the mixture was refluxed for 2 h under N_2. After the mixture was cooled to room temperature, the yellow solid was filtered, washed with acetonitrile, and dried in vacuo to give $PdCl_2$(*S*-BINAP) in quantitative yield. To a suspension of $PdCl_2$(*S*-BINAP) (800 mg, 1.0 mmol) in CH_2Cl_2 (35 mL) were added benzonitrile (5 mL) and $AgBF_4$ (487 mg, 2.5 mmol) dissolved in nitromethane (10 mL) with stirring under N_2. A white precipitate of AgCl appeared immediately. After stirring for 3 h the solution was filtered through a membrane filter (0.45 μm) and reduced to ca. 5 mL in vacuo. A yellow solid was precipitated by dropwise addition of diethyl ether (50−100 mL) with stirring, and the precipitate was filtered, washed with diethyl ether (10 mL), and dried in vacuo to give up to 90% yield of [Pd(*S*-BINAP)-$(PhCN)_2](BF_4)_2$. [Pd(*S*-BINAP)$(PhCN)_2](PF_6)_2$ and [Pt(*S*-BINAP)-$(PhCN)_2](BF_4)_2$ were prepared similarly using $AgPF_6$ and $PtCl_2$, respectively.

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[Pd(*S*-BINAP)$(PhCN)_2](BF_4)_2$: IR (KBr) 1065 cm^{-1}. Anal. Calcd for $C_{58}H_{42}B_2F_8N_2P_2Pd$: C, 62.82; H, 3.82; N, 2.53. Found: C, 62.26; H, 3.94; N, 2.52.

[Pd(*S*-BINAP)$(PhCN)_2](PF_6)_2$: IR (KBr) 838 cm^{-1}. Anal. Calcd for $C_{58}H_{42}F_{12}N_2P_4Pd$: C, 56.85; H, 3.46; N, 2.29. Found: C, 56.54; H, 3.45; N, 2.26.

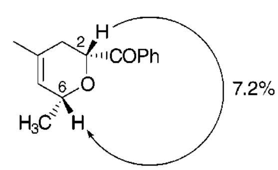
[Pt(*S*-BINAP)$(PhCN)_2](BF_4)_2$: IR (KBr) 1061 cm^{-1}. Anal. Calcd for $C_{58}H_{42}B_2F_8N_2P_2Pt$: C, 58.17; H, 3.53; N, 2.34. Found: C, 57.62; H, 3.63; N, 2.38.

Catalytic Hetero DA Reaction of Dienes with Arylglyoxals. A typical procedure (Table 3, entry 1) is as follows. To a mixture of [Pd(*S*-BINAP)$(PhCN)_2](BF_4)_2$ (44.3 mg, 0.04 mmol), powder of 3 Å molecular sieves (100 mg), and $CHCl_3$ (4 mL) were added phenylglyoxal (268 mg, 2.0 mmol) and 2,3-dimethyl-1,3-butadiene (246 mg, 3.0 mmol), and the mixture was stirred at 0 °C for 24 h under N_2 atmosphere. Diethyl ether (25 mL) was added to the mixture, and the solution was filtered through a short silica gel column and eluted with diethyl ether. After the solvent was removed, the residue was purified by silica gel column chromatography using hexane/EtOAc (10:1) as the eluent to give the hetero DA product (290 mg, 67%) as a colorless oil.

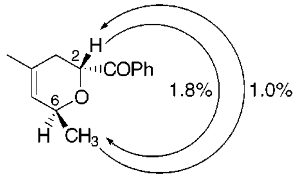
(*R*)-(+)-2-Benzoyl-4,5-dimethyl-3,6-dihydro-2*H*-pyran (3aa): ^{1}H NMR (400 MHz) δ 8.00 (approximate d, 2H, J_{app} = 7.8 Hz), 7.58−7.44 (m, 3H), 4.91 (dd, 1H, J = 10.2, 4.0 Hz), 4.19−4.09 (m, 2H), 2.42−2.38 (m, 1H), 2.12 (br d, 1H, J = 16.2 Hz), 1.68 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (100 MHz) δ 198.1, 135.2, 133.3, 128.8, 128.5, 124.3, 122.9, 76.4, 69.5, 32.9, 18.4, 13.9; IR (neat) 1694, 1114, 694 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 105 (100), 216 (M^+, 1.5). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.23; H, 7.43. $[\alpha]^{26}_D$ +155° (*c* 1.1, $CHCl_3$) 99% ee.

(+)-2-Benzoyl-4-methyl-3,6-dihydro-2*H*-pyran (3ba): ^{1}H NMR (500 MHz) δ 8.01 (approximate d, 2H, J_{app} = 7.8 Hz), 7.59−7.45 (m, 3H), 5.49 (s, 1H), 4.90 (dd, 1H, J = 9.9, 4.0 Hz), 4.31 (br s, 2H), 2.47−2.41 (m, 1H), 2.14 (br d, 1H, J = 16.9 Hz), 1.75 (s, 3H); ^{13}C NMR (125 MHz) δ 198.0, 135.2, 133.3, 131.1, 128.9, 128.6, 119.4, 75.8, 65.9, 32.0, 23.0; IR (neat) 1693, 1123, 693 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 105 (100), 202 (M^+, 2.9). Anal. Calcd for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.17; H, 6.96. $[\alpha]^{24}_D$ +108° (*c* 1.0, $CHCl_3$) 91%ee.

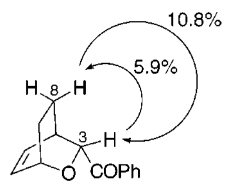
***cis*-(+)-2-Benzoyl-4,6-dimethyl-3,6-dihydro-2*H*-pyran (*cis*-3ca):** This isomer was assigned to the *cis* form on the basis of the NOE enhancement of 7.2% to the hydrogen attached to the 6-position from the hydrogen attached to the 2-position. ^{1}H NMR (500 MHz) δ 8.02 (approximate d, 2H, J_{app} = 8.3 Hz), 7.58−7.45 (m, 3H), 5.41−5.40 (m, 1H), 4.89 (dd, 1H, J = 11.1, 3.6 Hz), 4.42−4.40 (m, 1H), 2.46−2.39 (m, 1H), 2.06 (dt, 1H, J = 16.9, 2.9 Hz), 1.76 (s, 3H), 1.30 (d, 3H, J = 6.7 Hz); ^{13}C NMR (125 MHz) δ 197.7, 135.3, 133.2, 131.3, 129.1, 128.5, 128.1, 125.1, 71.9, 32.1, 22.8, 21.5; IR (neat) 1693, 1118, 697 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 105 (100), 216 (M^+, 2.0). $[\alpha]^{24}_D$ +24° (*c* 1.0, $CHCl_3$) 38% ee.



***trans*-(+)-2-Benzoyl-4,6-dimethyl-3,6-dihydro-2*H*-pyran (*trans*-3ca):** This isomer was assigned to the *trans* form on the basis of the NOE enhancement of 1.8% to the methyl group attached to the 6-position from the hydrogen attached to the 2-position and 1.0% to the hydrogen attached to the 2-position from the methyl group attached to the 6-position. ^{1}H NMR (400 MHz) δ 8.07 (approximate d, 2H, J_{app} = 7.8 Hz), 7.59−7.44 (m, 3H), 5.38−5.36 (m, 1H), 5.10 (dd, 1H, J = 8.4, 6.1 Hz), 4.36−4.30 (m, 1H), 2.41 (dd, 1H, J = 21.5, 7.6 Hz), 2.18 (dd, 1H, J = 21.5, 5.4 Hz), 1.75 (s, 3H), 1.27 (d, 3H, J = 6.7 Hz). $[\alpha]^{24}_D$ +17° (*c* 1.1, $CHCl_3$) 80% ee.



(+)-3-Benzoyl-2-oxabicyclo[2.2.2]oct-5-ene (3da): This product was assigned to the *endo* form on the basis of the NOE enhancement of 5.9% to the hydrogen attached to the 8-position from the hydrogen attached to the 3-position and 10.8% to the hydrogen attached to the 3-position from the hydrogen attached to the 8-position. Mp 83−83.5 °C; ^{1}H NMR (500 MHz) δ 7.91 (approximate d, 2H, J_{app} = 7.8 Hz), 7.53−7.39 (m, 3H), 6.48−6.45 (m, 1H), 6.27−6.24 (m, 1H), 5.04 (d, 1H, J = 1.6 Hz), 4.59−4.57 (m, 1H), 3.15−3.13 (m, 1H), 2.20−2.12 (m, 1H), 1.87−1.81 (m, 1H), 1.46−1.36 (m, 2H); ^{13}C NMR (100 MHz) δ 198.7, 135.7, 134.2, 132.9, 131.5, 128.7, 128.4, 78.4, 66.7, 32.9, 25.9, 21.3; IR (KBr) 1688, 1165, 696 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 77 (100), 105 (74). Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.19; H, 6.64. $[\alpha]^{23}_{D}$ +1.3° (*c* 1.1, $CHCl_3$) 99.6% ee.



(+)-4-Benzoyl-8,8-diethoxycarbonyl-3-oxabicyclo[4.3.0]-non-1(6)-ene (3ea): ^{1}H NMR (500 MHz) δ 7.99 (approximate d, 2H, J_{app} = 7.8 Hz), 7.59−7.45 (m, 3H), 4.85 (dd, 1H, J = 9.8, 4.0 Hz), 4.31 (br s, 2H), 4.22 (q, 2H, J = 7.1 Hz), 4.21 (q, 2H, J = 7.1 Hz), 3.09−2.99 (m, 4H), 2.48−2.43 (m, 1H), 2.25 (br d, 1H, J = 16.8 Hz), 1.27 (t, 3H, J = 7.1 Hz), 1.26 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz) δ 197.6, 172.1, 171.7, 135.2, 133.4, 130.4, 129.5, 129.0, 128.6, 75.7, 66.1, 61.7, 58.1, 43.4, 40.5, 28.0, 14.1; IR(neat) 1731, 1691, 1257 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 105 (100), 372 (M^{+}, 6.0). $[\alpha]^{21}_{D}$ +68° (*c* 1.2, $CHCl_3$) 98% ee.

(+)-4,5-Dimethyl-2-(4′-methylbenzoyl)-3,6-dihydro-2*H*-pyran (3ab): ^{1}H NMR (400 MHz) δ 7.90 (d, 2H, J = 8.2 Hz), 7.25 (d, 2H J = 8.2 Hz), 4.89 (dd, 1H, J = 10.1, 3.9 Hz), 4.19−4.09 (m, 2H), 2.44−2.38 (m, 4H), 2.11 (br d, 1H, J = 16.3 Hz), 1.69 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (100 MHz) δ 197.7, 144.1, 132.7, 129.3, 129.0, 124.3, 123.0, 76.4, 69.6, 33.0, 21.7, 18.4, 13.9; IR (neat) 1694, 1229, 1007 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 119 (100), 230 (M^{+}, 1.0). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 77.98; H, 7.72. $[\alpha]^{25}_{D}$ +134° (*c* 1.0, $CHCl_3$) 93% ee.

(+)-4,5-Dimethyl-2-(4′-methoxybenzoyl)-3,6-dihydro-2*H*-pyran (3ac): mp 109.5−111.0 °C; ^{1}H NMR (400 MHz) δ 8.01 (d, 2H, J = 8.9 Hz), 6.94 (d, 2H J = 8.9 Hz), 4.86 (dd, 1H, J = 10.2, 3.9 Hz), 4.19−4.09 (m, 2H), 3.87 (s, 3H), 2.46−2.39 (m, 1H), 2.11 (br d, 1H, J = 16.3 Hz), 1.69 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (100 MHz) δ 196.5, 163.6, 131.3, 128.2, 124.2, 123.0, 113.7, 76.4, 69.5, 55.5, 33.0, 18.4, 13.9; IR (KBr) 1675, 1605, 1262 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 135 (100), 218 (15). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.08; H, 7.47. $[\alpha]^{26}_{D}$ +129° (*c* 1.1, $CHCl_3$) 98% ee.

(+)-2-(4′-Chlorobenzoyl)-4,5-dimethyl-3,6-dihydro-2*H*-pyran (3ad): mp 56.5−57.5 °C; ^{1}H NMR (250 MHz) δ 7.96 (d, 2H, J = 8.6 Hz), 7.43 (d, 2H J = 8.6 Hz), 4.83 (dd, 1H, J = 9.9, 4.0 Hz), 4.20−4.05 (m, 2H), 2.48−2.37 (m, 1H), 2.12 (br d, 1H, J = 15.5 Hz), 1.69 (s, 3H), 1.57 (s, 3H); ^{13}C NMR (62.5 MHz) δ 197.0, 139.6, 133.4, 130.4, 128.8, 124.2, 122.8, 76.6, 69.4, 32.5, 18.3, 13.8; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 55 (100), 250 (M^{+}, 1.9); IR (KBr) 1693, 1588, 1087 cm^{-1}. Anal. Calcd for $C_{14}H_{15}ClO_2$: C, 67.07; H, 6.03; Cl, 14.14. Found: C, 66.76; H, 6.04; Cl, 14.23. $[\alpha]^{24}_{D}$ +121° (*c* 1.0, $CHCl_3$) 97% ee.

Catalytic Hetero DA Reaction of Dienes with Glyoxylate Esters. The reaction was carried out in a method similar to that used for dienes with arylglyoxals. Typically, 2,3-dimethyl-1,3-butadiene (370 mg, 4.5 mmol) and ethyl glyoxylate (306 mg, 3.0 mmol) were reacted in the presence of $[Pd(S\text{-}BINAP)(PhCN)_2](BF_4)_2$ (66 mg, 0.06 mmol) and powder of 3 Å molecular sieves (150 mg) in $CHCl_3$ (6 mL) at room temperature for 20 h under N_2 atmosphere. The purification by silica gel column chromatography using hexane/EtOAc (5:1) gave the hetero DA product (198 mg, 36%) and the ene product (194 mg 35%), respectively, as colorless oils.

(*R*)-(+)-Methyl 4,5-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (8aa): ^{1}H NMR (500 MHz) δ 4.22 (dd, 1H, J = 9.9, 4.2 Hz), 4.14−4.05 (m, 2H), 3.78 (s, 3H), 2.35−2.29 (m, 1H), 2.19 (br d, 1H, J = 15.4 Hz), 1.67 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (125 MHz) δ 172.0, 124.3, 122.5, 72.9, 69.3, 52.1, 33.0, 18.2, 13.8; IR (neat) 1762, 1741, 1196, 1119 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 55 (100), 170 (M^{+}, 5.6). $[\alpha]^{19}_{D}$ +181° (*c* 1.1, $CHCl_3$) 95% ee. The absolute configuration was determined to be *R* by the reported method.[4a]

(−)-Methyl 2-hydroxy-5-methyl-4-methylene-5-hexanoate (9aa): ^{1}H NMR (500 MHz) δ 5.25 (s, 1H), 5.12 (s, 1H), 5.10 (s, 1H), 5.04 (s, 1H), 4.38−4.34 (m, 1H), 3.77 (s, 3H), 2.86 (dd, 1H, J = 14.3, 4.1 Hz), 2.72−2.70 (m, 1H), 2.56 (dd, 1H, J = 14.3, 8.3 Hz), 1.93 (s, 3H); ^{13}C NMR (125 MHz) δ 175.0, 142.7, 142.1, 115.8, 113.4, 69.6, 52.4, 39.1, 21.1; IR (neat) 3480, 1741, 1216, 1097 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 41 (100), 170 (M^{+}, 0.2). $[\alpha]^{20}_{D}$ −5.3° (*c* 1.3, $CHCl_3$) 57% ee.

(*R*)-(+)-Ethyl 4,5-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (8ab):[4a] ^{1}H NMR (400 MHz) δ 4.24 (q, 2H, J = 7.1 Hz), 4.19 (dd, 1H, J = 9.8, 4.2 Hz), 4.14−4.04 (m, 2H), 2.35−2.28 (m, 1H), 2.18 (br d, 1H, J = 16.1 Hz), 1.67 (s, 3H), 1.54 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz); IR (neat) 1757, 1738, 1187, 1119 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 55 (100), 184 (M^{+}, 3.4). $[\alpha]^{26}_{D}$ +159° (*c* 0.9, $CHCl_3$) 95% ee (lit.[4a] $[\alpha]^{20}_{D}$ −138° (*c* 1.7, $CHCl_3$) 83% ee (*S*)).

(−)-Ethyl 2-hydroxy-5-methyl-4-methylene-5-hexanoate (9ab):[4a] ^{1}H NMR (400 MHz) δ 5.24 (s, 1H), 5.13 (s, 1H), 5.10 (s, 1H), 5.04 (s, 1H), 4.35−4.30 (m, 1H), 4.26−4.20 (m, 2H), 2.85 (dd, 1H, J = 14.3, 4.2 Hz), 2.69 (d, 1H, J = 6.5 Hz), 2.55 (dd, 1H, J = 14.3, 8.2 Hz), 1.94 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz); IR (neat) 3478, 1732, 1209, 1095 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 41 (100), 184 (M^{+}, 0.2). $[\alpha]^{24}_{D}$ −0.9° (*c* 1.1, $CHCl_3$) 62% ee (lit.[4a] $[\alpha]^{20}_{D}$ +1° (*c* 1.7, $CHCl_3$) 88% ee).

(*R*)-(+)-Isopropyl 4,5-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (8ac): ^{1}H NMR (400 MHz) δ 5.11 (sept, 1H, J = 6.2 Hz), 4.15 (dd, 1H, J = 9.7, 4.3 Hz), 4.12−4.03 (m, 2H), 2.32−2.26 (m, 1H), 2.16 (br d, 1H, J = 16.6 Hz), 1.67 (s, 3H), 1.54 (s, 3H), 1.27 (d, 6H, J = 6.2); ^{13}C NMR (100 MHz) δ 171.2, 124.3, 122.5, 73.0, 69.2, 68.4, 33.1, 27.8, 18.3, 13.8; IR (neat) 1755, 1731, 1188, 1107 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 55 (100), 198 (M^{+}, 1.9). $[\alpha]^{28}_{D}$ +157° (*c* 1.1, $CHCl_3$) 97% ee. The absolute configuration was determined to be *R* by the reported method.[4a]

Isopropyl 2-hydroxy-5-methyl-4-methylene-5-hexanoate (9ac): ^{1}H NMR (400 MHz) δ 5.24 (s, 1H), 5.14 (s, 1H), 5.10 (s, 1H), 5.11−5.05 (m, 1H), 5.04 (s, 1H), 4.31−4.26 (m, 1H), 2.84 (dd, 1H, J = 14.3, 4.2 Hz), 2.68 (d, 1H, J = 6.4), 2.52 (dd, 1H, J = 14.3, 8.2 Hz), 1.94 (s, 3H), 1.28 (d, 3H, J = 6.2), 1.27 (d, 3H, J = 6.2); ^{13}C NMR (100 MHz) δ 174.2, 142.9, 142.2, 115.6, 113.4, 69.6, 69.5, 39.2, 21.8, 21.2; IR (neat) 3483, 1732, 1215, 1107 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 43 (100), 198 (M^{+}, 0.1). Optical rotation was too small to measure correctly.

(*R*)-(+)-Butyl 4,5-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (8ad): ^{1}H NMR (400 MHz) δ 4.21−4.18 (m, 3H), 4.15−4.03 (m, 2H), 2.34−2.28 (m, 1H), 2.18 (br d, 1H, J = 16.4 Hz), 1.69−1.62 (m, 5H), 1.54 (s, 3H), 1.39 (sext, 2H, J = 7.4 Hz), 0.94 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz) δ 171.7, 124.3, 122.5, 72.9, 69.2, 64.9, 33.0, 30.7, 19.1, 18.3, 13.8, 13.7; IR (neat) 1759, 1736, 1185, 1119 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) *m/z* 41 (100), 212 (M^{+}, 2.2). $[\alpha]^{26}_{D}$ +139°

(c 1.0, $CHCl_3$) 96% ee. The absolute configuration was determined to be *R* by the reported method.[4a]

Butyl 2-hydroxy-5-methyl-4-methylene-5-hexanoate (9ad): ^{1}H NMR (400 MHz) δ 5.24 (s, 1H), 5.13 (s, 1H), 5.10 (s, 1H), 5.04 (s, 1H), 4.35−4.31 (m, 1H), 4.20−4.14 (m, 2H), 2.86 (dd, 1H, J = 14.3, 4.2 Hz), 2.72 (d, 1H, J = 6.3 Hz), 2.54 (dd, 1H, J = 14.3, 8.2 Hz), 1.93 (s, 3H), 1.65 (quint, 2H, J = 7.4 Hz), 1.39 (sext, 2H, J = 7.4 Hz), 0.95 (t, 3H, J = 7.4 Hz); ^{13}C NMR (100 MHz) δ 174.8, 142.8, 142.2, 115.6, 113.3, 69.7, 65.4, 39.2, 30.6, 21.1, 19.1, 13.7; IR (neat) 3483, 1736, 1207, 1095 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 41 (100), 194 (0.8). Optical rotation was too small to measure correctly.

(+)-Ethyl 4-methyl-3,6-dihydro-2*H*-pyran-2-carboxylate (8bb):[4a] ^{1}H NMR (400 MHz) δ 5.44−5.42 (m, 1H), 4.35−4.15 (m, 5H), 2.35−2.28 (m, 1H), 2.23−2.18 (m, 1H), 1.73 (s, 3H), 1.31 (t, 3H, J = 7.1 Hz); IR (neat) 1758, 1736, 1186, 1135 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 41 (100), 170 (M$^+$, 1.7). $[\alpha]^{24}_D$ +25° (c 1.1, $CHCl_3$) 11% ee (lit.[4a] $[\alpha]^{20}_D$ −90° (c 1.8, $CHCl_3$) 80% ee).

Ethyl 2-hydroxy-4-methylene-5-hexanoate (9bb):[4a] ^{1}H NMR (400 MHz) δ 6.40 (dd, 1H, J = 17.7, 10.8 Hz), 5.29 (d, 1H, J = 17.7 Hz), 5.27−5.10 (m, 3H), 4.35 (ddd, 1H, J = 8.0, 6.2, 4.1 Hz), 4.29−4.18 (m, 2H), 2.81−2.76 (m, 2H), 2.51 (ddd, 1H, J = 14.5, 8.0, 0.7 Hz), 1.31 (t, 3H, J = 7.1 Hz); IR (neat) 3479, 1737, 1207, 1097 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 41 (100), 170 (M$^+$, 2.2). Optical rotation was too small to measure correctly (lit.[4a] $[\alpha]^{20}_D$ +2° (c 0.9, $CHCl_3$) 91% ee).

***cis*-(+)-Ethyl 4,6-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (*cis*-8cb):** ^{1}H NMR (400 MHz) δ 5.33 (br s, 1H), 4.27−4.17 (m, 4H), 2.31−2.24 (m, 1H), 2.12 (br d, 1H, J = 16.7 Hz), 1.72 (s, 3H), 1.30 (t, 3H, J = 7.1 Hz), 1.28 (d, 3H, J = 6.6 Hz); ^{13}C NMR (100 MHz) δ 171.4, 130.9, 125.1, 73.2, 71.6, 61.0, 32.5, 22.7, 21.4, 14.2; IR (neat) 1759, 1736, 1184, 1126 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 43 (100), 184 (M$^+$, 0.9). $[\alpha]^{28}_D$ +13° (c 1.2, $CHCl_3$) 12% ee.

***trans*-(+)-Ethyl 4,6-dimethyl-3,6-dihydro-2*H*-pyran-2-carboxylate (*trans*-8cb):** ^{1}H NMR (400 MHz) δ 5.36 (br s, 1H), 4.51−5.54 (m, 1H), 4.41 (t, 1H, J = 4.7 Hz), 4.23 (q, 2H, J = 7.1 Hz), 2.27−2.25 (m, 2H), 1.72 (s, 3H), 1.29 (t, 3H, J = 7.1 Hz), 1.23 (d, 3H, J = 6.7 Hz); GC−MS (EI, 70 eV, relative intensity, %) m/z 43 (100), 184 (M$^+$, 1.4). $[\alpha]^{29}_D$ +34° (c 0.9, $CHCl_3$) 33% ee.

***trans*-(−)-Ethyl 2-hydroxy-4-methylene-5-heptenoate (9cb):** ^{1}H NMR (400 MHz) δ 6.10 (d, 1H, J = 15.8 Hz), 5.79 (dq, 1H, J = 15.8, 6.6 Hz), 5.04 (s, 1H), 4.97 (s, 1H), 4.34−4.32 (m, 1H), 4.26−4.20 (m, 2H), 2.76 (dd, 1H, J = 14.3, 4.2 Hz), 2.68 (d, 1H, J = 6.3 Hz), 2.48 (dd, 1H, J = 14.3, 8.1 Hz), 1.78 (d, 3H, J = 6.6 Hz), 1.30 (t, 3H, J = 7.1 Hz); ^{13}C NMR (100 MHz) δ 174.5, 141.0, 132.7, 125.7, 116.2, 69.4, 61.6, 37.6, 18.2, 14.2; IR (neat) 3500, 1737, 1204, 1105 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 55 (100), 184 (M$^+$, 4.9). $[\alpha]^{28}_D$ −1.6° (c 1.1, $CHCl_3$) 30% ee.

(1*S*,3*R*,4*R*)-(+)-Ethyl 2-oxabicyclo[2.2.2]oct-5-ene-3-calboxylate (8db):[4a] ^{1}H NMR (400 MHz) δ 6.55−6.51 (m, 1H), 6.29−6.26 (m, 1H), 4.59−4.56 (m, 1H), 4.30 (br s, 1H), 4.15 (q, 2H, J = 7.1 Hz), 3.11−3.09 (m, 1H), 2.10−2.01 (m, 1H), 1.78−1.72 (m, 1H), 1.43−1.26 (m, 2H), 1.25 (t, 3H, J = 7.1 Hz); IR (neat) 1757, 1723, 1191, 1053 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 79 (100), 182 (M$^+$, 1.6). $[\alpha]^{23}_D$ +5.2° (c 1.1, $CHCl_3$) 98% ee (lit.[4a] $[\alpha]^{20}_D$ −3.4° (c 3.0, $CHCl_3$) 60% ee (1*R*,3*S*,4*S*)).

Reduction of (*R*)-(+)-3aa. A mixture of **3aa** (99% ee, 516 mg, 2.39 mmol) and $NaBH_4$ (91 mg, 2.4 mmol) in methanol (25 mL) was stirred at room temperature for 2 h. After the reaction was quenched by adding a small amount of water, the solvent was removed in vacuo. The residue was dissolved in ether (20 mL), washed with saturated NaCl (20 mL × 3), and then dried over $MgSO_4$. After the solvent was removed in vacuo, the residue was purified by medium-pressure preparative liquid chromatography (Yamazen Corp., Ultra Pack column, silica gel, 40 μm, 60 Å, 26 mm × 300 mm) eluting with hexane/EtOAc (2:1) to give **4a** (309 mg, 59%) and **4b** (136 mg, 26%), respectively, as colorless oils.

Table 5. Summary of Crystal Data and Datails of Intensity Collection and Least-Squares Refinement Parameters for (a*S*,2*R*,9*R*)-5b and [Pd(*S*-BINAP)(PhCN)$_2$](PF$_6$)$_2$

	(a*S*,2*R*,9*R*)-**5b**	[Pd(*S*-BINAP)-(PhCN)$_2$](PF$_6$)$_2$
empirical formula	$C_{38}H_{32}O_4$	$C_{58}H_{42}F_{12}N_2P_4Pd$
formula weight	528.65	1225.26
crystal dimensions (mm)	0.40 × 0.15 × 0.40	0.40 × 0.40 × 0.40
crystal system	orthorhombic	orthorhombic
space group	$P2_12_12_1$ (No. 19)	$P2_12_12_1$ (No. 19)
a (Å)	14.337(2)	16.420(4)
b (Å)	18.281(2)	20.972(4)
c (Å)	10.827(2)	15.491(3)
V (Å^3)	2837.9(6)	5334(1)
Z	4	4
D_{calc} (g/cm^3)	1.237	1.526
μ(Mo Kα) (cm^{-1})	0.79	5.51
F(000)	1120.00	2472.00
radiation	Mo Kα (λ = 0.71069 Å) graphite monochromated	Mo Kα (λ = 0.71069 Å) graphite monochromated
temp (°C)	23	23
scan type	ω- 2θ	ω- 2θ
scan width (deg)	1.78 + 0.30 tan θ	1.26 + 0.30 tan θ
2θ_{max} (deg)	55.0	55.0
no. of unique reflections	3672	6755
no. of observations ($I > 3.00\sigma(I)$)	1740	5198
no. of variables	369	694
R	0.046	0.033
R_w	0.042	0.033
GOF	1.44	1.05
max shift/error in final cycle	0.03	0.01
min and max peak in final diff. map (e$^-$/Å^3)	−0.20, 0.35	−0.26, 0.33

(2*R*,9*S*)-(+)-4,5-Dimethyl-2-(1-hydroxybenzyl)-3,6-dihydro-2*H*-pyran (4a): ^{1}H NMR (500 MHz) δ 7.38−7.31 (m, 4H), 7.28−7.24 (m, 1H), 4.92 (t, 1H, J = 3.3 Hz), 4.09 (br d, 1H, J = 15.3 Hz), 4.00 (br d, 1H, J = 15.3 Hz), 3.73 (dt, 1H, J = 10.9, 3.6 Hz), 2.76 (d, 1H, J = 2.8 Hz), 2.26−2.20 (m, 1H), 1.56 (s, 3H), 1.50 (s, 3H), 1.40 (br d, 1H, J = 17.0 Hz); ^{13}C NMR (125 MHz) δ 140.1, 128.2, 127.4, 126.3, 123.65, 123.59, 77.4, 75.0, 70.1, 29.0, 18.4, 13.8; IR (neat) 3443, 1103, 701 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 111 (100), 218 (M$^+$, 3.2). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.05; H, 8.48. $[\alpha]^{25}_D$ +134° (c 1.1, $CHCl_3$).

(2*R*,9*R*)-(+)-4,5-Dimethyl-2-(1-hydroxybenzyl)-3,6-dihydro-2*H*-pyran (4b): ^{1}H NMR (500 MHz) δ 7.38−7.30 (m, 5H), 4.49 (dd, 1H, J = 8.1, 1.6 Hz), 4.11−4.03 (m, 2H), 3.57 (ddd, 1H, J = 11.1, 8.1, 3.4 Hz), 3.25 (d, 1H, J = 1.6 Hz), 2.00−1.94 (m, 1H), 1.54 (s, 3H), 1.53 (s, 3H), 1.37 (br d, 1H, J = 16.8 Hz); ^{13}C NMR (125 MHz) δ 139.9, 128.4, 128.1, 127.3, 124.3, 123.1, 78.7, 77.5, 69.8, 32.5, 18.3, 13.8; IR (neat) 3451, 1107, 701 cm^{-1}; GC−MS (EI, 70 eV, relative intensity, %) m/z 111 (100), 218 (M$^+$, 3.2). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.01; H, 8.49. $[\alpha]^{26}_D$ +46° (c 1.1, $CHCl_3$).

Preparation of Ester (a*S*,2*R*,9*R*)-5b. A mixture of **4b** (49.5 mg, 0.227 mmol), the acid chloride of (a*S*)-**6** prepared from (a*S*)-**6** with $SOCl_2$ (87 mg, 0.251 mmol),[18a] and 4-(dimethylamino)pyridine (42 mg, 0.344 mmol) in benzene (1 mL) was stirred at room temperature for 15 h. The reaction mixture was diluted with EtOAc (30 mL) and THF (20 mL), washed with 2 M HCl (30 mL × 2), 1 M Na_2CO_3 (30 mL × 2), and saturated NaCl (30 mL × 2), and then dried over $MgSO_4$. After the solvent was removed in vacuo, the residue was recrystallized from MeOH/CH_2Cl_2 to give **5b** (96.3 mg, 80%) as white crystals: mp 205.5−207.0 °C; ^{1}H NMR (500 MHz) δ 8.23 (d, 1H, J = 8.7 Hz), 8.02 (d, 1H, J = 9.0 Hz), 7.96 (d, 1H, J = 8.7 Hz), 7.93−7.90 (m, 2H), 7.52−7.48 (m, 1H), 7.44 (d, 1H, J = 9.0 Hz), 7.37−7.34 (m, 1H), 7.25−7.23 (m, 2H), 7.17−7.14 (m, 1H), 7.12−7.08 (m, 1H), 7.01 (t, 2H, $J = 7.6$ Hz), 6.92 (d, 1H, $J = 8.5$ Hz), 6.48 (d, 2H, $J = 7.9$ Hz), 5.61 (d, 1H, $J = 7.6$ Hz), 3.89−3.82 (m, 2H), 3.70 (s, 3H), 3.07 (ddd, 1H, $J = 11.2$, 7.6, 3.6 Hz), 1.61−1.53 (m, 1H), 1.49 (s, 3H), 1.44 (s, 3H), 1.00 (br d, 1H, $J = 16.6$ Hz); ^{13}C NMR (125 MHz) δ 166.97, 154.28, 137.02, 136.97, 135.29, 134.21, 132.98, 129.12, 128.90, 128.80, 127.97, 127.96, 127.87, 127.81, 127.76, 127.62, 127.60, 127.46, 127.16, 126.57, 126.53, 125.45, 124.16, 123.48, 122.682, 122.679, 113.93, 78.35, 75.11, 69.21, 56.54, 32.16, 18.19, 13.92; IR (KBr) 1696, 1272, 1125 cm^{-1}. Anal. Calcd for $C_{36}H_{32}O_4$: C, 81.79; H, 6.10. Found: C, 81.71; H, 6.26.

X-ray Crystal Structure Determination. (a*S*,2*R*,9*R*)-**5b** was crystallized from MeOH/EtOAc, and [Pd(*S*-BINAP)(PhCN)$_2$]-(PF$_6$)$_2$ was crystallized from CH_2Cl_2 layered with hexane. A summary of selected crystallographic data is given in Table 5. Data were collected on a Rigaku AFC7R diffractometer with graphite monochromated Mo Kα radiation and a rotating anode generator. Unit cell dimensions were obtained from a least-squares refinement using the setting angles of 25 reflections in the range 22° < 2θ < 25° for **5b** and 28° < 2θ < 30° for [Pd(*S*-BINAP)(PhCN)$_2$](PF$_6$)$_2$. The intensities of three representative reflections, measured after every 150 reflections, showed no decay. The data were corrected for absorption and for Lorentz and polarization effects.

Calculations were performed using the teXsan crystallographic software package from Molecular Structure Corporation. The structures were solved by direct methods (SIR92) and expanded using Fourier techniques (DIRDIF94). The structures were refined by full-matrix least squares with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms attached to asymmetric carbons on **5b** (H1 and H12) were refined isotropically, and all the other hydrogen atoms were included in calculated positions and were not refined.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for new compounds lacking analyses and X-ray crystallographic data for **5b** and [Pd(*S*-BINAP)(PhCN)$_2$](PF$_6$)$_2$. This material is available free of charge via the Internet at http://pubs.acs.org.

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