Ligand-Controlled Asymmetric Induction at a Transition Metal-Bonded α-Carbon in Ester and Amide Enolates. Diastereoselective Formation of Oxapalladacycles Applied to the Synthesis of a Chiral Nonracemic 2*H*-1-Benzopyran

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Stable benzannelated oxapalladacycles [−(P−P)Pd-1-C_6H_4-2-OCHY−] possessing chiral nonracemic bidentate phosphine ligands, (P−P) = (4*S*,5*S*)-(+)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((*S*,*S*)-DIOP) or (2*S*,4*S*)-(−)-2,4-bis(diphenylphosphino)pentane ((*S*,*S*)-BDPP), and a palladium-bonded stereogenic carbon representing an α-carbon in ester (Y = COOEt) or amide (Y = $CONEt_2$) enolates, have been synthesized in diastereomeric excess 46−80% exploiting asymmetric induction from the chiral ligands. The stereoselective event involved an intramolecular displacement of the iodide in complexes (P−P)IPd-1-C_6H_4-2-OCH_2Y by an in situ generated lithium or potassium ester or amide enolate. Only one enantiomer of each ligand was used, and the absolute sense of stereoinduction could be controlled by the choice of the base (*t*-BuOK or LDA) to afford both diastereomers of each palladacycle in a diastereomerically enriched form. Treatment of the palladacycles with an excess of *t*-BuOK allowed for further enrichment in the content of "thermodynamic" diastereomers. An X-ray structure of the complex [−((*S*,*S*)-BDPP)Pd-1-C_6H_4-2-(*R*)-OCHCOOEt−] was obtained. Ligand exchange reactions of the palladacycles with an achiral 1,2-bis(diphenylphosphino)ethane (dppe) ligand afforded enantiomerically enriched palladacycles [−(dppe)Pd-1-C_6H_4-2-OCHCOOEt−] in the corresponding enantiomeric purities without a loss of the stereochemical information. Reaction of dimethyl acetylenedicarboxylate (dmad) with complex [−((*S*,*S*)-DIOP)Pd-1-C_6H_4-2-$OCHCONEt_2$−], enriched via chromatography to 96% de, afforded (−)-2-*N*,*N*-diethylcarbonyl-3,4-bis(methoxycarbonyl)-2*H*-1-benzopyran in 88.4% ee with only a minimal (8%) racemization of the metal-bonded stereocenter.

Introduction

Carbon−carbon bond-forming reactions of intermediates possessing a transition metal−carbon bond play a major role in selective syntheses of complex organic molecules.[1] If organometallics with a transition metal-bonded sp^3-hybridized stereogenic carbon could be used in these transformations,[2] a convenient approach to the creation of stereogenic carbon centers would arise. For this reason, stereoselective synthesis of complexes with a transition metal−Csp^3 bond has recently received much attention.[3] Classical resolution techniques[4] or diastereoselective cyclometalations of chiral nonracemic organic substrates[5] have been explored. In contrast, an approach relying on communication of stereochemical information from chiral auxiliary ligands into achiral organic substrates giving rise to metal-bonded stereogenic carbons has only a few precedents.[6,7] Transition metal enolates, in most cases existing as the Csp^3-

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(4) (a) Spencer, J.; Maassarani, F.; Pfeffer, M. *Tetrahedron: Asymmetry* **1994**, *5* (3), 321−324. (b) Yoneda, A.; Hakushi, T.; Newkome, G. R.; Fronczek, F. R. *Organometallics* **1994**, *13* (12), 4912−4918.

(5) Cyclometalation at a Csp^2−H bond giving rise to the element of planar chirality has been extensively studied, see: (a) Stevens, A. M.; Richards, C. J. *Organometallics* **1999**, *18* (7), 1346−1348. (b) Zhao, G.; Yang, Q.-C.; Mak, T. C. W. *Organometallics* **1999**, *18* (18), 3623−3636. Stereoinduction at metal-bonded stereocenters (carbon and sulfur) has only recently been demonstrated, see: (c) Dupont, J.; Gruber, A. S.; Fonseca, G. S.; Monteiro, A. L.; Ebeling, G. *Organometallics* **2001**, *20* (1), 171−176. (d) Garcia-Ruano, J. L.; Gonzalez, A. M.; Barcena, A. I.; Camazon, M. J.; Navarro-Ranninger, C. *Tetrahedron: Asymmetry* **1996**, *7* (1), 139−148.

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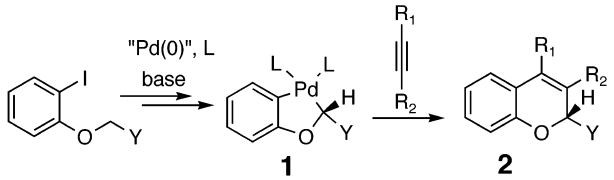
bonded forms,[8] have been established[9] as intermediates in the synthetically powerful catalytic arylation and alkenylation of ketones,[10] esters,[11] amides,[12] and cyano derivatives.[13] While catalytic asymmetric arylation of ketones afforded products in excellent enantiomeric purities,[14] palladium-catalyzed arylation of esters and amides has been found to be much less stereoselective.[15] Thus, it is rather surprising that studies on the preparation of *stable* transition metal ester or amide enolates[16] remain rare in the organometallic literature. To date, only a few examples of stereoselective syntheses[17] of transition metal enolates have been reported, and methods relying on asymmetric induction from chiral nonracemic ligands appear virtually unexplored.[6]

As a part of our program that investigates synthetic applications of palladacycles, we have recently described the preparation of racemic oxapalladacycles **1** and demonstrated their conversion into highly substituted 2*H*-1-benzopyrans **2** via a regiocontrolled insertion of unsymmetrical alkynes (Scheme 1).[18]

Scheme 1



Y = CO_2Et, $CONEt_2$; L = dppb, PPh_3; base = LDA, *t*-BuOK

R_1 = Me, *n*-Bu, Ph, 1-cyclohexenyl, TMS; R_2 = CO_2Et, COMe

Herein, we wish to report that the metal-bonded stereogenic carbon in stable oxapalladacycles **1** representing a carbon-bonded ester or amide enolate can be generated in a stereoselective manner (de up to 80%) via asymmetric induction from commercially available chiral nonracemic bidentate phosphine ligands (4*S*,5*S*)-(+)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane ((*S*,*S*)-DIOP) or (2*S*,4*S*)-(−)-2,4-bis(diphenylphosphino)pentane ((*S*,*S*)-BDPP). Insertion of dimethyl acetylenedicarboxylate (dmad) into a diastereomerically enriched palladacycle **1** (96% de after chromatography) proceeded with only minimal racemization, providing a chiral nonracemic 2*H*-1-benzopyran **2** (88.4% ee, $R_1 = R_2 =$ COOMe, Y = $CONEt_2$).[19] We have systematically explored factors that control asymmetric induction in the synthesis of palladacycles **1** and evaluated the configurational stability of the metal-bonded stereocenter. Absolute sense of stereoinduction could be controlled by the choice of the base (*t*-BuOK vs LDA), and good diastereoselectivity was achieved under both "kinetic" and "thermodynamic" conditions. Results described herein provide a proof of concept for the future development of a new approach to asymmetric synthesis of 2*H*-1-benzopyrans[20] and additional diverse applications of palladacycles **1** to asymmetric organic synthesis.

Results and Discussion

Synthesis and Structure Elucidation of Palladacycles 5a−c. Iodopalladium complexes **4a−c** possessing commercially available enantiomerically pure phosphine ligands (*S*,*S*)-DIOP[21] and (*S*,*S*)-BDPP[22] were obtained by straightforward ligand exchange reactions[23] with known[18] complexes **3a** and **3b** (Scheme 2). Bidentate

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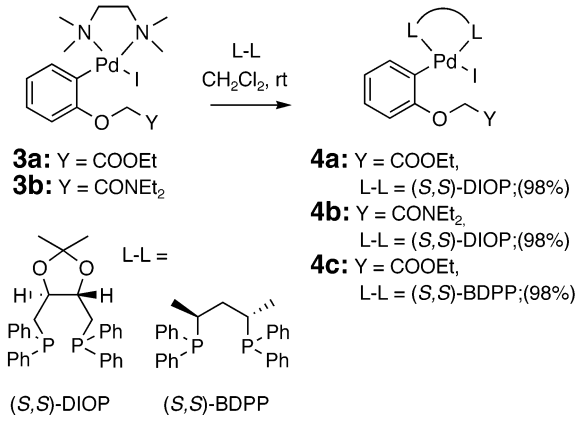
(23) Ludwig, M.; Strömberg, S.; Svensson, M.; Åkermark, B. *Organometallics* **1999**, *18* (6), 970−975.

Scheme 2



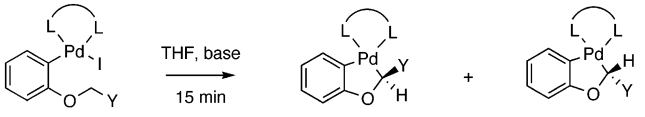
ligands with three- and four-carbon tethers were selected because a synthesis of a 2*H*-1-benzopyran via alkyne insertion into a racemic palladacycle bearing a structurally related achiral 1,4-bis(diphenylphosphino)-butane (dppb) ligand has been described.[18]

^{1}H and ^{31}P NMR spectra of iodopalladium complexes **4a**−**c** showed temperature-dependent features. ^{31}P NMR spectra of complexes **4a**−**c** consisted of one major and one minor pair of doublets corresponding to nonequivalent phosphorus atoms present in two distinct conformations of the seven-membered and six-membered "chelate" rings.[24] Changes in chemical shifts and relative intensities of the two pairs of doublets were noted when ^{31}P NMR spectra recorded at 25 and 55 °C were compared.[25]

Treatment of iodopalladium complexes **4a**−**c** with appropriate bases (e.g., *t*-BuOK or LDA) afforded the corresponding palladacycles **5a**−**c** in good overall yields (71−99%) as moisture- and air-stable solids in variable diastereomeric purities (8−80% de) (vida infra) (Table 1).

Spectroscopic data for complexes **5a**−**c** fully support the structures depicted in Table 1. Resonances at δ 5.35 and 5.22 (dd, $J(^1H-^{31}P) = 10.6$ Hz, 8.1 Hz), δ 5.94 and 5.69 (dd, $J(^1H-^{31}P) = 8.6-9.9$ Hz, 6.8−7.3 Hz), and δ 5.50 and 5.17 (t, $J(^1H-^{31}P) = 8.5-8.7$ Hz) in the ^{1}H NMR (500 MHz, $CDCl_3$) spectra of palladacycles **5a**, **5b**, and **5c**, respectively, were assigned to the methine protons attached to stereogenic metal-bonded carbons. The palladium-bonded methine carbons were found to resonate at δ 97.1 and 98.3 (dd, $J(^{13}C-^{31}P) = 85.0-85.4$ Hz, 5.6−5.9 Hz), δ 104.3 (dd, $J(^{13}C-^{31}P) = 89.2-92.0$ Hz, 4.3−4.9 Hz), and δ 95.9 and 98.5 (dd, $J(^{13}C-^{31}P) = 84.4-85.3$ Hz, 5.4−5.7 Hz) in the ^{13}C NMR (125 MHz, $CDCl_3$) spectra for complexes **5a**, **5b**, and **5c**, respectively. The corresponding H−C correlations were established via 2D NMR (HMQC) analyses on complexes **5a**, **5b**, and **5c**. Two pairs of doublets were detected in ^{31}P NMR (162 MHz, $CDCl_3$) spectra of complexes **5a**−**c** (**5a**: δ 10.72 (d, $J = 30.3$ Hz), 7.50 (d, $J = 30.1$ Hz) and δ 12.28 (d, $J = 30.7$ Hz), 3.42 (d, $J = 30.3$ Hz); **5b**: δ 8.38 (d, $J = 31.1$ Hz), 7.61 (d, $J = 31.2$ Hz) and δ 8.76 (d, $J = 30.9$ Hz), 3.52 (d, $J = 30.8$ Hz); **5c**: δ 21.74 (d, $J = 45.8$ Hz), 14.34 (d, $J = 46.0$ Hz) and δ 22.34 (d, $J = 43.1$ Hz), 16.65 (d, $J = 43.0$ Hz)). Thus, the indicative spectral features appeared as two clearly distinguishable sets in various ratios in ^{1}H and ^{31}P NMR spectra recorded for products **5a**−**c** of products **5a**−**c** of the ring-closure reactions of complexes **4a**−**c** (Table 1). Careful thin-layer chromatography (silica, EtOAc/hexanes) of these materials indicated the presence of two compounds with close retention factors (R_f), and variable-temperature NMR studies did not reveal any temperature-dependent features in ^{1}H and ^{31}P NMR spectra within the range of temperatures examined (25−55 °C). On the basis of this evidence, integration of the two ^{1}H NMR signals corresponding to methine protons at 5.17−5.94 ppm was employed as a convenient method for determining the ratios of diastereomers **5.1a**−**c**:**5.2a**−**c**[26] shown in Table 1.

Table 1. Effects of Reaction Conditions on Diastereoselectivity in the Synthesis of Stable Oxapalladacycles



4a-c **5.1a- 5.1c** **5.2a - 5.2c**

a: Y = COOEt, L-L = (*S*,*S*)-DIOP; **b:** Y = $CONEt_2$, L-L = (*S*,*S*)-DIOP;
c: Y = COOEt, L-L = (*S*,*S*)-BDPP

	substrate	base	temp (°C)	diastereomeric ratio **5.1a−c** (%)	diastereomeric ratio **5.2a−c** (%)	de (%)	combined yield (%)
	4a			**5.1a**	**5.2a**		
1		KHMDS[a]	−78	35	65	30	94
2		*t*-BuOK	rt	44	56	12	72
3			−78	69	31	38	88
4		LDA	rt	63	37	26	72
5			−78	86	14	72	89
6		(R*)MeNLi[b]	−78	90	10	80	98
	4b			**5.1b**[c]	**5.2b**[c]		
7		*t*-BuOK	rt	24	76	52	71
8			0	25	75	50	88
9			−78	44	56	12	*d*
10		LDA	rt	54	46	8	82
11			−78	77	23	54	91
	4c			**5.1c**	**5.2c**		
12		*t*-BuOK	rt	64	36	28	99
13			−78	87	13	74	99
14		LDA	rt	42	58	16	94
15			−78	12	88	76	99

[a] Reaction time was extended to 2 h. [b] R* = PhCH(Me)− with a *R* configuration. [c] The assignment of the absolute configuration is arbitrary. See ref 26. [d] The reaction proceeded with only a partial conversion of the starting material.

Crystallization of palladacycle **5c** (L = (*S*,*S*)-BDPP, Y = COOEt) (72% de, **5.1c**:**5.2c** = 14:86 by ^{1}H NMR) via slow diffusion of hexane into a methylene chloride solution at room temperature afforded diffraction-quality crystals of a pure major diastereomer, **5.2c**, as confirmed by spectroscopic analyses of the crystalline material (^{1}H NMR: δ 5.17 (t, $J(^1H-^{31}P) = 8.5$ Hz)). The

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(25) For example, see data for complex **4a**: ^{31}P NMR (202 MHz, $CDCl_3$, 25 °C): δ 11.31 (d, $J = 38.8$ Hz, 0.24 P), 11.24 (d, $J = 38.9$ Hz, 0.76 P), −3.70 (d, $J = 38.9$ Hz, 0.76 P), −6.15 (d, $J = 39.0$ Hz, 0.24 P); ^{31}P NMR (202 MHz, $CDCl_3$, 55 °C) δ 11.04 (d, $J = 39.0$ Hz, 1 P), −3.62 (d, $J = 39.0$ Hz, 0.35 P), −5.53 (d, $J = 39.0$ Hz, 0.65 P).

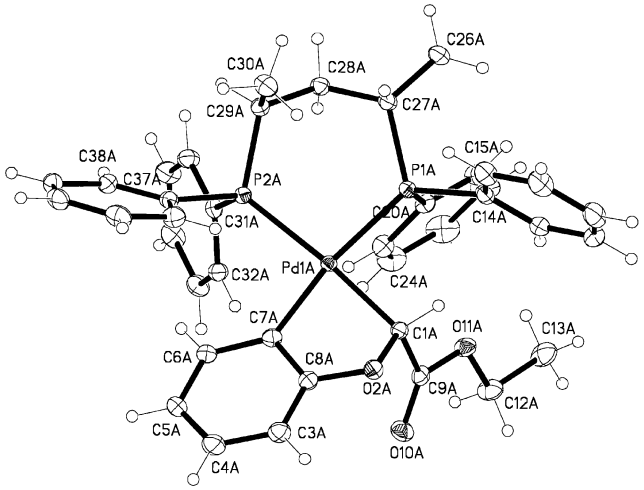


Figure 1. Crystal structure of complex **(+)-(*R*,*S*,*S*)-5.2c**. Ellipsoids represent a 50% probability level.

X-ray crystal structure of complex **5.2c** depicted in Figure 1 indicates the absolute configuration of the metal-bonded sp^3-hybridized stereogenic carbon as *R*, allowing for the assignment of the absolute configuration of the diastereomer **5.2c** as (*R*,*S*,*S*) and the diastereomer **5.1c** (^{1}H NMR: δ 5.50 (t, $J(^1H-^{31}P) = 8.4$ Hz)) as (*S*,*S*,*S*).

However, attempts to obtain diffraction-quality crystals of palladacycles **5a** and **5b** were unsuccessful. Diastereomeric purity of palladacycles **5.1a** (78% de) and **5.1b** (50% de) could be further increased by flash column chromatography over silica, which afforded diastereomer **5.1a**[26] (^{1}H NMR: δ 5.35 (dd, $J(^1H-^{31}P) =$ 10.6 Hz, 8.1 Hz) in 94% de, diastereomer **5.1b**[26] (^{1}H NMR: δ 5.94 (dd, $J(^1H-^{31}P) = 8.7$ Hz, 6.8 Hz) in 94% and 96% de, and a fraction containing the diastereomer **5.2b**[26] (^{1}H NMR: δ 5.70 (dd, $J(^1H-^{31}P) = 9.9$ Hz, 7.3 Hz) in 94% de.

Investigation of the Factors that Control Asymmetric Induction and Configurational Stability of the Metal-Bonded Stereocenters. The choice of the base and the reaction temperature proved to be the most important parameters for the control of asymmetric induction in the preparation of palladacycles **5a**−**c**. However, no common trends in responses to these factors could be identified among substrates **4a**−**c** that differ in the nature of ligands L−L and the electron-withdrawing group Y. In experiments reported in Table 1, care was taken not to alter the diastereomeric compositions of the crude products **5a**−**c** upon isolation.[27]

Diastereoselectivity of the preparation of palladacycle **5.1a** (Y = COOEt, L−L = (*S*,*S*)-DIOP) via the treatment of complex **4a** with either *t*-BuOK or LDA was increased to 72% de by lowering the reaction temperature to −78 °C (entries 2−5, Table 1). Further improvement in the diastereomeric excess of complex **5.1a** up to 80% de was achieved by employing a chiral nonracemic base generated in situ via deprotonation of (*R*)-(+)-*N*,α-dimethylbenzylamine by *n*-BuLi[28] (entry 6, Table 1). The opposite diastereomer **5.2a** was prepared in 30% de when the ring closure reaction of complex **4a** was mediated by KHMDS at −78 °C (entry 1, Table 1). Application of *t*-BuOLi, chiral alkoxide bases (potassium (1*R*,2*S*)- or (1*S*,2*R*)-[α-[1-(dimethylamino)ethyl]benzenemethoxide),[29] LiHMDS, NaHMDS, and variations in the nature of solvents (benzene) and additives ($AgNO_3$) did not prove effective for the ring closure, or did not significantly improve the observed diastereoselectivities.

Different trends were observed with complex **4b** featuring the amide functionality (entries 7−11, Table 1). Diastereomer **5.2b** was isolated in 52% de from the reaction mediated by *t*-BuOK at room temperature (entry 7, Table 1). Surprisingly, reaction at 0 °C afforded essentially the same result (entry 8, Table 1), and a further decrease in the reaction temperature to −78 °C led to incomplete conversion (entry 9, Table 1). The ring closure mediated by LDA at −78 °C was selective for the opposite diastereomer, providing complex **5.1b** in 54% de (entry 11, Table 1). Attempts to mediate the ring closure by chiral nonracemic lithium bases (lithium (*R*)- or (S)-*N*,α-dimethylbenzylamides)[28] or chiral alkoxide bases (potassium (1*R*,2*S*)- or (1*S*,2*R*)-[α-[1-(dimethylamino)ethyl]benzenemethoxide])[29] were unsuccessful.

Complex **4c**, featuring the (*S*,*S*)-BDPP ligand, participated in highly diastereoselective ring closure reactions when treated with either *t*-BuOK or LDA at low temperatures (entries 13 and 15, Table 1). Notably, while the ring closure with *t*-BuOK afforded diastereomer **5.1c** (74% de), the reaction mediated by LDA afforded the opposite diastereomer **5.2c** (76% de).

The observed differences in diastereoselectivity between reactions mediated by *t*-BuOK and LDA at variable temperatures prompted us to assess the configurational stability of the metal-bonded stereogenic center in the presence of an excess of *t*-BuOK (Table 2). Generation of enolates **6a**−**c** in low equilibrium concentrations may allow for either an "enrichment" or an "erosion" of the diastereomeric purities of palladacycles

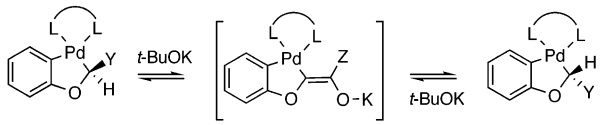
(26) In the ^{1}H NMR spectra of the diastereomers designated as **5.1**, the signal for the methine proton attached to the palladium-bonded carbon is found at *lower field* than in the spectra of the diastereomers designated as **5.2** (Table 1). Absolute configurations of the metal-bonded stereocenters for the diastereomers **5.1a** *S*, **5.1c** *S*, **5.2a** *R*, and **5.2c** *R* as shown in Table 1 were assigned via a combination of X-ray crystallographic studies on the complex **5.2c**, stereospecific ligand exchange, and specific optical rotations of complexes **7** (see Schemes 3 and 4 in the text). Note that the absolute configurations for the complexes **5.1b** and **5.2b** as shown in Tables 1 and 2 have been assigned arbitrarily.

(27) Workup procedures for the preparations of palladacycles **5a**−**c** as described in Table 1: Solutions of complexes **4a**−**c** in THF were treated with the indicated base at the indicated temperature. Crude reaction mixtures were filtered through a short plug of basic alumina eluting with ethyl acetate or ethyl acetate/hexanes mixtures with compositions that allowed for a complete elution of all the organometallic material. Solvents were removed under reduced pressure to afford the palladacycles **5a**−**c** as yellow solids. The diastereomeric composition of this material was determined by ^{1}H NMR spectroscopic analysis.

(28) (a) Cain, C. M.; Cousins, R. P. C.; Coumbarides, G.; Simpkins, N. S. *Tetrahedron* **1990**, *46* (2), 523−544. (b) Majewski, M.; Gleave, D. M.; Nowak, P. *Can. J. Chem.* **1995**, *73* (10), 1616−1626. When the opposite enantiomer of the chiral base, lithium (*S*)-(−)-*N*,α-dimethylbenzylamide, was applied to the ring closure of complex **4a**, a complete conversion into the palladacycle **5a** could not be achieved, even when an excess of the base was used for a prolonged reaction time. Both enantiomers of the base, lithium (*R*)- or (*S*)-*N*,α-dimethylbenzylamide, failed to allow for a complete conversion of complex **4b** into palladacycle **5b**.

(29) Plaquevent, J.-C.; Perrard, T.; Cahard, D. *Chem. Eur. J.* **2002**, *8* (15), 3301−3307. Attempted formation of palladacycles **5a** and **5b** via the treatment of complexes **4a** and **4b** with chiral alkoxides, potassium (1*R*,2*S*)- and (1*S*,2*R*)-[α-[1-(dimethylamino)ethyl]benzenemethoxide, obtained by the reaction of potassium hydride with *N*-methylephedrine in THF, afforded mixtures consisting of unreacted complexes **4a** or **4b** and palladacycles **5a** or **5b** with approximately 1:1 ratios of the diastereomers.

Table 2. Assessment of Configurational Stability of Palladium-Bonded Stereogenic Carbons in Stable Oxapalladacycles



5.1a-c **6a-c** **5.2a-c**

a: Y = COOEt, Z = OEt, L-L = (*S,S*)-DIOP;

b: Y = $CONEt_2$, Z = NEt_2, L-L = (*S,S*)-DIOP;

c: Y = COOEt, Z = OEt, L-L = (*S,S*)-BDPP

	diastereomeric ratio in substrate		time[a]	diastereomeric ratio in product		product de (%)	recovery (%)
	5.1 (%)	**5.2** (%)	(h)	**5.1** (%)	**5.2** (%)		
	5a			**5a**			
1	82	18	1	71	29	42	76
2	43	57	1	27	73	46	81
3	43	57	3	38	62	24	69
	5b[b]			**5b**[b]			
4	69	31	1	55	45	10	71
5	27	73	1	18	82	64	76
6	28	72	3	13	87	74	61
	5c			**5c**			
7	87	13	1	36	64	28	93
8	19	81	1	14	86	72	95
9	19	81	3	12	88	76	90

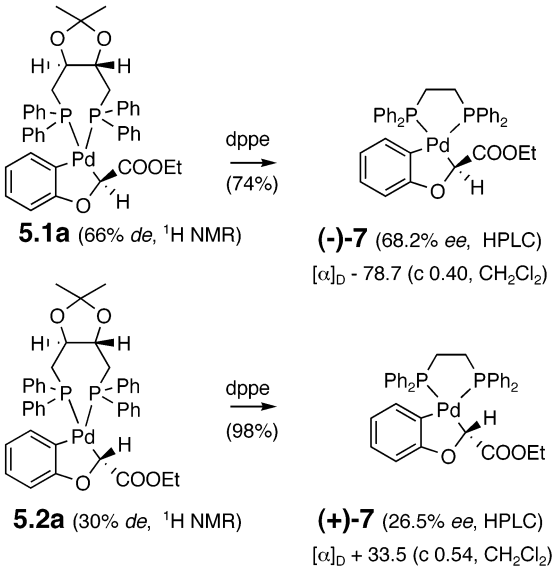
[a] To solutions of the substrates **5a**−**c** in THF was added 1.1 mol equiv of *t*-BuOK (1 M solutions in THF). Reaction mixtures were stirred for the indicated time period at room temperature. Diastereomeric composition of the recovered palladacycles **5a**−**c** was determined by ^{1}H NMR. [b] The assignment of the absolute configuration is arbitrary. See ref 26.

5a−**c**. Thus, treatment of palladacycles **5a**−**c** with 1.1 mol equiv of *t*-BuOK in THF for at least 1 h[30] resulted in significant shifts in the diastereomeric ratios measured for the recovered palladacycles (compare entries 1−3, 4−6, and 7−9 in Table 2) favoring the generation of the "thermodynamic" products **5.2a**, **5.2b**, and **5.2c**. The equilibration process described in Table 2 allowed us to raise the maximum diastereomeric purity of palladacycle **5.2a** to 46% de (entry 2, Table 2), and in the case of palladacycle **5.2b** to 74% de (entry 6, Table 2).

In summary, both diastereomers of palladacycles **5a** (in 80% and 46% de), **5b** (in 54% and 74% de), and **5c** (in 74% and 76% de) have been prepared via transfer of asymmetry using only one enantiomer of a chiral nonracemic ligand and employing either kinetic or thermodynamic conditions. The structures of the in situ generated alkaline metal ester and amide enolates appeared to play a critical role[31] in this process, since the choice of the base allowed us to control the absolute sense of asymmetric induction.

Ligand Exchange Reactions of the Diastereomerically Enriched Palladacycles. Assignments of Absolute Configurations. Both enantiomers of palladacycle **7** have been synthesized via ligand exchange reactions of palladacycles **5.1a**[26] and **5.2a**[26] with an achiral 1,2-bis(diphenylphosphino)ethane (dppe) ligand without affecting the configurational integrity of the metal-bonded stereocenter (Scheme 3).[32]

Scheme 3



5.1a (66% *de*, ^{1}H NMR) **(-)-7** (68.2% *ee*, HPLC) $[\alpha]_D$ - 78.7 (c 0.40, CH_2Cl_2)

5.2a (30% *de*, ^{1}H NMR) **(+)-7** (26.5% *ee*, HPLC) $[\alpha]_D$ + 33.5 (c 0.54, CH_2Cl_2)

Enantiomeric purities of complexes **(**−**)-7** (68.2% ee) and **(**+**)-7** (26.5% ee), determined by HPLC analyses on a chiral stationary phase (Chiralpak AD), were in acceptable agreement[33] with the diastereomeric ratios of substrates **5.1a** (66% de) and **5.2a** (30% de) measured by ^{1}H NMR spectroscopy (Scheme 3). In both the reactions, care was taken to ensure that complete conversion of the complexes **5.1a** and **5.2a** was achieved. Enantiomerically enriched palladacycle **(**−**)-7** (74.1% ee)[33] did not racemize to a significant degree when dissolved in 2-propanol at room temperature, showing 73.1% ee in an HPLC analysis repeated after 7 days, or when the solution of the complex **(**−**)-7** (74.1% ee)[33] in ethyl acetate was treated with silica for 1 h, yielding recovered complex **(**−**)-7** in 73.8% ee.

An exchange of (*S,S*)-BDPP ligand in complex **5.2c** (62% de) for the achiral dppe ligand afforded complex **(**+**)-7** (62.1% ee by HPLC) (Scheme 4). Assuming that the ligand exchange proceeded with retention of the absolute configuration *R* at the metal-bonded stereogenic carbon[32] in substrate **5.2c** (Figure 1), a correlation of the signs of optical rotation measured for complexes **7** (Schemes 3 and 4) was used to assign the absolute configurations of the metal-bonded stereocenters for

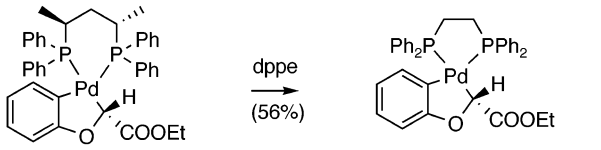
(30) However, no changes in the diastereomeric composition of palladacycles **5a**−**c** could be detected when the complexes were treated in neat THF (rt, 1 h), in THF with 0.1 mol equiv of *t*-BuOK (rt, 1 h), and in THF with 0.5 mol equiv of *t*-BuOK (rt, 1 h).

(31) For a discussion of the differences in the structure and the aggregation state of enolate anions of lithium and potassium metals, see: Smith, M. B. *Organic Synthesis*; McGraw-Hill: New York, 1994; Chapter 9, pp 865−869.

(32) Stability of a Pd−C bond during a ligand exchange process has been previously established (see ref 4b) and used for the preparation of enantiomerically enriched transition metal complexes with achiral ligands, see refs 4a, 6 and: Ryabov, A. D.; Panyashkina, I. M.; Polyakov, V. A.; Howard, J. A. K.; Kuzmina, L. G.; Datt, M. S.; Sacht, C. *Organometallics* **1998**, *17* (16), 3615−3618.

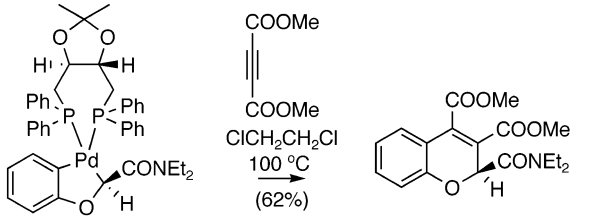
(33) In the case of palladacycle **(**−**)-7**, the agreement between the value of the diastereomeric ratio in substrates **5.1a** (determined by ^{1}H NMR) and the enantiomeric excess of complex **(**−**)-7** measured by chiral phase HPLC analyses was lower than expected. This could have been caused by the tendency of complex **(**−**)-7** to selectively precipitate during the removal of solvents under reduced pressure. Although all the solvents were removed to avoid a net enantiomeric enrichment, the bulk of the solid material was not homogeneous. This explanation is supported by a relatively large discrepancy noted for repeated HPLC analyses of the same sample (up to relative 3%). Conversion of complex **5.1a** into the enantiomerically enriched palladacycle **(**−**)-7** was repeated several times with the following results: (i) complex **5.1a** (60% de) yielded palladacycle **(**−**)-7** (62% yield, 56.9% ee); (ii) complex **5.1a** (70% de) yielded palladacycle **(**−**)-7** (84% yield, 72.7% ee); (iii) complex **5.1a** (80% de) yielded palladacycle **(**−**)-7** (61% yield, 74.1% ee).

Scheme 4



5.2c (62% *de,* ^{1}H NMR) **(+)-7** (62.1% *ee*, HPLC)
$[\alpha]_D$ + 71.7 (c 0.52, CH_2Cl_2)

Scheme 5 [a]



5.1b (96% *de,* ^{1}H NMR)[a] **(-)-8** (88.4% *ee*, HPLC)[a]

[a] Assignments of the absolute configuration are arbitrary.

palladacycles **5.1a** as *S* and **5.2a** as *R* (Scheme 3, and Tables 1 and 2).

Synthesis of a Chiral Nonracemic 2*H*-1-Benzopyran. To explore the applicability of palladacycles **5** for asymmetric organic synthesis, insertion of dimethyl acetylenedicarboxylate (dmad) into palladacycles **5a**−**c** was studied.[18] Optimum reactivity was observed for complexes **5b**, bearing a sterically demanding amide functionality.[34] The reaction of diastereomer **5.1b** enriched to 96% de (by ^{1}H NMR) by column chromatography, with dmad ($ClCH_2CH_2Cl$, 6 h at 100 °C and 16 h at room temperature) afforded benzopyran **(−)-8**[18] in good yield (62%) and only moderately diminished (8% racemization) enantiomeric excess of 88.4% ee, as established by HPLC on a chiral stationary phase (Chiralpak AD) (Scheme 5). The extent of racemization increased slightly when palladacycle **5.1b** enriched to 94% de (by ^{1}H NMR) was treated with dmad for an extended time at elevated temperature (10 h at 100 °C and 16 h at room temperature) yielding benzopyran **(−)-8** in 82.1% ee (by HPLC, 12.6% racemization). The reaction period at room temperature (16 h) allowed for gradual precipitation of palladium(0) and thus facilitated chromatographic purification of benzopyran **(−)-8** without significantly affecting its enantiomeric purity. Thus, benzopyran **(−)-8** with 87.2% ee was obtained when palladacycle **5.1b** (96% de by ^{1}H NMR) was reacted with dmad at elevated temperature ($ClCH_2CH_2Cl$, 6 h at 100 °C) followed by an immediate isolation of the product. Decreasing the reaction temperature from 100 °C to 80 °C eliminated the racemization, but HPLC analysis of benzopyran **(−)-8** detected the presence of less than 5% unreacted palladacycle **5.1b**, which was difficult to separate by column chromatography. Although 2*H*-1-benzopyran **(−)-8** proved relatively resistant to racemization[35] during chromatographic purification and extended solution manipulations without protection from light, the possibility that a slow racemization of benzopyran **(−)-8** accounts for the slight loss of the stereochemical information in the alkyne insertion reaction cannot be ruled out. This work represents a rare study on the fate of a nonracemic transition metal-bonded stereocenter in subsequent carbon−carbon bond forming reactions.[19] At present we are unable to assign the absolute configurations of benzopyran **(−)-8** and palladacycles **5b**,[26] and work toward this goal is in progress.

(34) Under the optimized reaction conditions (dmad 2.2 mol equiv, $ClCH_2CH_2Cl$, 6 h at 100 °C and 16 h at room temperature), palladacyle **5a** afforded after repeated chromatographic purification a 45% yield of the corresponding benzopyran[18] in 80% purity (by ^{1}H NMR), and palladacycles **5c** and **7** failed to yield the desired organic product.

Conclusions

In conclusion, an efficient transfer of asymmetry from chiral nonracemic ligands into a transition metal-bonded stereogenic sp^3-hybridized carbon has been demonstrated. The transformation allowed for a diastereoselective (46−80% de) synthesis of novel oxapalladacycles representing rare examples of stable chiral nonracemic palladium ester and amide enolates with a metal-bonded stereogenic α-carbon. Our studies revealed that for a selected enantiomer of the ligand, the absolute sense of stereoinduction could be controlled by the choice of the base, operating under either kinetic or thermodynamic conditions. Absolute configurations of palladacycles **5a** and **5c** were assigned relying on an X-ray crystallographic analysis and stereoselective ligand exchange reactions. A synthetically valuable highly substituted 2*H*-1-benzopyran was synthesized in a good enantiomeric purity (88.4% ee) via a stereoselective insertion of an alkyne into a diastereomerically enriched (96% de) palladacycle. In this transformation, the palladium-bonded stereogenic carbon was incorporated into a carbon framework with only a minimal loss (8% racemization) of the stereochemical information. Further generalization of this concept with respect to ligand structures and reaction types of the novel palladacycles is being pursued in our laboratories.

Experimental Section

Unless otherwise indicated, all NMR data were collected at room temperature in $CDCl_3$ with internal $CHCl_3$ as the reference (δ 7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C) and "internal" (present in a sealed capillary inserted into the NMR tube) H_3PO_4 (85%) (δ 0 ppm) as the reference for ^{31}P NMR. Specific rotation was measured on an AUTOPOL IV polarimeter (Rudolph Research Analytical) at room temperature in methylene chloride. IR spectra were measured in KBr pellets or as thin films on salt (NaCl) plates. Melting points are uncorrected and were taken in open capillary tubes. MS were measured under fast atom bombardment (FAB) or electron impact (EI) conditions. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN. Analytical thin-layer chromatography (TLC) was carried out on commercial Merck silica gel 60 plates, 0.25 μm thickness, with fluorescent indicator (F-254) or stained with aqueous $KMnO_4$ solution. Column chromatography was performed with 40−63 μm silica gel (Merck) or basic alumina (150 mesh, Brokmann I). Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone. 1,2-Dichloroethane was freshly distilled from CaH_2.

(35) (a) See ref 20a. (b) Van Gemert, B. In *Organic Photochromic and Thermochromic Compounds*; Crano, J. C., Guglielmetti, R. J., Eds.; Plenum: New York, 1999; Vol. 1, Chapter 3, p 111. Treatment of benzopyran **(−)-8** (82.1% ee) in 1,2-dichloroethane for 6 h at 100 °C in light or for 6 h at room temperature in light afforded the recovered benzopyrans **(−)-8** in 78.6% ee (4.2% racemization) and 76.8% ee (6.5% racemization), respectively. Treatment of benzopyran **(−)-8** (78.6%) dissolved in ethyl acetate with silica for 1 h afforded recovered benzopyran **(−)-8** in 76.3% ee (2.9% racemization).

Benzene was distilled from CaH_2 and kept over 3 Å (8−12 mesh) molecular sieves under an atmosphere of dry argon. Methylene chloride was kept over 3 Å (8−12 mesh) molecular sieves under an atmosphere of dry argon; other solvents were used as received. Unless otherwise specified, all reactions were carried out under an atmosphere of dry nitrogen or argon in oven-dried (at least 6 h at 140 °C) glassware. Single crystals for X-ray analysis were obtained by slow diffusion of hexanes into a methylene chloride solution of the palladium complex.

General Procedure for the Synthesis of Iodopalladium Complexes 4a−c. A solution of the complex **3a** or **3b** (1.0 mmol) and (*S*,*S*)-DIOP (1.1 mmol) or (*S*,*S*)-BDPP (1.1 mmol) in methylene chloride (55 mL for **4a**,**b** and 13.5 mL for **4c**) was stirred for the indicated time at room temperature under argon. The solvent was removed under reduced pressure, and the crude product was triturated with small amounts of ether/hexanes (3:1) to afford pure complexes **4a**−**c** as pale yellow or orange solids.

(+)-[2-(Ethoxycarbonylmethoxy)phenyl]iodo[(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (4a). Complex **3a** (0.789 g, 1.49 mmol), (*S*,*S*)-DIOP (0.845 g, 1.64 mmol), and methylene chloride (80 mL) were treated according to the general procedure described above for 1 h to afford complex **4a** (1.33 g, 98%) as a yellow solid: mp 152−153 °C dec (EtOAc/hexanes, 1:2); R_f = 0.58 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +115.2 (*c* 0.65, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 5 °C) δ 8.05 (t, J = 9.3 Hz, 1.3 H), 7.99−7.91 (m, 0.3 H), 7.82 (t, J = 9.4 Hz, 1.7 H), 7.74−7.71 (m, 2.7 H), 7.57−7.36 (m, 10 H), 7.20−7.10 (m, 2 H), 7.03 (t, J = 7.9 Hz, 1 H), 6.93 (td, J = 7.6 Hz, 2.3 Hz, 1 H), 6.85 (t, J = 9.4 Hz, 1 H), 6.48 (t, J = 7.1 Hz, 1 H), 6.43−6.38 (m, 1 H), 6.03−6.02 (m, 0.3 H), 5.90−5.88 (m, 0.7 H), 4.65 (d, J = 15.7 Hz, 0.3 H), 4.49 (d, J = 15.3 Hz, 0.7 H), 4.37−4.27 (m, 2 H), 4.21 (d, J = 15.7 Hz, 0.3 H), 4.06 (d, J = 15.3 Hz, 0.7 H), 3.90−3.82 (m, 1 H), 3.72−3.67 (m, 0.7 H), 3.40−3.29 (m, 1 H), 3.08 (t, J = 15.4 Hz, 0.7 H), 2.69 (t, J = 14.4 Hz, 0.7 H), 2.64−2.62 (m, 0.3 H), 2.48−2.44 (m, 0.3 H), 2.28−2.21 (m, 0.7 H), 2.11 (dd, J = 14.5 Hz, 9.5 Hz, 0.6 H), 1.37 (t, J = 7.1 Hz, 2 H), 1.33 (t, J = 7.1 Hz, 1 H), 1.25 (s, 3 H), 1.21 (s, 0.3 H), 1.15 (s, 0.7 H), 0.88 (d, J = 12.8 Hz, 1.4 H), 0.87 (d, J = 13.6 Hz, 0.6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ [169.6], 169.5, 157.7, [142.0], 141.0, [138.5 (d, $J(^{13}C-^{31}P)$ = 2.9 Hz)], 137.9 (d, $J(^{13}C-^{31}P)$ = 2.9 Hz), 135.4 (d, $J(^{13}C-^{31}P)$ = 12.4 Hz), [135.3 (d, $J(^{13}C-^{31}P)$ = 10.3 Hz)], 134.7 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz), 133.8, 133.7 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz), [133.6 (d, $J(^{13}C-^{31}P)$ = 11.0 Hz)], 133.3 (d, $J(^{13}C-^{31}P)$ = 9.5 Hz), [133.0 (d, $J(^{13}C-^{31}P)$ = 11.5 Hz)], 132.4 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz), 131.6 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 131.0 (d, $J(^{13}C-^{31}P)$ = 9.0 Hz), [130.8 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz)], 130.7 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 130.2 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 130.1 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 129.9 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), [129.7 (d, $J(^{13}C-^{31}P)$ = 2.9 Hz)], 128.9 (d, $J(^{13}C-^{31}P)$ = 10.5 Hz), 128.7 (d, $J(^{13}C-^{31}P)$ = 2.6 Hz), [128.5 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz)], 128.4 (d, $J(^{13}C-^{31}P)$ = 10.1 Hz), 127.9 (d, $J(^{13}C-^{31}P)$ = 9.2 Hz), [127.7 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz)], 127.0 (d, $J(^{13}C-^{31}P)$ = 10.4 Hz), 123.9, [123.8], [122.0 (d, $J(^{13}C-^{31}P)$ = 8.6 Hz)], 121.8 (d, $J(^{13}C-^{31}P)$ = 8.4 Hz), [112.3 (d, $J(^{13}C-^{31}P)$ = 5.6 Hz)], 111.1 (d, $J(^{13}C-^{31}P)$ = 5.5 Hz), 108.4, [107.9], 78.3 (dd, $J(^{13}C-^{31}P)$ = 7.6 Hz, 2.4 Hz), [77.0 (d, $J(^{13}C-^{31}P)$ = 9.2 Hz)], 76.5 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz), [66.1], 65.2, 60.8, [60.7], 31.9 (dd, $J(^{13}C-^{31}P)$ = 21.0 Hz, 3.8 Hz), 31.2 (dd, $J(^{13}C-^{31}P)$ = 17.9 Hz, 3.6 Hz), 26.8, [26.7], 26.5, [26.2], 14.4, [14.2], signals for the minor conformer are given in brackets, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 11.60 (d, J = 38.8 Hz, 0.25 P), 11.54 (d, J = 39.0 Hz, 0.75 P), −3.43 (d, J = 38.9 Hz, 0.75 P), −5.93 (d, J = 38.7 Hz, 0.25 P); IR (KBr, cm^{-1}) 3050 (m), 2980 (m), 1755 (s), 738 (s), 692 (s). Anal. Calcd for $C_{41}H_{43}IO_5P_2Pd$: C, 54.05; H, 4.76. Found: C, 54.56; H, 4.93.

(+)-[2-(*N*,*N*-Diethylcarbonylmethoxy)phenyl]iodo-[(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (4b). Complex **3b** (0.500 g, 0.899 mmol), (*S*,*S*)-DIOP (0.492 g, 0.987 mmol), and methylene chloride (50 mL) were treated according to the general procedure described above for 1 h to afford complex **4b** (0.844 g, 98%) as a yellow solid: mp 139−140 °C dec (EtOAc/hexanes, 1:1); R_f = 0.26 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +54.0 (*c* 0.74, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 5 °C) δ 7.95 (t, J = 9.5 Hz, 0.7 H), 7.85−7.82 (m, 2 H), 7.77 (t, J = 8.6 Hz, 1.3 H), 7.59 (t, J = 9.0 Hz, 1 H), 7.47−7.37 (m, 10 H), 7.30−7.11 (m, 6 H), 6.50−6.45 (m, 2 H), 6.95−6.89 (m, 1 H), 4.45−4.41 (m, 1 H), 4.25−4.22 (m, 0.3 H), 4.04−3.94 (m, 1.3 H), 3.91−3.84 (m, 1.3 H), 3.59−3.51 (m, 0.7 H), 3.47−3.41 (m, 1 H), 3.35−3.26 (m, 2 H), 3.19−3.14 (m, 1 H), 3.01 (t br, J = 14.2 Hz, 0.7 H), 2.73−2.67 (m, 0.3 H), 2.43 (t br, J = 12.2 Hz, 0.7 H), 2.30−2.18 (m, 1.7 H), 1.25 (s, 3 H), 1.17−1.11 (m, 3 H), 1.08 (t, J = 7.4 Hz, 2 H), 0.99 (s, 2 H), 0.97 (s, 1 H), 0.87 (t, J = 7.1 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7, 158.0, 137.8 (dd, $J(^{13}C-^{31}P)$ = 8.8 Hz, 2.6 Hz), 134.8 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz), 134.3 (t, $J(^{13}C-^{31}P)$ = 10.9 Hz), 134.0 (d, $J(^{13}C-^{31}P)$ = 4.3 Hz), [133.9 (d, $J(^{13}C-^{31}P)$ = 5.5 Hz)], [133.7], [133.0 (d, $J(^{13}C-^{31}P)$ = 10.4 Hz)], [132.5 (d, $J(^{13}C-^{31}P)$ = 10.7 Hz)], [131.8 (d, $J(^{13}C-^{31}P)$ = 10.0 Hz)], 131.7 (d, $J(^{13}C-^{31}P)$ = 10.0 Hz), 131.0 (d, $J(^{13}C-^{31}P)$ = 3.4 Hz), [130.9 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz)], 130.3 (dd, $J(^{13}C-^{31}P)$ = 23.9 Hz, 1.9 Hz), 129.5 (d, $J(^{13}C-^{31}P)$ = 2.9 Hz), 128.1 (t, $J(^{13}C-^{31}P)$ = 10.4 Hz), 128.0 (d, $J(^{13}C-^{31}P)$ = 9.2 Hz), 127.6 (d, $J(^{13}C-^{31}P)$ = 10.5 Hz), 124.0, 121.5 (t, $J(^{13}C-^{31}P)$ = 8.3 Hz), 111.6 (d, $J(^{13}C-^{31}P)$ = 4.8 Hz), [111.3 (d, $J(^{13}C-^{31}P)$ = 4.8 Hz)], 108.2, [107.9], 77.6 (dd, $J(^{13}C-^{31}P)$ = 7.5 Hz, 2.8 Hz), 76.5 (d, $J(^{13}C-^{31}P)$ = 2.2 Hz), [68.1], 67.6, [42.4], 42.2, [40.5], 40.4, 31.4 (dd, $J(^{13}C-^{31}P)$ = 21.0 Hz, 2.4 Hz), 29.8 (d, $J(^{13}C-^{31}P)$ = 23.6 Hz), 26.6, 26.5, [26.4], [14.8], 14.7, [14.2], 13.2, signals for the minor conformer are given in brackets, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 12.32 (d, J = 39.4 Hz, 0.69 P), 11.06 (d, J = 39.0 Hz, 0.31 P), −4.55 (d, J = 39.0 Hz, 0.31 P), −4.63 (d, J = 39.4 Hz, 0.69 P); IR (KBr, cm^{-1}) 3050 (m), 2979 (m), 2931 (m), 1663 (s), 739 (s), 692 (s). Anal. Calcd for $C_{43}H_{48}INO_4P_2Pd$: C, 55.05; H, 5.16; N, 1.49. Found: C, 54.97; H, 5.30; N, 1.50.

(+)-[2-(Ethoxycarbonylmethoxy)phenyl]iodo[(2*S*,4*S*)-2,4-bis(diphenylphosphino)pentane]palladium (4c). Complex **3a** (0.400 g, 0.757 mmol), (*S*,*S*)-BDPP (0.366 g, 0.831 mmol), and methylene chloride (10 mL) were treated according to the general procedure described above for 12 h to afford complex **4c** (0.633 g, 98%) as an orange solid: mp 173−174 °C dec (hexanes); R_f = 0.57 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +79.8 (*c* 0.54, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$, 5 °C) δ 8.31−8.27 (m, 2 H), 8.09−8.00 (m, 0.3 H), 7.78 (t, J = 9.2 Hz, 2 H), 7.70 (t, J = 8.7 Hz, 1.7 H), 7.67−7.62 (m, 0.3 H), 7.53 (s br, 2.7 H), 7.45 (s br, 0.3 H), 7.41 (t, J = 7.3 Hz, 1 H), 7.36−7.31 (m, 3 H), 7.17−7.13 (m, 3 H), 6.95 (t, J = 6.3 Hz, 1.7 H), 6.90−6.84 (m, 2.7 H), 6.51 (t, J = 7.3 Hz, 1 H), 6.43 (t, J = 7.2 Hz, 1 H), 6.20−6.15 (m, 0.3 H), 5.80−5.75 (m, 1 H), 4.41 (d, J = 15.1 Hz, 1 H), 4.36−4.31 (m, 1.7 H), 4.29−4.17 (m, 0.3 H), 3.60 (d, J = 15.1 Hz, 1 H), 3.20−3.10 (s br, 1 H), 2.85−2.80 (m, 0.7 H), 1.94−1.81 (m, 2.3 H), 1.39 (t, J = 7.1 Hz, 3 H), 1.29 (dd, J = 14.5 Hz, 7.0 Hz, 3 H), 0.91 (dd, J = 11.2 Hz, 7.1 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, [163.9], 158.7, 143.2, 142.3, 137.2 (d, $J(^{13}C-^{31}P)$ = 12.6 Hz), 136.6 (d, $J(^{13}C-^{31}P)$ = 2.8 Hz), 135.6 (d, $J(^{13}C-^{31}P)$ = 11.2 Hz), [135.2 (d, $J(^{13}C-^{31}P)$ = 10.6 Hz)], 134.2 (d, $J(^{13}C-^{31}P)$ = 9.6 Hz), [134.1 (d, $J(^{13}C-^{31}P)$ = 10.9 Hz)], 133.7, 133.4, 131.5 (d, $J(^{13}C-^{31}P)$ = 7.8 Hz), 131.3 (d, $J(^{13}C-^{31}P)$ = 2.8 Hz), 131.1, [130.8], 130.2 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 130.0 (d, $J(^{13}C-^{31}P)$ = 2.8 Hz), 129.8 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 128.7 (d, $J(^{13}C-^{31}P)$ = 8.8 Hz), 128.3 (d, $J(^{13}C-^{31}P)$ = 2.6 Hz), 127.8 (d, $J(^{13}C-^{31}P)$ = 10.7 Hz), 127.4 (d, $J(^{13}C-^{31}P)$ = 10.1 Hz), 126.6 (d, $J(^{13}C-^{31}P)$ = 9.9 Hz), 125.9, [125.6], 123.9, 121.4 (d, $J(^{13}C-^{31}P)$ = 8.4 Hz), 110.9 (d, $J(^{13}C-^{31}P)$ = 5.2 Hz), [66.1], 64.9, 60.5, [60.4], 35.6 (t, $J(^{13}C-^{31}P)$ = 6.7 Hz), 26.4 (dd, $J(^{13}C-^{31}P)$ = 20.4 Hz, 3.8 Hz), 23.3 (dd, $J(^{13}C-^{31}P)$ = 20.8 Hz, 6.3 Hz), 19.7 (d, $J(^{13}C-^{31}P)$ = 7.6 Hz), 16.3 (d, $J(^{13}C-^{31}P)$ = 5.9 Hz), 14.5, [14.3], signals for the minor

conformer are given in brackets, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.57 (d, J = 50.3 Hz, 0.13 P), 20.30 (d, J = 47.9 Hz, 0.87 P), 6.92 (d, J = 48.1 Hz, 0.87 P), 6.28 (d, J = 50.2 Hz, 0.13 P); IR (KBr, cm^{-1}) 3049 (m), 2978 (m), 1756 (s), 1192 (s), 744 (m), 695 (s); HRMS (FAB) calcd for $C_{39}H_{42}IO_3P_2Pd$ (M + H^+), 870.0954, found 870.0969. Anal. Calcd for $C_{39}H_{41}IO_3P_2Pd$: C, 54.91; H, 4.84. Found: C, 54.95; H, 5.08.

Synthesis of Palladacycles 5a−c. (−)-[(*S*)-(Ethoxycarbonylmethineoxy-1,2-phenylene)][(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (5.1a). To a solution of iodopalladium complex **4a** (0.150 g, 0.165 mmol) in THF (7.5 mL) at −78 °C was added a solution of lithium (*R*)-(+)-*N*,α-dimethylbenzylamide[29b] (1.1 mL, 0.173 mmol, in THF). The mixture was stirred at −78 °C for 15 min, quenched with 0.1 mL of MeOH, and filtered through a small plug of basic alumina, eluting with EtOAc. The solvent was removed under reduced pressure to afford palladacycle **5.1a** (0.126 g, 98%) as a yellow solid in 80% de (**5.1a**:**5.2a** = 90:10 by ^{1}H NMR). Palladacycle **5.1a** with diastereomeric excess 78% de was further purified by flash chromatography over silica eluting with EtOAc/hexanes (2:3), to afford complex **5.1a** in 94% de, **5.1a**:**5.2a** = 97:3 (by ^{1}H NMR): mp 155−158 °C dec (EtOAc/hexanes, 2:3); R_f = 0.42 (EtOAc/hexanes, 1:1); $[\alpha]_D$ −80.3 (*c* 0.40, CH_2Cl_2).

Analytical data for 5.1a as a 97:3 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (t, J = 8.9 Hz, 2 H), 7.87 (t, J = 8.9 Hz, 2 H), 7.61 (t, J = 8.7 Hz, 2 H), 7.53 (t, J = 8.9 Hz, 2 H), 7.48 (dd, J = 7.1 Hz, 1.6 Hz, 1 H), 7.43 (t, J = 7.9 Hz, 3 H), 7.36 (dd, J = 14.2 Hz, 7.1 Hz, 4 H), 7.34−7.25 (m, 4 H), 6.87−6.81 (m, 2 H), 6.45 (td, J = 7.9 Hz, 3.3 Hz, 1 H), 6.11−6.07 (m, 1 H), 5.35 (dd, J = 10.6 Hz, 8.1 Hz, 0.97 H), 5.22 (dd, J = 10.6 Hz, 8.1 Hz, 0.03 H), 4.07 (dq, J = 7.0 Hz, 3.6 Hz, 1 H), 3.99−3.94 (m, 1 H), 3.81 (dq, J = 7.1 Hz, 3.6 Hz, 1 H), 3.78−3.72 (m, 1 H), 3.19 (td, J = 13.3 Hz, 3.3 Hz, 1 H), 2.77 (ddd, J = 13.7 Hz, 11.2 Hz, 4.7 Hz, 1 H), 2.20 (t br, J = 5.0 Hz, 2 H), 1.21 (s, 3 H), 1.00 (t, J = 7.1 Hz, 3 H), 0.94 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.1, 174.0 (t, $J(^{13}C-^{31}P)$ = 4.8 Hz), 147.6 (dd, $J(^{13}C-^{31}P)$ = 106.2 Hz, 10.1 Hz), 140.3 (dd, $J(^{13}C-^{31}P)$ = 10.1 Hz, 2.9 Hz), 136.2 (dd $J(^{13}C-^{31}P)$ = 36.3 Hz, 2.9 Hz), 135.6 (d, $J(^{13}C-^{31}P)$ = 14.6 H), 134.1 (d, $J(^{13}C-^{31}P)$ = 13.2 Hz), 133.8 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz), 132.5 (d, $J(^{13}C-^{31}P)$ = 1.0 Hz), 132.2 (d, $J(^{13}C-^{31}P)$ = 11.0 Hz), 131.1 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 131.0 (d, $J(^{13}C-^{31}P)$ = 2.0 Hz), 130.8, 130.6 (t, $J(^{13}C-^{31}P)$ = 2.4 Hz), 130.5, 130.2, 130.1 (d, $J(^{13}C-^{31}P)$ = 1.8 Hz), 128.6 (dd, $J(^{13}C-^{31}P)$ = 10.1 Hz, 1.3 Hz), 128.5 (d, $J(^{13}C-^{31}P)$ = 7.1 Hz), 128.4 (d, $J(^{13}C-^{31}P)$ = 6.4 Hz), 126.1, 117.7 (dd, $J(^{13}C-^{31}P)$ = 8.6 Hz, 4.2 Hz), 109.1 (d, $J(^{13}C-^{31}P)$ = 2.3 Hz), 107.9, 97.1 (dd, $J(^{13}C-^{31}P)$ = 85.4 Hz, 5.9 Hz), 78.1 (dd, $J(^{13}C-^{31}P)$ = 14.9 Hz, 7.7 Hz), 76.7 (d, $J(^{13}C-^{31}P)$ = 10.3 Hz), 59.0, 31.1 (dd, $J(^{13}C-^{31}P)$ = 21.4 Hz, 5.5 Hz), 29.9 (d, $J(^{13}C-^{31}P)$ = 17.6 Hz), 26.7, 26.4, 14.5, only signals for the major diastereomer have been detected, some signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 12.28 (d, J = 30.7 Hz, 0.03 P), 10.72 (d, J = 30.3 Hz, 0.97 P), 7.50 (d, J = 30.1 Hz, 0.97 P), 3.42 (d, J = 30.3 Hz, 0.03 P).

(+)-[(*R*)-(Ethoxycarbonylmethineoxy-1,2-phenylene)]-[(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (5.2a). To a solution of iodopalladium complex **4a** (0.150 g, 0.165 mmol) in THF (7.5 mL) at −78 °C was added a solution of potassium bis(trimethylsilyl)amide (KHMDS) (0.5 M in toluene, 0.43 mL, 0.215 mmol). The mixture was stirred at −78 °C for 2 h, quenched with 0.1 mL of MeOH, and filtered through a small plug of basic alumina, eluting with EtOAc. The solvent was removed under reduced pressure to afford palladacycle **5.2a** (0.121 g, 94%) as a yellow solid in 30% de, **5.1a**:**5.2a** = 35:65 (by ^{1}H NMR). Palladacycle **5.2a** with diastereomeric excess 22% de was further purified by flash column chromatography over silica eluting with EtOAc/hexanes (2:3), to afford complex **5.2a** in 68% de, **5.1a**:**5.2a** = 16:84 (by ^{1}H NMR): mp 152−155 °C dec (EtOAc/hexanes, 1:1); R_f = 0.50 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +46.8 (*c* 0.34, CH_2Cl_2).

Analytical data for 5.2a as a 16:84 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (t, J = 8.9 Hz, 0.32 H), 8.03 (t, J = 8.7 Hz, 1.68 H), 7.87 (t, J = 8.9 Hz, 0.32 H), 7.81 (t, J = 8.6 Hz, 1.68 H), 7.61 (t, J = 8.7 Hz, 0.32 H), 7.55 (t, J = 9.7 Hz, 2 H), 7.49 (t, J = 8.4 Hz, 2 H), 7.45−7.40 (m, 3 H), 7.36 (q, J = 6.8 Hz, 2 H), 7.32−7.27 (m, 4 H), 7.24 (td, J = 7.4 Hz, 1.5 Hz, 1 H), 6.93 (t, J = 7.0 Hz, 1.68 H), 6.87−6.81 (m, 2 H), 6.59 (td, J = 8.1 Hz, 3.5 Hz, 0.84 H), 6.45 (td, J = 7.9 Hz, 0.16 H), 6.16 (tt, J = 7.1 Hz, 1.6 Hz, 0.84 H), 6.11−6.07 (m, 0.16 H), 5.35 (dd, J = 10.6 Hz, 8.1 Hz, 0.16 H), 5.22 (dd, J = 10.1 Hz, 8.5 Hz, 0.84 H), 4.27 (dq, J = 7.1 Hz, 3.6 Hz, 0.84 H), 4.16−4.05 (m, 1.84 H), 3.99−3.94 (m, 0.16 H), 3.86 (t, J = 9.5 Hz, 0.84 H), 3.81−3.72 (m, 0.32 H), 3.25 (td, J = 13.5 Hz, 4.6 Hz, 0.84 H), 3.19 (td, J = 13.7 Hz, 3.3 Hz, 0.16 H), 3.10 (ddd, J = 13.6 Hz, 10.9 Hz, 4.0 Hz, 0.84 H), 2.77 (ddd, J = 13.7 Hz, 11.2 Hz, 4.7 Hz, 0.16 H), 2.58 (td, J = 14.0 Hz, 4.1 Hz, 0.84 H), 2.20 (t br, J = 5.0 Hz, 0.32 H), 1.74 (dd, J = 14.7 Hz, 7.2 Hz, 0.84 H), 1.26 (t, J = 7.1 Hz, 2.52 H), 1.26 (s, 2.52 H), 1.21 (s, 3 H), 1.00 (t, J = 7.1 Hz, 0.48 H), 0.94 (s, 0.48 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.0 (q, $J(^{13}C-^{31}P)$ = 1.3 Hz), 174.6 (t, $J(^{13}C-^{31}P)$ = 4.8 Hz), 147.9 (dd, $J(^{13}C-^{31}P)$ = 107.1 Hz, 9.9 Hz), 140.5 (dd, $J(^{13}C-^{31}P)$ = 10.7 Hz, 3.1 Hz), 136.2 (dd, $J(^{13}C-^{31}P)$ = 38.1 Hz, 2.9 Hz), [136.6 (d, $J(^{13}C-^{31}P)$ = 14.8 Hz)], 135.2 (d, $J(^{13}C-^{31}P)$ = 13.2 Hz), [134.1 (d, $J(^{13}C-^{31}P)$ = 13.4 Hz)], 133.9 (dd, $J(^{13}C-^{31}P)$ = 14.8 Hz, 1.4 Hz), [133.8 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz)], 133.7 (dd, $J(^{13}C-^{31}P)$ = 1.4 Hz), 133.4 (d, $J(^{13}C-^{31}P)$ = 13.5 Hz), 132.4 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 132.2 (d, $J(^{13}C-^{31}P)$ = 10.9 Hz), 132.1 (d, $J(^{13}C-^{31}P)$ = 0.95 Hz), 131.7 (d, $J(^{13}C-^{31}P)$ = 10.0 Hz), 131.1 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), [131.0 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz)], 130.7 (dd, $J(^{13}C-^{31}P)$ = 38.6 Hz, 2.4 Hz), [130.7 (t, $J(^{13}C-^{31}P)$ = 2.4 Hz)], [130.2], [130.1 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz)], 129.7, 129.4, 129.3 (d, $J(^{13}C-^{31}P)$ = 1.8 Hz), 128.8 (d, $J(^{13}C-^{31}P)$ = 9.9 Hz), [128.6 (dd, $J(^{13}C-^{31}P)$ = 9.8 Hz, 1.6 Hz)], [128.5 (d $J(^{13}C-^{31}P)$ = 7.1 Hz)], 128.4 (d, $J(^{13}C-^{31}P)$ = 10.4 Hz), [128.4 (d, $J(^{13}C-^{31}P)$ = 6.4 Hz)], 128.3 (d, $J(^{13}C-^{31}P)$ = 9.4 Hz), [126.1], 126.0, 117.5 (q, $J(^{13}C-^{31}P)$ = 4.3 Hz), 109.2 (d, $J(^{13}C-^{31}P)$ = 2.1 Hz), [109.1], 108.3, [107.9], 98.3 (dd, $J(^{13}C-^{31}P)$ = 85.0 Hz, 5.6 Hz), 79.0 (dd, $J(^{13}C-^{31}P)$ = 9.6 Hz, 5.4 Hz), 76.3 (dd, $J(^{13}C-^{31}P)$ = 16.7 Hz, 2.4 Hz), 59.3, [59.0], 32.5 (dd, $J(^{13}C-^{31}P)$ = 24.7 Hz, 6.0 Hz), 27.6 (d, $J(^{13}C-^{31}P)$ = 14.7 Hz), 26.9, [26.7], 26.6, [26.4], 14.9, [14.5], signals for the minor diastereomer are shown in brackets, some signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 12.28 (d, J = 30.7 Hz, 0.84 P), 10.73 (d, J = 30.2 Hz, 0.16 P), 7.51 (d, J = 30.1 Hz, 0.16 P), 3.42 (d, J = 30.7 Hz, 0.84 P).

Analytical data for a mixture of diastereomers 5.1a:5.2a (86:14): IR (KBr, cm^{-1}) 3051 (m), 2981 (m), 2931 (w), 1706 (s), 1240 (s), 745 (s), 696 (s); HRMS (FAB) calcd for $C_{41}H_{43}O_5P_2Pd$ (M + H^+), 783.1621 found 783.1618.

(−)-[(*R* or *S*)-(*N*,*N*-Diethylcarbonylmethineoxy-1,2-phenylene)][(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (5.1b). To a solution of iodopalladium complex **4b** (0.686 g, 0.732 mmol) in THF (34 mL) at −78 °C was added a solution of LDA (1.5 M in cyclohexane, 0.53 mL, 0.795 mmol). The mixture was stirred at −78 °C for 15 min, quenched with 0.1 mL of MeOH, and filtered through a small plug of basic alumina, eluting with EtOAc/hexanes (1:1). The solvent was removed under reduced pressure to afford palladacycle **5.1b** (0.542 g, 91%) as a yellow solid in 54% de, **5.1b**:**5.2b** = 77:23 (by ^{1}H NMR). Palladacycle **5.1b** with diastereomeric excess 50% de was further purified by flash chromatography over silica eluting with EtOAc/hexanes (2:3), to afford complex **5.1b** in 94% de, **5.1b**:**5.2b** = 97:3 (by ^{1} H NMR): mp 143−147 °C dec (EtOAc/hexanes); R_f = 0.29 (EtOAc/hexanes, 1:1); $[\alpha]_D$ −45.8 (*c* 0.45, CH_2Cl_2).

Analytical data for 5.1b as a 97:3 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (ddd, J = 10.0 Hz,

8.2 Hz, 2.2 Hz, 2 H), 8.00 (t, J = 8.6 Hz, 2 H), 7.86 (t, J = 8.6 Hz, 2 H), 7.62 (t, J = 8.7 Hz, 2 H), 7.49 (td, J = 7.3 Hz, 1.5 Hz, 1 H), 7.46 (td, J = 7.6 Hz, 1.5 Hz, 2 H), 7.39−7.35 (m, 4 H), 7.32 (td, J = 7.7 Hz, 1.7 Hz, 2 H), 7.28 (td, J = 7.4 Hz, 1.4 Hz, 1 H), 7.21 (td, J = 7.8 Hz, 1.7 Hz, 2 H), 6.78 (td, J = 8.2 Hz, 1.4 Hz, 1 H), 6.68 (ddd, J = 7.9 Hz, 3.0 Hz, 1.2 Hz, 1 H), 6.65 (tdd, J = 7.9 Hz, 3.4 Hz, 1.4 Hz, 1 H), 6.11 (tt, J = 7.4 Hz, 1.5 Hz, 1 H), 5.94 (dd, J = 8.7 Hz, 6.8 Hz, 0.97 H), 5.69 (dd, J = 9.9 Hz, 7.3 Hz, 0.03 H), 4.00−3.95 (m, 1 H), 3.66−3.61 (m, 1 H), 3.61−3.17 (s br, 2 H), 3.14 (td, J = 13.5 Hz, 2.4 Hz, 1 H), 3.05 (t br, J = 6.5 Hz, 2 H), 2.55 (ddd, J = 13.9 Hz, 10.8 Hz, 4.7 Hz, 1 H), 2.33 (tt, J = 15.1 Hz, 5.1 Hz, 1 H), 2.18−2.11 (m, 1 H), 1.18 (s, 3 H), 1.01 (t, J = 7.0 Hz, 6 H), 0.90 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.1 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 174.7 (t, $J(^{13}C-^{31}P)$ = 5.6 Hz), 148.8 (dd, $J(^{13}C-^{31}P)$ = 103.4 Hz, 9.4 Hz), 140.5 (dd, $J(^{13}C-^{31}P)$ = 10.5 Hz, 2.9 Hz), 136.3 (dd, $J(^{13}C-^{31}P)$ = 35.3 Hz, 2.9 Hz), 135.0 (d, $J(^{13}C-^{31}P)$ = 14.0 Hz), 134.2 (d, $J(^{13}C-^{31}P)$ = 13.5 Hz), 133.2 (d, $J(^{13}C-^{31}P)$ = 12.5 Hz), 132.9 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 132.2 (d, $J(^{13}C-^{31}P)$ = 11.4 Hz), 131.9 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 131.7 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 131.4, 131.1, 130.9 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 130.4 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 130.1 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 129.7 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 128.6 (dd, $J(^{13}C-^{31}P)$ = 11.5 Hz, 10.0 Hz), 128.3 (dd, $J(^{13}C-^{31}P)$ = 9.4 Hz, 2.6 Hz), 125.7, 117.2 (dd, $J(^{13}C-^{31}P)$ = 8.2 Hz, 4.2 Hz), 108.6 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 107.7, 104.3 (dd, $J(^{13}C-^{31}P)$ = 89.2 Hz, 4.3 Hz), 77.9 (dd, $J(^{13}C-^{31}P)$ = 17.0 Hz, 7.1 Hz), 77.1 (d, $J(^{13}C-^{31}P)$ = 31.5 Hz), 41.1 (s br, 2 C), 31.7 (dd, $J(^{13}C-^{31}P)$ = 19.8 Hz, 5.5 Hz), 29.8 (d, $J(^{13}C-^{31}P)$ = 18.5 Hz), 26.8, 26.4, 13.7 (s br, 2 C), only signals for the major diastereomer were detected, some signals account for more than one carbon, broadening of certain signals is the result of a hindered rotation about the C−N bond in the amide group; ^{31}P NMR (162 MHz, $CDCl_3$) δ 8.38 (d, J = 31.1 Hz, 1 P), 7.61 (d, J = 31.2 Hz, 1 P); only signals for the major diastereomer were detected.

(+)-[(*R* or *S*)-(*N*,*N*-Diethylcarbonylmethineoxy-1,2-phenylene)][(4*S*,5*S*)-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane]palladium (5.2b). To a solution of iodopalladium complex **4b** (0.151 g, 0.160 mmol) in THF (7.5 mL) at room temperature was added a solution of *t*-BuOK (1.0 M in THF, 0.18 mL, 0.180 mmol). The mixture was stirred at room temperature for 15 min and filtered through a small plug of basic alumina eluting with EtOAc/hexanes (1:1). The solvent was removed under reduced pressure to afford palladacycle **5.2b** (0.092 g, 71%) as a yellow solid in 52% de (**5.1b**:**5.2b** = 24:76 by ^{1}H NMR). In a subsequent step, a solution of palladacycle **5.2b** (0.031 g, 0.038 mmol) with 44% de (**5.1b**:**5.2b** = 28:72 by ^{1}H NMR) in THF (2.5 mL) at room temperature was resubjected to the closing conditions by adding a solution of *t*-BuOK (1.0 M in THF, 0.042 mL, 0.042 mmol). The mixture was stirred at room temperature for 3 h and filtered through a small plug of basic alumina eluting with EtOAc/hexanes (1:1). The solvent was removed under reduced pressure to afford palladacycle **5.2b** (0.019 g, 61%) in 74% de, **5.1b**:**5.2b** = 13:87 (by ^{1}H NMR).

Palladacycle **5.1b** with diastereomeric excess 50% de was further purified by flash chromatography over silica eluting with EtOAc/hexanes (2:3) to afford a fraction containing complex **5.2b** in 94% de, **5.1b**: **5.2b** = 3:97 (by ^{1}H NMR): mp 144−147 °C dec (EtOAc/hexanes, 2:3); R_f = 0.37 (EtOAc/hexanes, 1:1); $[\alpha]_D$ +31.0 (*c* 0.51, CH_2Cl_2).

Analytical data for 5.2b as a 3:97 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (t, J = 8.5 Hz, 2 H), 7.83 (t, J = 8.8 Hz, 2 H), 7.56 (t, J = 7.3 Hz, 2 H), 7.51 (td, J = 8.2 Hz, 1.6 Hz, 2 H), 7.43 (ddd, J = 9.9 Hz, 7.7 Hz, 2.2 Hz, 2 H), 7.33 (td, J = 7.2 Hz, 1.5 Hz, 1 H), 7.28 (td, J = 7.9 Hz, 1.4 Hz, 6 H), 7.16 (td, J = 7.4 Hz, 1 H), 6.86 (td, J = 7.7 Hz, 1.4 Hz, 2 H), 6.81 (td, J = 7.5 Hz, 1.3 Hz, 1 H), 6.72 (td, J = 7.9 Hz, 2.8 Hz, 1 H), 6.67 (ddd, J = 7.8 Hz, 3.1 Hz, 1.0 Hz, 1 H), 6.18 (t, J = 7.4 Hz, 1 H), 5.93 (dd, J = 8.6 Hz, 6.8 Hz, 0.03 H) 5.70 (dd, J = 9.9 Hz, 7.3 Hz, 0.97 H), 4.23 (dt, J = 13.2 Hz, 8.2 Hz, 1 H), 3.82−3.77 (m, 1 H), 3.46 (s br 2 H), 3.30−3.21 (m, 2 H), 3.03 (s br, 2 H), 2.67 (td, J = 14.4 Hz, 4.2 Hz, 1 H), 1.66 (dd, J = 14.6 Hz, 8.4 Hz, 1 H), 1.27 (s, 3 H), 1.24 (s, 3 H), 1.10 (s br, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 174.9 (t, $J(^{13}C-^{31}P)$ = 5.7 Hz), 148.9, 141.0 (dd, $J(^{13}C-^{31}P)$ = 10.7 Hz, 2.6 Hz), 136.7 (dd, $J(^{13}C-^{31}P)$ = 38.6 Hz, 3.8 Hz), 135.3 (d, $J(^{13}C-^{31}P)$ = 13.4 Hz), 135.0 (t, $J(^{13}C-^{31}P)$ = 1.9 Hz), 133.8 (d, $J(^{13}C-^{31}P)$ = 13.5 Hz), 133.3 (dd, $J(^{13}C-^{31}P)$ = 32.0 Hz, 1.9 Hz), 133.1 (d, $J(^{13}C-^{31}P)$ = 13.0 Hz), 131.6 (d, $J(^{13}C-^{31}P)$ = 10.0 Hz), 130.9 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 130.5 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 130.2 (d, $J(^{13}C-^{31}P)$ = 2.4 Hz), 130.0, 129.7, 128.8 (d, $J(^{13}C-^{31}P)$ = 9.8 Hz), 128.7 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 128.3, 128.2 (d, $J(^{13}C-^{31}P)$ = 2.0 Hz), 127.9 (d, $J(^{13}C-^{31}P)$ = 9.5 Hz), 125.7, 117.4 (dd, $J(^{13}C-^{31}P)$ = 8.6 Hz), 108.6, 108.1, 104.3 (dd, $J(^{13}C-^{31}P)$ = 92.0 Hz, 4.9 Hz), 79.3 (dd, $J(^{13}C-^{31}P)$ = 9.5 Hz, 4.3 Hz), 76.4 (dd, $J(^{13}C-^{31}P)$ = 17.6 Hz, 2.9 Hz), 41.1 (s br, 2 C), 33.3 (dd, $J(^{13}C-^{31}P)$ = 24.1 Hz, 5.5 Hz), 26.9, 26.8, 26.1 (d, $J(^{13}C-^{31}P)$ = 15.1 Hz), 13.7 (s, br, 2 C), only signals for the major diastereomer were detected, several signals account for more than one carbon, broadening of certain signals is the result of a hindered rotation about the C−N bond in the amide group; ^{31}P NMR (162 MHz, $CDCl_3$) δ 8.76 (d, J = 30.9 Hz, 1 P), 3.52 (d, J = 30.8 Hz, 1 P); only the signals for the major diastereomer were detected.

Analytical data for a mixture of diastereomers 5.1b:5.2b (69:31): IR (KBr, cm^{-1}) 3051 (m), 2981 (m), 2930 (m), 1582 (m), 1223 (m), 743 (s), 696 (s); HRMS (FAB) calcd for $C_{43}H_{48}NO_4P_2Pd$ ($M + H^+$), 810.2093, found 810.2119.

(+)-[(*S*)-(Ethoxycarbonylmethineoxy-1,2-phenylene)]-[(2*S*,4*S*)-2,4-bis(diphenylphosphino)pentane]palladium (5.1c). To a solution of iodopalladium complex **4c** (0.150 g, 0.176 mmol) in THF (7.5 mL) at −78 °C was added a solution of *t*-BuOK (1.0 M in THF, 0.20 mL, 0.200 mmol). The mixture was stirred at −78 °C for 15 min and filtered through a small plug of basic alumina eluting with EtOAc. The solvent was removed under reduced pressure to afford palladacycle **5.1c** (0.126 g, 99%) as an orange solid in 74% de, **5.1c**:**5.2c** = 87:13 (by ^{1}H NMR); R_f = 0.32 (EtOAc/hexanes, 2:3); $[\alpha]_D$ +1.1 (*c* 0.55, CH_2Cl_2).

Analytical data for 5.1c as a 87:13 mixture of diastereomers: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05−8.02 (m, 0.26 H), 7.84 (t, J = 6.6 Hz, 1.74 H), 7.71 (t, J = 8.6 Hz, 0.26 H), 7.67−7.62 (m, 3.48 H), 7.60 (t, J = 8.8 Hz, 0.26 H), 7.53 (td, J = 8.6 Hz, 1.5 Hz, 3.26 H), 7.46−7.39 (m, 3 H), 7.38−7.34 (m, 2 H), 7.33−7.30 (m, 1.74 H), 7.28−7.25 (m, 2 H), 7.11 (td, J = 7.7 Hz, 1.4 Hz, 2 H), 6.85−6.84 (m, 1.74 H), 6.79−6.77 (m, 0.26 H), 6.51 (td, J = 7.9 Hz, 3.3 Hz, 0.87 H), 6.50 (td, J = 7.9 Hz, 3.6 Hz, 0.13 H), 6.21−6.15 (m, 0.87 H), 6.12−6.09 (m, 0.13 H), 5.50 (t, J = 8.7 Hz, 0.87 H), 5.17 (t, J = 8.5 Hz, 0.13 H), 3.92 (dq, J = 7.0 Hz, 3.6 Hz, 1 H), 3.69 (dq, J = 7.1 Hz, 3.6 Hz, 0.87 H), 2.91−2.87 (m, 0.13 H), 2.84−2.78 (m, 0.87 H), 2.77−2.68 (m, 1 H), 2.08−1.92 (m, 1 H), 1.91−1.78 (m, 1 H), 1.73−1.66 (m, 0.13 H), 1.91 (dd, J = 11.0 Hz, 7.0 Hz, 2.61 H), 1.13−1.07 (m, 3 H), 0.93 (t, J = 7.1 Hz, 2.61 H), 0.92−0.88 (m, 0.39 H), 0.63 (t, J = 7.1 Hz, 0.39 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 174.5 (t, J = 4.3 Hz), 148.8 (dd, $J(^{13}C-^{31}P)$ = 103.6 Hz, 7.7 Hz), 139.9 (dd, $J(^{13}C-^{31}P)$ = 9.5 Hz, 2.4 Hz), [137.0 (d, $J(^{13}C-^{31}P)$ = 14.2 Hz)], 135.8 (d, $J(^{13}C-^{31}P)$ = 12.0 Hz), [134.9 (d, $J(^{13}C-^{31}P)$ = 11.9 Hz)], 134.4 (d, $J(^{13}C-^{31}P)$ = 12.6 Hz), [134.3 (d, $J(^{13}C-^{31}P)$ = 12.7 Hz)], 134.0 (d, $J(^{13}C-^{31}P)$ = 11.8 Hz), 133.9 (d, $J(^{13}C-^{31}P)$ = 10.2 Hz), [132.1 (d, $J(^{13}C-^{31}P)$ = 9.2 Hz)], 131.2 (d, $J(^{13}C-^{31}P)$ = 1.4 Hz), 131.2, 131.1 (dd, $J(^{13}C-^{31}P)$ = 6.2 Hz, 2.4 Hz), 130.9, [130.7 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz)], 130.6 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), 130.4, 130.3 (dd, $J(^{13}C-^{31}P)$ = 13.4 Hz, 2.0 Hz), 130.2 (d, $J(^{13}C-^{31}P)$ = 2.1 Hz), 130.1 (d, $J(^{13}C-^{31}P)$ = 2.1 Hz), 129.5 (d, $J(^{13}C-^{31}P)$ = 1.9 Hz), [129.1 (d, $J(^{13}C-^{31}P)$ = 9.5 Hz)], 128.7 (d, $J(^{13}C-^{31}P)$ = 9.3 Hz), [128.3 (d, $J(^{13}C-^{31}P)$ = 8.8 Hz)], 128.2 (d, $J(^{13}C-^{31}P)$ = 9.6 Hz), 127.9 (d, $J(^{13}C-^{31}P)$ = 9.0 Hz), [127.8 (d, $J(^{13}C-^{31}P)$ = 9.7 Hz)], 127.6 (d, $J(^{13}C-^{31}P)$ = 9.5 Hz), [127.5 (d, $J(^{13}C-^{31}P)$ = 10.2 Hz)], 125.7, [125.6], 117.5 (dd, $J(^{13}C-^{31}P)$ = 8.3 Hz, 4.4 Hz),

109.0 (d, $J(^{13}C-^{31}P) = 2.5$ Hz), [108.6 (d, $J(^{13}C-^{31}P) = 2.5$ Hz)], 95.9 (dd, $J(^{13}C-^{31}P) = 84.4$ Hz, 5.4 Hz), 58.5, [58.2], 35.4 (t, $J(^{13}C-^{31}P) = 6.3$ Hz), 29.7, [29.1 (dd, $J(^{13}C-^{31}P) = 22.2$ Hz, 5.0 Hz)], 28.1 (dd, $J(^{13}C-^{31}P) = 21.9$ Hz, 6.0 Hz), 25.6 (dd, $J(^{13}C-^{31}P) = 16.6$ Hz, 1.8 Hz), [19.1 (d, $J(^{13}C-^{31}P) = 7.5$ Hz)], 17.9 (d, $J(^{13}C-^{31}P) = 2.5$ Hz), [16.9 (d, $J(^{13}C-^{31}P) = 4.9$ Hz)], 16.7 (d, $J(^{13}C-^{31}P) = 3.2$ Hz), 14.6, [14.0], signals for the minor diastereomer are given in brackets, several signals account for more than one carbon; ^{31}P NMR (162 MHz, $CDCl_3$) δ 22.34 (d, $J = 43.1$ Hz, 0.13 P), 21.74 (d, $J = 45.8$ Hz, 0.87 P), 16.65 (d, $J = 43.0$ Hz, 0.13 P), 14.34 (d, $J = 46.0$ Hz, 0.87 P).

(+)-[(*R*)-(Ethoxycarbonylmethineoxy-1,2-phenylene)]-[(2*S*,4*S*)-2,4-bis(diphenylphosphino)pentane]palladium (5.2c). To a solution of iodopalladium complex **4c** (0.148 g, 0.174 mmol) in THF (7.5 mL) at −78 °C was added a solution of LDA (1.5 M in cyclohexane, 0.13 mL, 0.195 mmol). The mixture was stirred at −78 °C for 15 min, quenched with 0.1 mL of MeOH, and filtered through a small plug of basic alumina eluting with EtOAc. The solvent was removed under reduced pressure to afford palladacycle **5.2c** (0.125 g, 99%) as an orange solid in 76% de, **5.1c**:**5.2c** = 12:88 (by ^{1}H NMR). Palladacycle **5.2c** with diastereomeric excess 72% de, **5.1c**:**5.2c** = 14:86 (by ^{1}H NMR), was crystallized by a slow diffusion of hexane into a methylene chloride solution of the palladacycle to afford palladacycle **5.2c** as a pure diastereomer: mp 212−214 °C dec (CH_2Cl_2/hexanes); $R_f = 0.38$ (EtOAc/hexanes, 2:3); $[\alpha]_D$ +99.4 (*c* 0.18, CH_2Cl_2).

Analytical data for a pure diastereomer 5.2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06−8.01 (m, 2 H), 7.71 (t, $J = 8.6$ Hz, 2 H), 7.59 (t, $J = 8.6$ Hz, 2 H), 7.56−7.53 (m, 5 H), 7.45−7.41 (m, 3 H), 7.37−7.35 (m, 2 H), 7.26 (t, $J = 7.5$ Hz, 2 H), 7.13 (td, $J = 7.3$ Hz, 1.5 Hz, 2 H), 6.79−6.77 (m, 2 H), 6.50 (td, $J = 7.9$ Hz, 3.3 Hz, 1 H), 6.14−6.07 (m, 1 H), 5.17 (t, $J = 8.5$ Hz, 1 H), 3.91 (dq, $J = 7.1$ Hz, 3.6 Hz, 1 H), 2.86 (dq, $J = 7.1$ Hz, 3.6 Hz, 1 H), 2.81−2.73 (m, 2 H), 1.85−1.72 (m, 1 H), 1.70−1.62 (m, 1 H), 1.11 (dd, $J = 14.1$ Hz, 7.1 Hz, 3 H), 0.90 (dd, $J = 9.7$ Hz, 7.0 Hz, 3 H) 0.62 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.7, 140.9 (dd, $J(^{13}C-^{31}P) = 9.3$ Hz, 2.4 Hz), 137.0 (d, $J(^{13}C-^{31}P) = 13.8$ Hz), 134.7 (dd, $J(^{13}C-^{31}P) = 70.0$ Hz, 12.2 Hz), 132.1 (d, $J(^{13}C-^{31}P) = 9.4$ Hz), 130.7 (dd, $J(^{13}C-^{31}P) = 16.0$ Hz, 2.1 Hz), 130.5, 130.2 (d, $J(^{13}C-^{31}P) = 1.9$ Hz), 129.1 (d, $J(^{13}C-^{31}P) = 9.5$ Hz), 128.3 (d, $J(^{13}C-^{31}P) = 8.8$ Hz), 127.7 (dd, $J(^{13}C-^{31}P) = 36.5$ Hz, 10.0 Hz), 127.1, 126.8, 125.6, 117.8 (dd, $J(^{13}C-^{31}P) = 8.3$ Hz, 4.1 Hz), 108.7 (d, $J(^{13}C-^{31}P) = 2.4$ Hz), 98.5 (dd, $J(^{13}C-^{31}P) = 85.3$ Hz, 5.7 Hz), 58.2, 35.6 (d, $J(^{13}C-^{31}P) = 5.2$ Hz), 29.0 (dd, $J(^{13}C-^{31}P) = 21.7$ Hz, 5.5 Hz), 25.8 (dd, $J(^{13}C-^{31}P) = 18.8$ Hz, 5.0 Hz), 19.1 (d, $J(^{13}C-^{31}P) = 7.5$ Hz), 16.9 (d, $J(^{13}C-^{31}P) = 4.9$ Hz), 14.0, several signals account for more than one carbon; ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.32 (d, $J = 43.0$ Hz, 1 P), 16.65 (d, $J = 42.7$ Hz, 1 P).

Analytical data for a mixture of diastereomers 5.1c:5.2c (87:13): IR (KBr, cm^{-1}) 3050 (m), 2975 (m), 2927 (m), 1701 (s), 1480 (m), 1157 (s), 746 (s), 697 (s); HRMS (FAB) calcd for $C_{39}H_{41}O_3P_2Pd$ ($M + H^+$), 725.1566, found 725.1541. Anal. Calcd for $C_{39}H_{40}O_3P_2Pd$: C, 64.60; H, 5.56. Found: C, 64.21; H, 5.88.

General Procedure for Preparation of (+)-[(*R*)-Ethoxycarbonylmethineoxy-1,2-phenylene)][1,2-bis(diphenylphosphino)ethane]palladium (+)-7 and (−)-[(*S*)-Ethoxycarbonylmethineoxy-1,2-phenylene)][1,2-bis(diphenylphosphino)ethane]palladium (−)-7. Solutions of complexes **5.1a** or **5.2a** (1.0 mmol) and dppe (1.1 mmol) in methylene chloride (78 mL) were stirred for 16 h at room temperature under argon. The crude reaction mixtures were purified by flash chromatography over silica eluting with EtOAc/hexanes (1:1) to afford pure palladacycles **(+)-7** or **(−)-7** as white solids.

(−)-[(*S*)-Ethoxycarbonylmethineoxy-1,2-phenylene)]-[1,2-bis(diphenylphosphino)ethane]palladium [(−)-7]. Complex **5.1a** (0.032 g, 0.407 mmol) with 66% de, **5.1a**:**5.2a** = 83:17 (by ^{1}H NMR), and dppe (0.036 g, 0.091 mmol) were treated according to the general procedure described above to afford complex **(−)-7** (0.021 g, 74%) as a yellow solid in 68.2% ee, **5.1a**:**5.2a** = 15.87:84.12 (by HPLC): $[\alpha]_D$ −78.7 (*c* 0.40, CH_2Cl_2).

(+)-[(*R*)-Ethoxycarbonylmethineoxy-1,2-phenylene)]-[1,2-bis(diphenylphosphino)ethane]palladium [(+)-7]. Complex **5.2a** (0.061 g, 0.077 mmol) with 30% de, **5.1a**:**5.2a** = 35:65 (by ^{1}H NMR), and dppe (0.035 g, 0.087 mmol) were treated according to the general procedure described above to afford complex **(+)-7** (0.052 g, 98%) as a white solid in 26.5% ee, **5.1a**:**5.2a** = 36.73:63.26 (by HPLC): $[\alpha]_D$ +33.5 (*c* 0.54, CH_2Cl_2).

(+)-[(*R*)-Ethoxycarbonylmethineoxy-1,2-phenylene)]-[1,2-bis(diphenylphosphino)ethane]palladium [(+)-7]. To a solution of **5.2c** (0.050 g, 0.069 mmol) with 62% de, **5.1c**:**5.2c** = 19:81 (by ^{1}H NMR) in methylene chloride (5 mL), was added dppe (0.095 g, 0.239 mmol) by a stepwise addition of a single equivalent over a period of 4 days. Solvents were removed under reduced pressure, and the resulting solid was triturated with ether to afford the crude product as a yellow solid. The crude product was purified by filtration through a short plug of silica eluting with EtOAc/hexanes (2:1) to afford complex **(+)-7** (0.263 g, 56%) as a pale yellow solid in 62.1% ee, **5.1c**:**5.2c** = 18.95:81.05 (by HPLC): $[\alpha]_D$ +71.7 (*c* 0.52, CH_2Cl_2).

Analytical data for palladacycle (±)-7: mp 213−214 °C dec (ether); $R_f = 0.70$ (EtOAc/hexanes, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94−7.90 (m, 2 H), 7.78−7.69 (m, 6 H), 7.50−7.38 (m, 12 H), 6.95 (ddd, $J = 7.9$ Hz, 3.4 Hz, 1.3 Hz, 1 H), 6.91 (dd, $J = 7.0$ Hz, 1.3 Hz, 1 H), 6.89−6.85 (m, 1 H), 6.31 (dd, $J = 9.9$ Hz, 3.8 Hz, 1 H), 6.26 (tt, $J = 7.2$ Hz, 1.6 Hz, 1 H), 3.86 (dq, $J = 7.1$ Hz, 3.4 Hz, 1 H), 3.22 (dq, $J = 7.1$ Hz, 3.6 Hz, 1 H), 2.64−2.48 (m, 1 H), 2.38−2.25 (m, 1 H), 2.06−1.99 (m, 1 H), 1.85−1.74 (m, 1 H), 0.76 (t, $J = 7.1$ Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4 (d, $J(^{13}C-^{31}P) = 3.0$ Hz), 175.4 (t, $J(^{13}C-^{31}P) = 4.6$ Hz), 140.4 (dd, $J(^{13}C-^{31}P) = 10.9$ Hz, 2.4 Hz), 134.7 (dd, $J(^{13}C-^{31}P) = 13.6$ Hz, 3.0 Hz), 134.0 (t, $J(^{13}C-^{31}P) = 5.4$ Hz), 133.5 (d, $J(^{13}C-^{31}P) = 12.9$ Hz), 132.6 (d, $J(^{13}C-^{31}P) = 11.5$ Hz), 132.0, 131.4, 131.3 (d, $J(^{13}C-^{31}P) = 7.9$ Hz), 131.1 (d, $J(^{13}C-^{31}P) = 9.9$ Hz), 131.0, 130.5 (dd, $J(^{13}C-^{31}P) = 69.1$ Hz, 2.4 Hz), 129.4, 129.0 (dd, $J(^{13}C-^{31}P) = 13.4$ Hz, 10.0 Hz), 128.8 (d, $J(^{13}C-^{31}P) = 6.8$ Hz), 128.7 (dd, $J(^{13}C-^{31}P) = 17.8$ Hz, 9.8 Hz), 126.3, 117.9 (dd, $J(^{13}C-^{31}P) = 8.1$ Hz, 4.9 Hz), 109.4 (d, $J(^{13}C-^{31}P) = 2.0$ Hz), 96.8 (dd, $J(^{13}C-^{31}P) = 85.6$ Hz, 5.3 Hz), 58.7, 29.7 (dd, $J(^{13}C-^{31}P) = 26.4$ Hz, 17.0 Hz), 28.9 (dd, $J(^{13}C-^{31}P) = 26.7$ Hz, 18.2 Hz), 14.1, several signals account for more than one carbon; ^{31}P NMR (202 MHz, $CDCl_3$) δ 44.23 (d, $J = 19.3$ Hz, 1 P), 41.39 (d, $J = 19.0$ Hz, 1 P); IR (KBr, cm^{-1}): 3049 (w), 2980 (w), 1692 (s), 1434 (m), 1176 (m), 747 (w), 699 (w); HRMS (FAB) calcd for $C_{36}H_{35}O_3P_2Pd$ ($M + H^+$), 683.1096, found 683.1073. Anal. Calcd for $C_{36}H_{34}O_3P_2Pd$: C, 63.30; H, 5.02. Found: C, 63.02; H, 5.13.

(−)-2-*N*,*N*-Diethylcarbonyl-3,4-bis(methoxycarbonyl)-2*H*-1-benzopyran [(−)-8].[18] To a solution of palladacycle **5.1b** with 96% de, **5.1b**:**5.2b** = 98:2 (by ^{1}H NMR) (0.146 g, 0.180 mmol) in methylene chloride (5.5 mL), was added dimethyl acetylenedicarboxylate (0.048 mL, 0.055 g, 0.390 mmol). The reaction mixture was stirred for 6 h at 100 °C and subsequently for 16 h at room temperature in a 25 mL sealed glass tube. The crude reaction mixture was purified by flash chromatography over silica eluting with EtOAc/hexanes (1:2) to afford pure 2*H*-1-benzopyran **(−)-8** (0.039 g, 62%) as a light yellow oil in 88.4% ee (by HPLC): $[\alpha]_D$ −13.4 (*c* 1.36 CH_2Cl_2); $R_f = 0.56$ (EtOAc/hexanes, 1:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (td, $J = 7.8$ Hz, 1.4 Hz, 1 H), 7.08 (dd, $J = 7.8$ Hz, 1.5 Hz, 1 H), 6.93 (td, $J = 7.6$ Hz, 1.0 Hz, 1 H), 6.84 (d, $J = 8.2$ Hz, 1 H), 5.95 (s, 1 H), 3.96 (s, 3 H), 3.77 (s, 3 H), 3.70−3.55 (m, 2 H), 3.36−3.23 (m, 2 H), 1.33 (t, $J = 7.1$ Hz, 3 H), 1.06 (t, $J = 7.1$ Hz, 3 H).

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Supporting Information Available: Descriptions of the X-ray crystallographic study on palladacycle **5.2c** and experimental procedures for the experiments in Table 2 and for the chiral-phase chromatographic analyses. Includes HPLC chromatograms of (±)**-7**, **(+)-7**, **(−)-7**, **(±)-8**, and **(−)-8** and photocopies of ^{1}H and ^{13}C NMR spectra of complexes **4a**−**c**, **5a**−**c**, and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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