Design and Preparation of 3,3′-Disubstituted 2,2′-Bis(oxazolyl)-1,1′-binaphthyls (boxax): New Chiral Bis(oxazoline) Ligands for Catalytic Asymmetric Wacker-Type Cyclization

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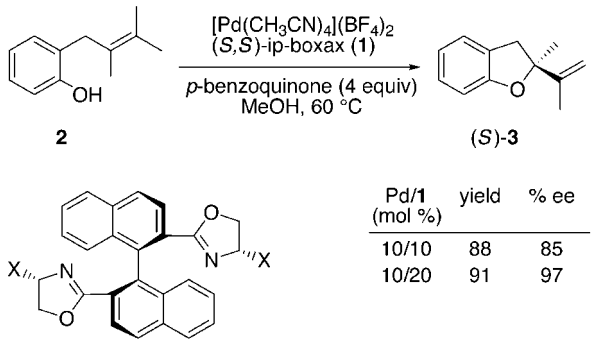
New optically active 2,2′-bis(oxazolyl)-1,1′-binaphthyls (boxax) bearing various substituents (methoxycarbonyl, trimethylsilyl, (dimethylamino)carbonyl, formyl, and iodo) at their C3 and C3′ positions were prepared via *ortho*-lithiation promoted by the oxazolyl groups. The 3,3′-disubstituted boxax ligands showed much higher enantioselectivity than the 3,3′-unsubstituted ones in the palladium(II)-catalyzed Wacker-type cyclization of an *o*-allylphenol. The cyclization of (*E*)-2-(2-methyl-2-butenyl)phenol (**10**) in the presence of a cationic palladium catalyst coordinated with (*S*)-2,2′-bis(4,4-dimethyloxazol-2-yl)-3,3′-bis(methoxycarbonyl)-1,1′-binaphthyl gave (*S*)-2-ethenyl-2-methyl-2,3-dihydrobenzofuran of 96% ee.

Introduction

Considerable efforts have been devoted to the development of new chiral ligands due to the growing importance of transition metal-catalyzed asymmetric synthesis.[1] In a series of our studies on asymmetric synthesis with chiral transition metal complexes, appropriate modification of the chiral ligands often provided us with highly enantioselective catalysts for a variety of asymmetric transformations.[2] Recently, we have developed optically active bis(oxazoline) ligands, (*S*)-2,2′-bis(oxazol-2-yl)-1,1′-binaphthyls ((*S*)-boxax),[3] which found utilities as chiral ligands for copper(I)-catalyzed asymmetric cyclopropanation[3a] and palladium(II)-catalyzed asymmetric Wacker-type cyclization.[3b,c] In both of these reactions, steric tuning of boxax by introduction of alkyl substituents at the C4 position of the oxazoline rings (e.g. (*S*)-2,2′-bis((*S*)-4-isopropyloxazol-2-yl)-1,1′-binaphthyls ((*S,S*)-ip-boxax, **1**)) was found to be effective to bring about high stereoselectivity. Palladium(II)-catalyzed Wacker-type cyclization of *o*-allylphenol **2** shown in Scheme 1 is one of the representatives. Described here is the design and the preparation of new boxax ligands where several functional groups were introduced at the C3 and C3′ positions, and their successful application to asymmetric Wacker-type cyclization.

Scheme 1



Pd/**1** (mol %)	yield	% ee
10/10	88	85
10/20	91	97

Results and Discussion

Preparation of 3,3′-Disubstituted Boxax. A series of new boxax ligands, all of which have C3 and C3′ substituents, were prepared in good to excellent yields via *ortho*-lithiation[4] of (*S,S*)-ip-boxax **1** or (*S*)-2,2′-bis(4,4-dimethyloxazol-2-yl)-1,1′-binaphthyl ((*S*)-dm-boxax, **6**). The dimethyloxazolyl derivative, (*S*)-dm-boxax (**6**), was prepared from (*S*)-1,1′-binaphthyl-2,2′-dicarboxylic acid (**4**)[5] according to the procedures reported for the preparation of **1**[3a] (Scheme 2). Treatment of dicarboxylic acid (*S*)-**4** with refluxing thionyl chloride followed by condensation of the resulting diacyl chloride with 2-amino-2-

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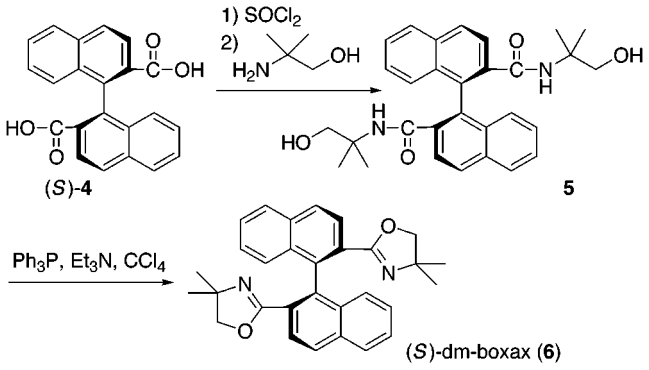
Scheme 2



Scheme 3

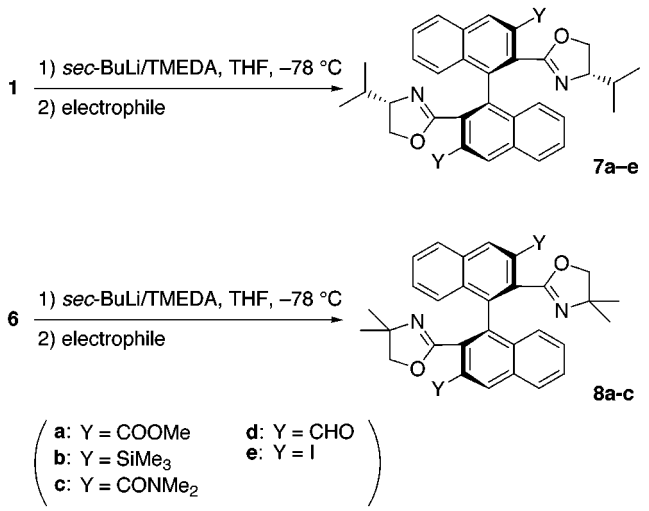


Table 1. Introduction of Various Substituents at C3 and C3′ Positions of Boxax 1 and 6[a]

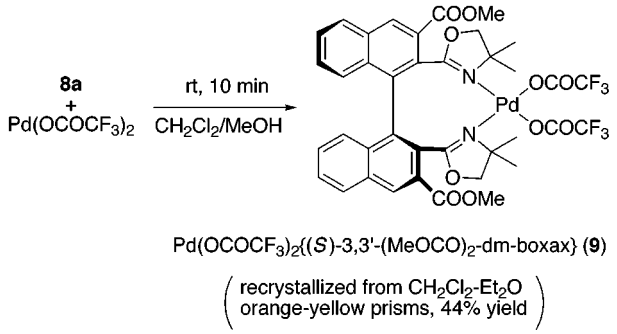
entry	substrate	reagent	electrophile	product	yield[b]
1	**1**	*sec*-BuLi	$(MeO)_2CO$	**7a**	73
2	**6**	*sec*-BuLi	$(MeO)_2CO$	**8a**	75
3	**6**	*n*-BuLi	$(MeO)_2CO$	*c*	
4	**6**	*tert*-BuLi	$(MeO)_2CO$	*c*	
5[d]	**6**	*sec*-BuLi	$(MeO)_2CO$	**8a**	<5
6	**1**	*sec*-BuLi	Me_3SiCl	**7b**	75
7	**6**	*sec*-BuLi	Me_3SiCl	**8b**	93
8	**1**	*sec*-BuLi	Me_2NCOCl	**7c**	82
9	**6**	*sec*-BuLi	Me_2NCOCl	**8c**	70
10[e]	**1**	*sec*-BuLi	Me_2NCHO	**7d**	99
11	**1**	*sec*-BuLi	I_2	**7e**	49

[a] A mixture of boxax **1** or **6**, butyllithium, and TMEDA in THF was stirred at −78 °C for 2 h. After the addition of the electrophile, the reaction mixture was allowed to warm from −78 °C to room temperature and stirred for 1 h. The ratio of boxax (**1** or **6**)/butyllithium/TMEDA/electrophile = 1/3/4/3.5, unless otherwise noted. [b] Isolated yield. [c] A complex mixture was obtained where the desired **8a** was not detected on TLC at all. [d] Without TMEDA. [e] The reaction was carried out in Et_2O.

methylpropanol gave binaphthyl bis(carboxamide) **5** in 96% yield. The oxazoline ring formation was performed by using triphenylphosphine and carbon tetrachloride in the presence of triethylamine to give (*S*)-dm-boxax **6** in 87% yield.

The *ortho*-lithiation[4] of boxax, **1** and **6**, took place at both C3 and C3′ positions by use of *sec*-butyllithium and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (Scheme 3, Table 1). Thus, (*S*,*S*)-ip-boxax **1** was allowed to react with 3 mol equiv of *sec*-butyllithium in THF at −78 °C in the presence of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA, 4 mol equiv) for 2 h, and the dilithiated boxax was treated with 3.5 mol equiv of dimethyl carbonate to give (*S*,*S*)-3,3′-bis(methoxycarbonyl)-ip-boxax, **7a** in 73% yield (Table 1, entry 1). Similarly, methoxycarbonyl group was introduced onto (*S*)-dm-boxax **6** to give 75% yield of (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax **8a** (entry 2). Lithiation of **6** with *n*-butyllithium or *tert*-butyllithium resulted in the formation of a complex mixture under otherwise the same reaction conditions (entries 3 and 4). Addition of TMEDA is essential to perform the *ortho*-lithiation of **6**. Thus, without TMEDA, lithiation of **6** with *sec*-butyllithium followed by treatment with dimethyl carbonate gave several unidentified byproducts on TLC, isolated yield of desired **8a** being <5% (entry 5). According to the same procedures, chlorotrimethylsilane, dimethylcarbamoyl chloride, *N*,*N*-dimethylformamide, and iodine were successfully used as electrophiles to give 3,3′-disubstituted boxax derivatives having trimethylsilyl (**7b** and **8b**, entries 6 and 7), dimethylaminocarbonyl (**7c** and **8c**, entries 8 and 9), formyl (**7d**, entry 10), and iodo (**7e**, entry 11) groups, respectively.

Scheme 4



X-ray Structure of Pd(OCOCF$_3$)$_2$\{(*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax\} (9). The coordination manner of (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax **8a** to a transition metal was studied by X-ray crystal structure analysis of the palladium complex Pd(OCOCF$_3$)$_2$\{(*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax\} (**9**). The complex **9** was prepared in a manner similar to the preparation of Pd(OCOCF$_3$)$_2$\{(*S*,*S*)-ip-boxax\},[3c] and the single crystals were obtained by recrystallization from dichloromethane−diethyl ether (Scheme 4). The molecular structure is shown in Figure 1. The complex **9** adopts square planer geometry with two nitrogen atoms of oxazoline rings and two oxygen atoms of trifluoroacetate groups. The bite angle of boxax ligand **8a** to palladium ∠{N(1)−Pd-N(2)} is 98.2° and the dihedral angle between two naphthyl rings ∠{C(2)−C(1)}−{C(18)−C(19)} is 83.2°. Two oxazoline rings are twisted to each other by 56.7° (∠{C(11)−N(1)}−{N(2)−C(28)}) of torsion angle due to rigid nature of the binaphthyl backbone.

Although the basic structure around palladium atom in **9** is essentially the same as that in Pd(OCOCF$_3$)$_2$-\{(*S*,*S*)-ip-boxax\} which we have previously reported,[3c] the chiral surroundings on the complex **9** are significantly different from those on Pd(OCOCF$_3$)$_2$\{(*S*,*S*)-ip-boxax\}. As can be seen from the schematic structure of a metal−boxax complex shown in Figure 2B, the substituents at C3 and C3′ positions (Y in Figure 2B) are situated in the regions of the first and the third quadrants (from the viewpoint of metal side), whereas the 4*S*-alkyl substituents of the oxazolines (X in Figure 2A) are situated in the second and the fourth quadrants. A proper choice of

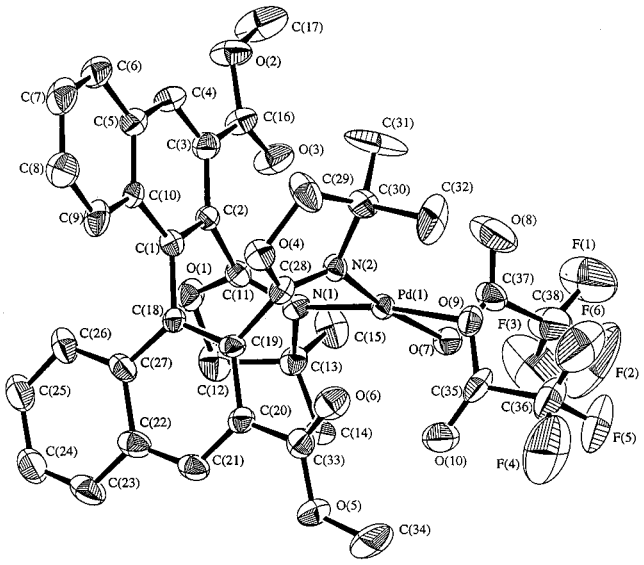


Figure 1. ORTEP drawing of $Pd(OCOCF_3)_2$\{3,3′-bis(MeOCO)-(*S*)-dm-boxax\} (**9**). The ellipsoids are drawn at 25% probability level. All protons are omitted for clarity.

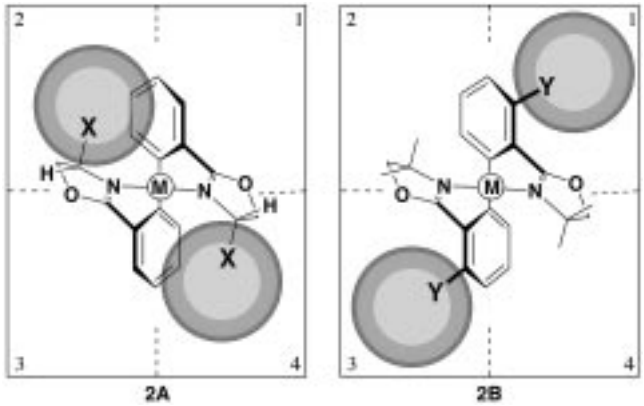


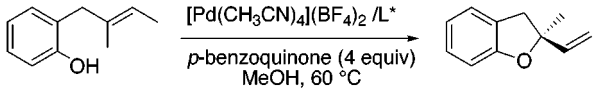
Figure 2. Schematic structure of metal complexes of 2,2′-bis-(oxazolyl)-1,1′-biaryls. 2A: With an *S*-chiral axis and *S*-chiral centers (e.g. compounds **1**). 2B: With an *S*-chiral axis and 3,3′-substituents (e.g. compounds **8**).

the combination of 4*S*- and/or 4*R*-alkyl substituents of the oxazolines and C3 and C3′ substituents of binaphthyl should realize further steric and/or electronic fine-tuning which will bring about high stereoselectivity in some transition metal-catalyzed transformations.

Catalytic Asymmetric Wacker-Type Cyclization. The enantiocontrolling abilities of 3,3′-disubstituted boxax ligands **7** and **8** obtained above were examined for palladium(II)-catalyzed asymmetric Wacker-type cyclization of (*E*)-2-(2-methyl-2-butenyl)phenol (**10**) forming 2-ethenyl-2-methyl-2,3-dihydrobenzofuran (**11**) (Scheme 5).[6,7] The results obtained are summarized in Table 2, which includes those obtained with (*S*,*S*)-ip-boxax **1** and (*S*)-dm-boxax **6** for comparison.

A palladium(II) complex of (*S*,*S*)-ip-boxax **1** has been demonstrated to be an effective catalyst for the Wacker-type cyclization,[3b,c] but the enantioselectivity is still not always high enough. For example, the enantioselectivity observed in the asymmetric intramolecular Wacker-type cyclization of trisubstituted olefin, (*E*)-2-(2-methyl-2-butenyl)phenol (**10**), with palladium(II)-(*S*,*S*)-ip-boxax catalyst forming 2-ethenyl-2-methyl-2,3-dihydrobenzofuran (**11**) was only 9% ee (*S*) (Table 2, entry 2), whereas the cyclization of **2** bearing tetrasubstituted olefin with the same catalyst system gave (*S*)-**3** of 97% ee[3c] (Scheme 1) (Table 2, entry 1). The enantioselectivity for trisubstituted *o*-allylphenol **10** was significantly improved by use of (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax **8a** (entry 3) which has methoxycarbonyl groups at the C3 and C3′ positions and does not have bulky alkyl substituents such as isopropyl group on the oxazoline rings. Thus, the asymmetric cyclization of (*E*)-2-(2-methyl-2-butenyl)phenol (**10**) was carried out in the presence of 5 mol % of palladium(II) catalyst generated from $[Pd(CH_3CN)_4]$-$(BF_4)_2$ and (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax **8a** (Pd/ligand = 1/2) at 60 °C for 2 h to give 90% yield of (*S*)-**11** whose enantiomeric purity was determined by HPLC analysis with a chiral stationary phase column to be 67% ee (entry 3). The cyclization carried out at 20 °C increased the enantiomeric purity of **11** to 88% ee (entry 4). The absolute configuration of **11** was determined by comparison of its specific rotation value with that of the authentic (*S*)-**11** prepared from (*S*)-**3** (Scheme 6). Thus, ozonolysis of (*S*)-**3** (96% ee), which was prepared by the asymmetric Wacker-type cyclization of **2** with palladium-(II)-(*S*,*S*)-ip-boxax complex, followed by treatment with zinc dust−acetic acid, gave 2-acetyl-2-methyl-2,3-dihydrobenzofuran ((*S*)-**12**). The acetyl group in (*S*)-**12** was transformed to vinyl group by a sequence of reactions including $LiAlH_4$ reduction, tosylate formation, and elimination with potassium *tert*-butoxide to give (*S*)-**11** of 96% ee.

Scheme 5



10 (*S*)-**11**

The enantioselectivity and/or catalytic activity of palladium−boxax complex was strongly affected by the combination of 4-substituents of oxazoline rings and the functional groups introduced at C3 and C3′ positions. Thus, the boxax derivative **6** which does not have C3 and C3′ functional groups showed lower catalytic activity and enantioselectivity to give 38% ee (*S*) of cyclized product **11** in 44% yield under the same reaction conditions (entry 5). The boxax derivative **7a**, which has both *S*-isopropyl substituents on the oxazoline rings and methoxycarbonyl groups at C3 and C3′ positions, gave **11** of 13% ee (*R*) (entry 6). Of the 3,3′-functionalized dm-boxax derivatives, **8b** and **8c**, which have trimethylsilyl groups and dimethylaminocarbonyl groups, respectively, were much less enantioselective than **8a** in the cyclization of **10** to give almost racemic **11** (entries 7 and 8). It is noteworthy that 3,3′-bis(methoxycarbonyl)-dm-boxax **8a** shows little asymmetric induction in the cyclization of tetrasubstituted substrate **2** (entry 9), indicating that **8a** plays a complementary role to (*S*,*S*)-alkyl-boxax, e.g. (*S*,*S*)-ip-boxax **1**, in the asymmetric Wacker-type cyclization of *o*-allylphenols.

We have previously reported that the enantioselectivity in the cyclization of **2** giving **3** is dependent on the ratio

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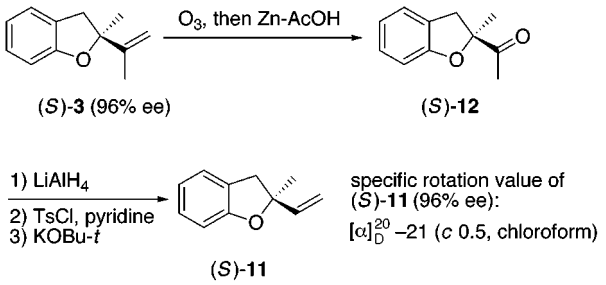
Table 2. Palladium-Catalyzed Asymmetric Wacker-Type Cyclization of *o*-allylphenols[a]

entry	substrate	ligand (equiv to Pd)	temp/time (°C/h)	product	yield[b] (%)	% ee[c] (abs config)[d]
1[e]	**2**	**1** (2.0)	60/0.8	**3**	91	97 (*S*)[f,g]
2	**10**	**1** (2.0)	60/0.5	**11**	90	9 (*S*)
3	**10**	**8a** (2.0)	60/0.5	**11**	90	67 (*S*)
4	**10**	**8a** (2.0)	20/2	**11**	90	88 (*S*)
5	**10**	**6** (2.0)	60/2	**11**	44	38 (*S*)
6	**10**	**7a** (2.0)	60/24	**11**	63	13 (*R*)
7	**10**	**8b** (2.0)	60/24	**11**	50	5 (*S*)
8	**10**	**8c** (2.0)	60/24	**11**	33	<1 (*S*)
9	**2**	**8a** (2.0)	60/24	**3**	30	4 (*S*)[g]
10	**10**	none	60/6	**11**	35	–
11	**10**	**8a** (1.1)	60/2	**11**	78	8 (*S*)
12	**10**	**8a** (3.0)	60/2	**11**	73	86 (*S*)
13	**10**	**8b** (3.0)	60/24	**11**	33	69 (*S*)
14	**10**	**8a** (3.0)	20/12	**11**	80	96 (*S*)[h]

[a] All reactions were carried out in the presence of palladium−boxax complex generated from $Pd(CH_3CN)_4(BF_3)_2$, boxax, and *p*-benzoquinone in methanol under oxygen atmosphere. The ratio of *o*-allylphenol (**2** or **10**)/Pd/benzoquinone = 1.0/0.05/4.0, unless otherwise noted. [b] Isolated yield by column chromatography. [c] Determined by HPLC analysis with a chiral stationary phase column (Daicel OD-H, eluent: hexane/2-propanol = 9/1). [d] See text. [e] 10 mol % of palladium was used. [f] Reported in ref 3c. [g] The enantiomeric excess of **3** was determined by GC analysis with a chiral stationary phase column (CP Cyclodex β236M) (ref 3b). [h] $[\alpha]_D^{20}$ −22 (*c* 1.0, chloroform).

Scheme 6



of boxax ligand to palladium, higher enantioselectivity being observed at higher ratio (Scheme 1).[3c] The same dependency was observed in the reaction of **10** catalyzed by palladium−**8** (entries 3, 7, 11, 12, and 13). The enantiomeric purities of **11** obtained in the reaction at 60 °C with 1.1, 2.0, and 3.0 equiv (to palladium) of **8a** were 8%, 67%, and 86% ee, respectively. The reaction at 20 °C with 3 equiv of **8a** gave the highest enantioselectivity of 96% ee (entry 14). The lower selectivity observed with the lower ratio of boxax ligand may be rationalized by dissociation of the ligand from palladium, which will result in the racemic product.

In summary, the structure of boxax, in which 2-oxazolyl groups are directly connected to the binaphthyl skeleton, underwent further modification of the ligands by functionalization at C3 and C3′ positions by way of *ortho*-lithiation of the binaphthyl skeleton. The fine-tuning of the chiral catalyst was achieved by a proper combination of the substituents at 4-position of oxazoline and 3-position of binaphthyl. For the palladium(II)-catalyzed asymmetric Wacker-type cyclization of the *o*-allylphenol having trisubstituted olefin, (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax **8a** turned out to be the most effective ligand.

Experimental Section

General. ^{1}H NMR spectra were run at 500 MHz and ^{13}C NMR spectra at 125 MHz in $CDCl_3$. All dry solvents were distilled under N_2. THF and Et_2O were distilled from sodium/benzophenone ketyl. Dichloromethane was distilled from CaH_2.

Preparation of (*S*)-2,2′-Bis(4,4-dimethyloxazol-2-yl)-1,1′-binaphthyl ((*S*)-dm-boxax) (6). (*S*)-*N*,*N*′-Bis[2-hydroxy-1,1-dimethylethyl]-1,1′-binaphthyl-2,2′-dicarboxamide (5). A mixture of (*S*)-1,1′-binaphthyl-2,2′-dicarboxylic acid (2.02 g, 5.90 mmol) and 30 mL (0.41 mol) of thionyl chloride was refluxed for 3 h. Excess thionyl chloride was removed under reduced pressure. The residue dissolved in 10 mL of THF was added to a solution of 1.6 g (18 mmol) of 2-amino-2-methylpropanol and 2.5 mL (18 mmol) of triethylamine in 15 mL of THF at 0 °C. The mixture was stirred at room temperature for 1 h, and the reaction mixture was concentrated under reduced pressure. The residue was extracted with EtOAc and washed with 5% hydrochloric acid, saturated sodium bicarbonate, and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was chromatographed on silica gel (eluent: EtOAc) to give 2.75 g (96%) of (*S*)-*N*,*N*′-bis[2-hydroxy-1,1-dimethylethyl]-1,1′-binaphthyl-2,2′-dicarboxamide (**5**) as white powder: $[\alpha]^{20}_D$ −206 (*c* 1.09, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.66 (s, 6 H), 0.72 (s, 6 H), 3.16 (s, 2 H), 3.17 (s, 2 H), 3.98 (br s, 2 H), 6.73 (br s, 2 H), 7.25 (d, J = 7.8 Hz, 2 H), 7.35 (dd, J = 8.3, 6.8 Hz, 2 H), 7.53 (dd, J = 7.8, 6.8 Hz, 2 H), 7.72 (d, J = 8.8 Hz, 2 H), 7.96 (d, J = 8.3 Hz, 2 H), 8.05 (d, J = 8.8 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.2, 23.7, 56.3, 69.8, 123.9, 126.3, 127.3, 127.5, 128.3, 129.1, 132.2, 132.5, 134.0, 135.2, 170.6. Anal. Calcd for $C_{30}H_{32}N_2O_4$: C, 74.36; H, 6.66; N, 5.78. Found: C, 74.39; H, 6.67; N, 5.74. **(*S*)-2,2′-Bis(4,4-dimethyloxazol-2-yl)-1,1′-binaphthyl ((*S*)-dm-boxax) (6).** To a solution of 3.9 g (15 mmol) of triphenylphosphine, 2.8 mL (20 mmol) of triethylamine, and 3.6 mL (37 mmol) of carbon tetrachloride in 60 mL of acetonitrile was added 2.75 g (5.67 mmol) of (*S*)-*N*,*N*′-bis[2-hydroxy-1,1-dimethylethyl]-1,1′-binaphthyl-2,2′-dicarboxamide (**5**) at room temperature. The mixture was refluxed for 3 h under nitrogen atmosphere. After being cooled, the reaction mixture was concentrated under reduced pressure. The residue was extracted with EtOAc and washed with saturated sodium bicarbonate and brine. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The crude mixture was chromatographed on silica gel (hexane/EtOAc/Et_3N = 20/3/1) to give 2.20 g (87%) of (*S*)-2,2′-(4,4-dimethyloxazol-2-yl)-1,1′-binaphthyl ((*S*)-dm-boxax) (**6**) as white powder: $[\alpha]^{20}_D$ −129 (*c* 1.08, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.95 (s, 6 H), 1.12 (s, 6 H), 3.24 (d, J = 7.8 Hz, 2 H), 3.50 (d, J = 7.8 Hz, 2 H), 7.26−7.30 (m, 4 H), 7.49 (ddd, J = 7.8, 5.8, 2.0 Hz, 2 H), 7.92 (d, J = 8.3 Hz, 2 H), 7.94 (d, J = 8.3 Hz, 2 H), 8.01 (d, J = 8.3 Hz, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.9, 66.8, 79.3, 126.3, 126.3, 126.4, 126.7, 127.3, 127.7, 127.8, 132.8, 134.0, 137.1, 163.6. Anal. Calcd for $C_{30}H_{28}N_2O_2$: C, 80.33; H, 6.29; N, 6.25. Found: C, 80.49; H, 6.38; N, 6.26.

Preparation of 3,3′-Disubstituted Boxax (Table 1). A typical procedure is given for the preparation of **(*S*)-2,2′-bis(4,4-dimethyloxazol-2-yl)-3,3′-bis(methoxycarbonyl)-1,1′-binaphthyl ((*S*)-(MeOCO)$_2$-dm-boxax) (8a)** (Table 1, entry 2). To a solution of 82 mg (0.18 mmol) of **6** and 0.11 mL (0.73 mmol) of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) in

3.0 mL of dry THF was added dropwise 0.53 mL (0.56 mmol) of 1.05 M *sec*-BuLi in cyclohexane at −78 °C. After 2 h of stirring at −78 °C under nitrogen atmosphere, 53 μL (0.63 mmol) of dimethyl carbonate was added at −78 °C. The reaction mixture was stirred for 1 h at ambient temperature and quenched with a small amount of saturated sodium bicarbonate. The mixture was extracted with saturated sodium bicarbonate and brine, dried over anhydrous sodium sulfate, and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc/Et_3N = 20/3/1) to give 77 mg of (*S*)-2,2′-bis(4,4-dimethyloxazol-2-yl)-3,3′-bis(methoxycarbonyl)-1,1′-binaphthyl ((*S*)-$(MeOCO)_2$-dm-boxax) (**8a**): 75%; $[\alpha]^{20}_D$ −169 (*c* 0.87, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.37 (s, 6 H), 1.00 (s, 6 H), 3.43 (d, *J* = 7.8 Hz, 2 H), 3.64 (d, *J* = 7.8 Hz, 2 H), 3.92 (s, 6 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.41 (t, *J* = 8.3 Hz, 2 H), 7.56 (t, *J* = 8.3 Hz, 2 H), 7.89 (d, *J* = 8.3 Hz, 2 H), 8.62 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.0, 27.2, 52.4, 67.2, 79.2, 126.8, 127.4, 127.6, 128.1, 128.7, 128.8, 131.7, 132.2, 134.5, 136.9, 160.8, 167.0. Anal. Calcd for $C_{34}H_{32}N_2O_6$: C, 72.32; H, 5.71; N, 4.96. Found: C, 72.13; H, 5.93; N, 4.92.

(*S*)-2,2′-Bis((*S*)-4-isopropyloxazol-2-yl)-3,3′-bis(methoxycarbonyl)-1,1′-binaphthyl ((*S*,*S*)-3,3′-$(MeOCO)_2$-ip-boxax) (7a) (entry 1): 73% yield; $[\alpha]^{20}_D$ −197 (*c* 0.68, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.52 (d, *J* = 6.3 Hz, 6 H), 0.59 (d, *J* = 6.3 Hz, 6 H), 0.87 (m, 2 H), 3.33−3.41 (m, 4 H), 3.76 (m, 2 H), 3.91 (s, 6 H), 7.32 (d, *J* = 8.3 Hz, 2 H), 7.38 (t, *J* = 8.3 Hz, 2 H), 7.55 (t, *J* = 8.3 Hz, 2 H), 7.98 (d, *J* = 8.3 Hz, 2 H), 8.53 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.7, 19.4, 32.8, 52.4, 70.8, 73.5, 126.7, 127.6, 127.6, 128.3, 128.4, 128.7, 131.1, 132.5, 133.8, 137.1, 161.8, 167.5. Anal. Calcd for $C_{36}H_{36}N_2O_6$: C, 72.95; H, 6.12; N, 4.73. Found: C, 72.80; H, 6.25; N, 4.62.

(*S*)-2,2′-Bis((*S*)-4-isopropyloxazol-2-yl)-3,3′-bis(trimethylsilyl)-1,1′-binaphthyl ((*S*,*S*)-3,3′-$(Me_3Si)_2$-ip-boxax) (7b) (entry 6): 75%; $[\alpha]^{20}_D$ −25 (*c* 0.28, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.36 (s, 18 H), 0.49 (d, *J* = 6.8 Hz, 6 H), 0.65 (d, *J* = 6.3 Hz, 6 H), 0.89 (m, 2 H), 2.98 (dd, *J* = 10.3, 8.3 Hz, 2 H), 3.42 (q, *J* = 9.8 Hz, 2 H), 3.84 (dd, *J* = 9.8, 8.3 Hz, 2 H), 7.25−7.26 (m, 4 H), 7.46 (dt, *J* = 8.3, 4.0 Hz, 2 H), 7.87 (d, *J* = 8.3 Hz, 2 H), 8.14 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 0.5, 18.8, 20.1, 32.9, 70.3, 74.0, 126.4, 126.4, 127.5, 127.7, 131.8, 132.8, 133.2, 135.5, 136.7, 136.9, 163.5. Anal. Calcd for $C_{38}H_{48}N_2O_2Si_2$: C, 73.50; H, 7.79; N, 4.51. Found: C, 73.26; H, 7.77; N, 4.58.

(*S*)-2,2′-Bis(4,4-dimethyloxazol-2-yl)-3,3′-bis(trimethylsilyl)-1,1′-binaphthyl ((*S*)-$(Me_3Si)_2$-dm-boxax) (8b) (entry 7): 93%; $[\alpha]^{20}_D$ −129 (*c* 1.08, chloroform), ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.38 (s, 18 H), 0.42 (s, 6 H), 0.96 (s, 6 H), 3.53 (s, 4 H), 7.18 (d, *J* = 8.3 Hz, 2 H), 7.27 (t, *J* = 8.3 Hz, 2 H), 7.45 (t, *J* = 8.3 Hz, 2 H), 7.86 (d, *J* = 8.3 Hz, 2 H), 8.13 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 0.2, 27.3, 27.5, 67.1, 77.8, 126.0, 126.6, 127.2, 127.5, 131.2, 131.9, 133.4, 135.1, 135.3, 136.5, 161.8. Anal. Calcd for $C_{36}H_{44}N_2O_2Si_2$: C, 72.93; H, 7.48; N, 4.72. Found: C, 72.86; H, 7.45; N, 4.59.

(*S*)-2,2′-Bis((*S*)-4-isopropyloxazol-2-yl)-3,3′-bis(dimethylaminocarbonyl)-1,1′-binaphthyl ((*S*,*S*)-3,3′-$(Me_2NCO)_2$-ip-boxax) (7c) (entry 8): 82% yield; $[\alpha]^{20}_D$ −173 (*c* 0.86, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.55 (d, *J* = 6.8 Hz, 6 H), 0.64 (d, *J* = 6.8 Hz, 6 H), 1.18 (m, 2 H), 2.97 (s, 6 H), 3.11 (s, 6 H), 3.45−3.47 (m, 4 H), 3.65 (m, 2 H), 7.25−7.30 (m, 4 H), 7.50 (t, *J* = 7.3 Hz, 2 H), 7.87−7.88 (m, 4 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 19.3, 32.7, 35.0, 39.2, 70.4, 73.3, 126.3, 127.3, 127.4, 127.4, 127.5, 127.8, 128.3, 132.5, 133.2, 134.8, 161.7, 171.2. Anal. Calcd for $C_{38}H_{42}N_4O_4$: C, 73.76; H, 6.84; N, 9.05. Found: C, 73.99; H, 6.55; N, 9.36.

(*S*)-2,2′-Bis(4,4-dimethyloxazol-2-yl)-3,3′-bis(dimethylaminocarbonyl)-1,1′-binaphthyl ((*S*)-$(Me_2NCO)_2$-dm-boxax) (8c) (entry 9): 70%; $[\alpha]^{20}_D$ −132 (*c* 0.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.74 (s, 6 H), 0.82 (s, 6 H), 2.95 (s, 6 H), 3.08 (s, 6 H), 3.27 (d, *J* = 7.8 Hz, 2 H), 3.42 (d, *J* = 7.8 Hz, 2 H), 7.30−7.38 (m, 4 H), 7.52 (t, *J* = 8.3 Hz, 2 H), 7.89 (d, *J* = 8.3 Hz, 2 H), 7.93 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 27.3, 27.5, 35.0, 39.3, 67.5, 78.8, 124.9, 126.3, 127.3, 127.4, 127.5, 127.9, 132.3, 133.2, 134.3, 137.1, 160.2, 170.7. Anal. Calcd for $C_{36}H_{38}N_4O_4$: C, 73.20; H, 6.48; N, 9.48. Found: C, 72.99; H, 6.51; N, 9.18.

(*S*)-2,2′-Bis((*S*)-4-isopropyloxazol-2-yl)-3,3′-diformyl-1,1′-binaphthyl ((*S*,*S*)-3,3′-$(CHO)_2$-ip-boxax) (7d) (entry 10): 99%; $[\alpha]^{20}_D$ −260 (*c* 0.94, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.57 (d, *J* = 6.3 Hz, 6 H), 0.64 (d, *J* = 6.8 Hz, 6 H), 1.07 (m, 2 H), 3.48−3.55 (m, 4 H), 3.73 (m, 2 H), 7.34 (d, *J* = 8.3 Hz, 2 H), 7.45 (t, *J* = 8.3 Hz, 2 H), 7.61 (t, *J* = 8.3 Hz, 2 H), 8.10 (d, *J* = 8.3 Hz, 2 H), 8.61 (s, 2 H), 10.38 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.5, 19.2, 32.7, 70.7, 73.4, 127.0, 127.3, 128.1, 129.3, 129.8, 130.9, 132.3, 132.7, 133.7, 137.2, 160.6, 191.1. Anal. Calcd for $C_{34}H_{32}N_2O_4$: C, 76.67; H, 6.06; N, 5.26. Found: C, 76.55; H, 5.90; N, 5.43.

(*S*)-2,2′-Bis((*S*)-4-isopropyloxazol-2-yl)-3,3′-diiodo-1,1′-binaphthyl ((*S*,*S*)-3,3′−I_2-ip-boxax) (7e) (entry 11): 49%; $[\alpha]^{20}_D$ −206 (*c* 0.77, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.55 (d, *J* = 6.8 Hz, 6 H), 0.67 (d, *J* = 6.8 Hz, 6 H), 0.90 (m, 2 H), 3.40−3.46 (m, 4 H), 3.73 (m, 2 H), 7.30−7.47 (m, 4 H), 7.51 (t, *J* = 7.8 Hz, 2 H), 7.77 (d, *J* = 7.8 Hz, 2 H), 8.52 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.6, 19.4, 32.6, 70.3, 73.1, 91.9, 126.4, 126.9, 127.7, 127.8, 131.2, 132.5, 134.7, 136.7, 139.0, 162.8. Anal. Calcd for $C_{32}H_{30}N_2O_2I_2$: C, 52.77; H, 4.15; N, 3.85. Found: C, 53.07; H, 4.14; N, 3.76.

[(*S*)-3,3′-Bis(methoxycarbonyl)-dm-boxax]palladium Bis(trifluoroacetate) (9). A solution of 66.9 mg (0.118 mmol) of (*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax (**8a**) in 0.5 mL of chloroform was added to 39.3 mg (0.118 mmol) of palladium bis(trifluoroacetate) in 0.5 mL of acetonitrile at room temperature. The reaction mixture was stirred at room temperature for 10 min and concentrated in vacuo to give brown powder (99 mg). The brown powder was recrystallized from dichloromethane and Et_2O to give 47.1 mg of [(*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax]palladium bis(trifluoroacetate) (**9**) as orange prisms: 44% yield; mp 223 °C (dec); $[\alpha]^{20}_D$ +55.6 (*c* 0.42, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.05 (s, 6 H), 1.48 (s, 6 H), 1.87 (d, *J* = 7.8 Hz, 2 H), 3.56 (d, *J* = 7.8 Hz, 2 H), 4.10 (s, 6 H), 7.31 (d, *J* = 7.8 Hz, 2 H), 7.55 (t, *J* = 7.8 Hz, 2 H), 7.73 (t, *J* = 7.8 Hz, 2 H), 8.18 (d, *J* = 7.8 Hz, 2 H), 8.98 (s, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 25.7, 25.9, 53.4, 71.4, 81.3, 125.7, 126.6, 126.9, 129.2, 129.5, 130.1, 132.9, 133.0, 133.1, 135.9, 164.7, 169.3. Anal. Calcd for $C_{38}H_{32}N_2O_{10}F_6Pd$: C, 50.88; H, 3.60; N, 3.12. Found: C, 50.58; H, 3.66; N, 3.00.

X-ray Diffraction Study of 9. The molecular structure of [(*S*)-3,3′-bis(methoxycarbonyl)-dm-boxax]palladium bis(trifluoroacetate) (**9**) determined by an X-ray diffraction study is shown in Figure 1. A single crystal (0.20 × 0.15 × 0.15 mm) of the palladium complex **9** obtained above was put on the top of a glass capillary tube. Intensity data were collected on a Rigaku AFC 7S diffractometer. Details of X-ray diffraction study of **9**, including crystal data and structure refinement, fractional coordinates and equivalent isotropic thermal factors, anisotropic displacement parameters, bond lengths, and bond angles are reported in the Supporting Information.

Palladium(II)-Catalyzed Asymmetric Wacker-Type Cyclization of *o*-Allylphenols (Table 2). A typical procedure is given for the reaction of (*E*)-2-(2-methyl-2-butenyl)phenol (**10**) with a palladium(II) complex of (*S*)-3,3′-$(MeOCO)_2$-dm-boxax (**8a**) forming **(*S*)-2-ethenyl-2-methyl-2,3-dihydrobenzofuran (11)** (Table 2, entry 13). Tetrakis(acetonitrile)palladium bis(tetrafluoroborate) ($[Pd(CH_3CN)_4](BF_4)_2$) (2.5 mg, 5.6 μmol) and 9.5 mg of **8a** (17 μmol) were dissolved in 0.1 mL of chloroform and 0.1 mL of acetonitrile. The solution was stirred for 10 min at room temperature and concentrated in vacuo. (*E*)-2-(2-methyl-2-butenyl)phenol (**10**) (18.5 mg, 0.114 mmol), 49 mg of *p*-benzoquinone (0.45 mmol), and 0.27 mL of methanol were added, and the mixture was stirred for 12 h at 20 °C and then chromatographed on silica gel (hexane/benzene = 2/1) to give 14.4 mg (79% yield) of (−)-2-ethenyl-2-methyl-2,3-dihydrobenzofuran ((−)-**11**).[5] Enantiomeric excess of **11** was determined to be 96% ee by HPLC analysis using a chiral stationary phase column (Chiralcel OD-H, eluent: hexane/2-propanol = 9/1). (−)-**11** (96% ee): $[\alpha]^{20}_D$ −22 (*c* 1.0, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.55 (s, 3 H), 3.06 (d, *J* = 15.6 Hz, 1 H), 3.18 (d, *J* = 15.6 Hz, 1 H), 5.09 (d, *J* = 10.7 Hz, 1 H), 5.31 (d, *J* = 17.1 Hz, 1 H), 6.05 (dd, *J* = 17.1, 10.7 Hz, 1 H), 6.79 (d, *J* = 7.8 Hz, 1 H), 6.83 (t, *J* = 7.6 Hz, 1 H), 7.10−7.14

(m, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 26.1, 42.0, 87.5, 109.5, 112.8, 120.2, 125.0, 126.4, 128.0, 141.7, 158.8.

Determination of Absolute Configuration of (−)-11. The absolute configuration of (−)-**11** was determined to be (*S*) by comparison of its specific rotation value with the authentic sample which was prepared from (*S*)-2-isopropenyl-2-methyl-2,3-dihydrobenzofuran ((*S*)-**3**)[3b] (Scheme 6). **(*S*)-2-Acetyl-2-methyl-2,3-dihydrobenzofuran ((*S*)-12).** (*S*)-**3** (96% ee) (260 mg, 1.49 mmol) was dissolved in 10 mL of dichloromethane, and the solution was cooled to −78 °C. Ozonized oxygen was bubbled through this solution for 1.5 h, and then dry nitrogen gas was bubbled for 10 min. Powdered zinc (0.1 g) and 0.5 mL of acetic acid were added at −78 °C, and the suspension was stirred for 1 h at 0 °C. Additional powdered zinc (0.1 g) and 0.5 mL of acetic acid were added at 0 °C, and the suspension was stirred for 30 min at room temperature. The suspension was filtered, and the filtrate was neutralized with saturated sodium bicarbonate. The mixture was extracted with EtOAc, and it was washed with brine, dried over anhydrous sodium sulfate, and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc = 5/1) to give 138 mg of (*S*)-2-acetyl-2-methyl-2,3-dihydrobenzofuran (*S*)-**12**: 53%; $[\alpha]^{20}_D$ −11.6 (*c* 0.70, chloroform); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.57 (s, 3 H), 2.28 (s, 3 H), 3.04 (d, J = 16.5 Hz, 1 H), 3.51 (d, J = 16.5 Hz, 1 H), 6.84 (d, J = 8.5 Hz, 1 H), 6.88 (t, J = 7.3 Hz, 1 H), 7.15−7.18 (m, 2 H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.7, 25.2, 39.4, 92.2, 109.6, 121.1, 125.0, 125.6, 128.3, 158.4, 211.0. Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.73; H, 6.81. **Transformation of (*S*)-2-acetyl-2-methyl-2,3-dihydrobenzofuran (*S*)-12 to (*S*)-11**. To a suspension of 15.2 mg (0.40 mmol) of $LiAlH_4$ in 2.0 mL of Et_2O, was added a solution of 132 mg (0.75 mmol) of (*S*)-**12** in 1.6 mL of Et_2O at 0 °C. The mixture was stirred for 2 h at room temperature and extracted with Et_2O and it was washed with brine and dried over anhydrous sodium sulfate and evaporated. The residue was chromatographed on silica gel (hexane/EtOAc = 1/3) to give 120 mg (90% yield) of a 1:1 mixture of (*S*)-2-((1*S*)-hydroxyethyl)-2-methyl-2,3-dihydrobenzofuran and (*S*)-2-((1*R*)-hydroxyethyl)-2-methyl-2,3-dihydrobenzofuran as colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.21 (d, J = 6.3 Hz, 3/2 H), 1.22 (d, J = 6.3 Hz, 3/2 H), 1.36 (s, 3/2 H), 1.40 (s, 3/2 H), 2.13 (s, 1/2 H), 2.26 (s, 1/2 H), 2.73 (d, J = 15.6 Hz, 1/2 H), 2.88 (d, J = 15.6 Hz, 1/2 H), 3.15 (d, J = 15.6 Hz, 1/2 H), 3.43 (d, J = 15.6 Hz, 1/2 H), 3.86 (m, 1/2 H), 3.99 (m, 1/2 H), 6.75 (m, 2/2 H), 6.84 (m, 2/2 H), 7.13 (m, 4/2 H). The mixture was taken on to the next step without separation. To a solution of 93 mg (0.52 mmol) of the mixture and 0.18 mL (2.2 mmol) of pyridine in 1,2-dichloroethane was added 0.20 g (1.0 mmol) of *p*-(toluene)-sulfonyl chloride at room temperature, and the mixture was refluxed for 1 day under nitrogen atmosphere. The mixture was diluted with chloroform and washed with brine. The organic layer was dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (hexane/EtOAc = 5/1) to give a diastereomeric mixture of (*S*)-2-(1-(*p*-toluenesulfonyl)oxyethyl)-2-methyl-2,3-dihydrobenzofuran. To the solution of the resulting mixture in 2.3 mL of DMSO was added 154 mg (1.38 mmol) of potassium *tert*-butoxide at room temperature, and the mixture was stirred for 10 h at 60 °C under nitrogen atmosphere. The mixture was diluted with Et_2O, washed with brine, and dried over anhydrous sodium sulfate. After removal of the solvent, the residue was chromatographed on silica gel (hexane/EtOAc = 7/1) to give 50 mg of (*S*)-**11**: 60%; $[\alpha]^{20}_D$ −21 (*c* 0.52, chloroform). The enantiomeric excess was determined to be 96% ee by HPLC analysis.

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Supporting Information Available: Tables for X-ray analysis of $Pd(OCOCF_3)_2${(*S*)-3,3′-bis(methoxycarbonyl)-dmboxax} (**9**); crystal data and structure refinement, fractional coordinates and equivalent isotropic thermal factors, anisotropic displacement parameters, bond lengths, and bond angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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