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Chelation-Induced Axially Chiral Palladium Complex System with Tetraoxazoline Ligands for Highly Enantioselective Wacker-Type Cyclization

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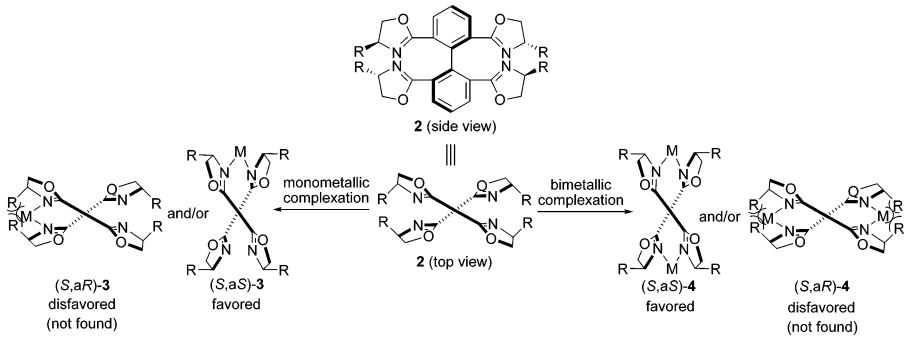
Received July 16, 2007



A new family of chelation-induced axially chiral palladium complexes by using biphenyl ligands **2** with four identical chiral oxazoline groups at four ortho positions has been developed. Although there is no axial chirality in ligands **2** due to the molecular symmetry, when they chelated with one or two palladium ions, the axial chirality could be induced by destroying the molecular symmetry. Significantly, only one diastereomeric metal complex with (*S*)-axial configuration was produced during the chelation-induced process. The chelation-induced axially chiral catalytic system, **2c**-Pd$(CF_3COO)_2$ (1:1 molar ratio), showed excellent catalytic activities and enantioselectivities in the Wacker-type cyclization of allylphenols with up to 99% ee.

Introduction

The design and development of effective chiral ligands have played a significant role in advancement of asymmetric catalysis and have attracted a great deal of attention from both academia and industry. Thousands of ligands with various chiral elements have been developed and applied in many catalytic asymmetric reactions to produce enantiomerically pure compounds.[1] Among them, axial chirality is one of the important stereogenic elements used for the development of chiral ligands such as BINAP,[2] BINOL,[3] and boxax,[4] which have been explored as effective templates for transition metal-catalyzed asymmetric reactions.[5]

In general, there are two necessary preconditions for axial chirality in biaryl molecules, that is, a rotationally stable biaryl axis and the presence of different ortho substituents on both sides of the biaryl axis. In contrast to traditional axially chiral molecules, we are introducing a new family of biphenyl ligands **1** with four constitutionally identical coordinating groups at the ortho positions of the biphenyl axis, in which there is no axial chirality due to the molecular symmetry. Significantly, as shown in Scheme 1, while the biphenyl ligand **1** chelated with one or two metal ions, the molecular symmetry could be destroyed by formation of metal chelating bridge at one or two side of biphenyl, giving a pair of enantiomers of monometallic or

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10.1021/jo701469y CCC: $37.00
Published on Web 10/31/2007

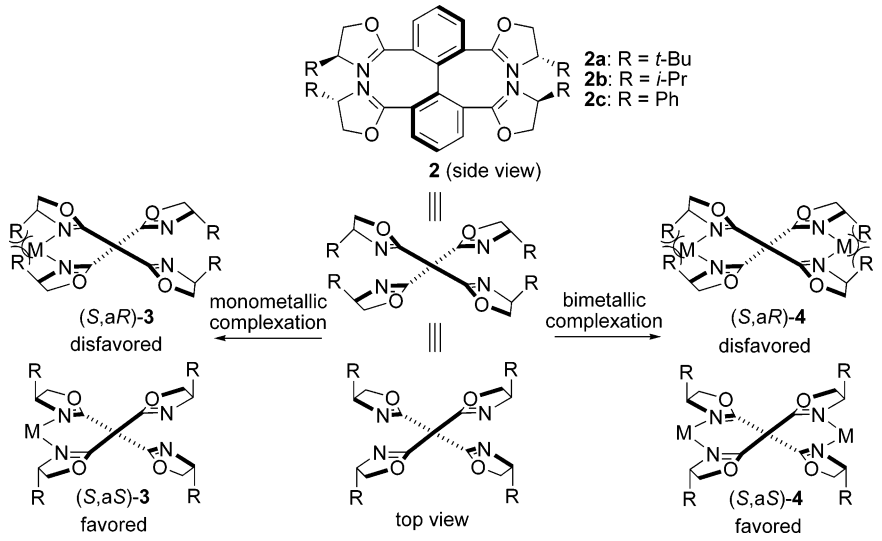
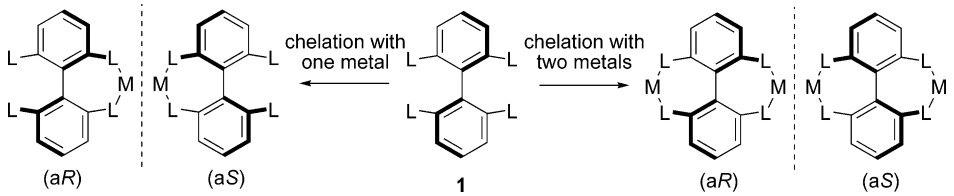


FIGURE 1. Model figures of diastereomeric monometallic and bimetallic complexes with tetraoxazoline ligands.

SCHEME 1. Chelation-Induced Axially Chiral Metal Complexes Formed by Destroying the Molecular Symmetry (L = Coordination Group)



bimetallic complexes. Moreover, if the L groups in the biphenyl **1** are chiral coordinating groups (e.g., chiral oxazolines), the diastereomeric metal complexes will be formed. Under ideal circumstances, these diastereomers will have sufficiently different energies, so that only one of the two possible diastereomeric metal complexes could be formed. Therefore, the axially chiral monometallic or bimetallic complexes could be formed by the chelation-induced concept upon complexing process of axially achiral ligands.

Numbers of C_2-symmetric chiral bisoxazolines with an axially chiral biaryl backbone have been successfully employed as chiral ligands.[6] However, this type of ligands requires inconvenient diastereomeric separation in their synthetic process, and generally, only one of the diastereomers works effectively in catalytic asymmetric reactions due to the configurational matching-mismatching effect. In contrast, the axially achiral tetraoxazoline ligands **2**, in which four identical chiral oxazoline groups were introduced into four ortho positions of biphenyl axis, may produce only one of the two possible diastereomeric metal complexes during the coordinating process based on our chelation-induced concept. As depicted in Figure 1, the diastereomeric monometallic complexes (*S*,a*R*)-**3** and (*S*,a*S*)-**3** and bimetallic complexes (*S*,a*R*)-**4** and (*S*,a*S*)-**4** should have different steric interactions between the substitutents on oxazoline rings and/or metal ions. It is not difficult to find that the metal complexes (*S*,a*S*)-**3** and (*S*,a*S*)-**4** are sterically more favorable compared with their diastereomers. Hence, under the ideal circumstances, we can expect that only one diastereomeric metal complex with (*S*)-axial configuration could be afforded during the chelation-induced process. In fact, the (*S*,a*S*)-configuration effectively matches in most of the well-developed transition metal catalyzed asymmetric reactions by using biaryl bisoxazoline ligands.[6] Thus, we report a new family of tetraoxazoline ligands **2** for the construction of chelation-induced axially chiral catalytic systems and their application to enantioselective Wacker-type cyclizations.

Results and Discussion

Ligand Preparation. The tetraoxazoline ligands **2** were readily prepared from the commercially available starting material pyrene as illustrated in Scheme 2. Oxidation of pyrene gave 2,2′,6,6′-tetracarboxy-1,1′-biphenyl (**5**) in 72% yield.[7] Treatment of tetraacid **5** with thionyl chloride produced tetraacid chloride, which was stirred with (*S*)-*tert*-leucinol and triethylamine in dichloromethane, followed by reaction with methanesulfonyl chloride in the presence of triethylamine to produce tetraoxazoline compound **2a** in 39% yield from tetraacid **5**.[8] In the same way, tetraoxazoline ligands **2b** and **2c** were prepared respectively in 45% and 47% yields from tetraacid **5** and the corresponding enantiomerically pure 2-amino alcohols.

Complexation Behavior of Ligands 2 with Palladium Salt. To evaluate the coordinating behavior of **2**, the reaction of **2a**

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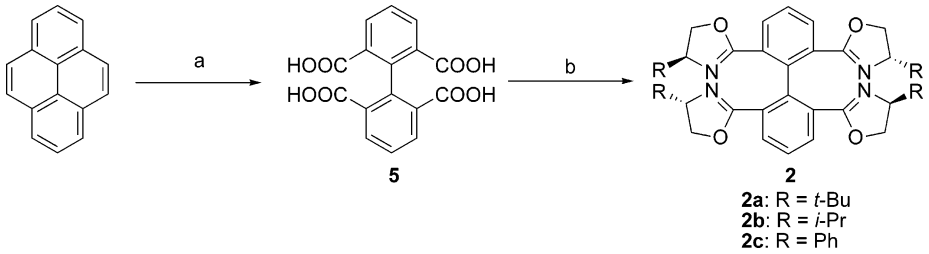
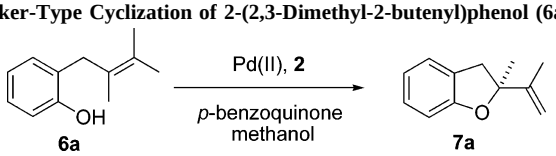
SCHEME 2 [a]



with 2 equiv of $Pd(CF_3COO)_2$ in acetone-d_6 was monitored by ^1H NMR spectroscopy. As expected, the resultant solution produced only one set of peaks in ^1H NMR spectroscopy. This observation obviously suggests that only one diastereomer is quantitively formed through the chelation with two palladium ions. The axial configuration of the complex **4a** was assigned as *S* by CPK models and the analysis of the nuclear Overhauser effect (NOE).[9] Thus, 3.9% and 3.4% NOEs were observed between the methyl protons of one oxazolinyl *tert*-butyl group and the 3- and 4-position protons at the other phenyl ring, respectively. Similarly, ligands **2b** and **2c** also produced only one diastereomeric bimetallic complex (*S*,a*S*)-**4b** and (*S*,a*S*)-**4c**, respectively. Interestingly, when the ratio of palladium to ligand **2c** was 1:1, a mixture of bimetallic complex (*S*,a*S*)-**4c**, monometallic complex (*S*,a*S*)-**3c** and residual free ligand **2c** was obtained with 1:1.4:1 ratio determined by ^1H NMR analysis. The axial configuration of the monometallic complex (*S*,a*S*)-**3c** was deduced by comparing with the corresponding bimetallic complex (*S*,a*S*)-**4c**.

Pd(II)-Catalyzed Asymmetric Wacker-Type Cyclization. Pd(II)-catalyzed intramolecular Wacker-type cyclizations have emerged as a versatile strategy in the construction of a range of heterocycles.[10] However, asymmetric oxidative cyclizations catalyzed with chiral Pd(II) complexes have received relatively little attention. Previous attempts at asymmetric versions of the oxidative cyclizations were reported by Hosokawa and Murahashi,[11] whose Wacker-type cyclization of 2-allylphenols by use of a chiral π-allylpalladium complex produced dihydrobenzofurans with only 29% ee. Although Hayashi and Uozumi have made an important breakthrough on the Pd(II)-catalyzed enantioselective Wacker-type cyclization of 2-allylphenols with chiral bisoxazoline ligands based on binaphthyl backbone (boxax),[12] only few ligands have been successfully applied to this type of cyclization.[13] To test the catalytic activity and enantioselectivity of our chelation-induced axially chiral Pd(II) complex in Wacker-type cyclizations, 2-(2,3-dimethyl-2-butenyl)phenol (**6a**) was selected as a model substrate. The reactions were catalyzed by 5 mol % of the bimetallic complexes in the presence of 4 equiv. *p*-benzoquinone as reoxidant in methanol at 60 °C for 24 h. As shown in Table 1, the catalytic efficiencies were largely depended not only on the substituents at the oxazoline rings but also on the kinds of anions in the catalyst systems. The complex (*S*,a*S*)-**4c**, derived from phenyl-substituted tetraoxazoline **2c**, showed remarkably higher catalytic activity and enantioselectivity compared with the complexes (*S*,a*S*)-**4a** and (*S*,a*S*)-**4b** (entries 1−3). The Pd(II) complexes formed from $Pd(OAc)_2$ and $Pd(CF_3COO)_2$ exhibited similar catalytic efficiencies (entries 3 and 4). However, markedly decreased enantioselectivities have been observed with the Pd(II)-complexes bearing chloride or tetrafluoroborate anions (entries 5 and 6). Moreover, the reaction was also proceeded well even in the presence of 1 mol % of catalyst (*S*,a*S*)-**4c** (entry 7).

TABLE 1. Optimization of Pd(II)-Catalyzed Asymmetric Wacker-Type Cyclization of 2-(2,3-Dimethyl-2-butenyl)phenol (6a)[a]



entry	Pd/**2** (mol %/mol %)	(*S*,a*S*)-**4**/(*S*,a*S*)-**3**/**2**[b]	yield[c] (%)	ee[d] (%)
1	$Pd(CF_3COO)_2$/**2a** (10/5)	1:0:0	43	38
2	$Pd(CF_3COO)_2$/**2b** (10/5)	1:0:0	87	80
3	$Pd(CF_3COO)_2$/**2c** (10/5)	1:0:0	89	90
4	$Pd(OAc)_2$/**2c** (10/5)	1:0:0	85	90
5	$Pd(CH_3CN)_2Cl_2$/**2c** (10/5)	1:0:0	39	55
6	$Pd(CH_3CN)_2(BF_4)_2$/**2c**/(10/5)	1:0:0	92	75
7	$Pd(CF_3COO)_2$/**2c** (2/1)	1:0:0	68	91
8	$Pd(CF_3COO)_2$/**2c** (10/7.5)	1:0.5:0.4	85	93
9	$Pd(CF_3COO)_2$/**2c** (10/10)	1:1.4:1	86	96
10	$Pd(CF_3COO)_2$/**2c** (10/20)	1:6:9	85	97

[a] The reactions were catalyzed by the Pd(II)−**2** complex generated in situ by mixing $Pd(OCOCF_3)_2$ with tetraoxazolines **2** in the presence of 4 equiv of *p*-benzoquinone in methanol at 60 °C for 24 h. [b] Determined by ^1H NMR analysis. [c] Isolated yield by column chromatography. [d] The enantiomeric excesses were determined by chiral GC on a CP-Chirasil-Dex CB column. The absolute configurations were determined by comparing the sign of the optical rotation with that reported in ref 12a.

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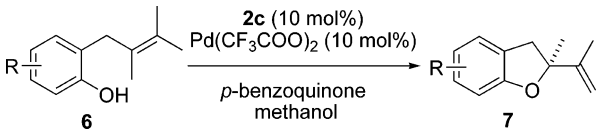
TABLE 2. Pd(II)-Catalyzed Asymmetric Wacker-Type Cyclization of Allylphenols 6[a]



entry	substrate	R	yield[b] (%)	ee[c] (%)
1	**6a**	H	86	96
2	**6b**	4-Me	84	98
3	**6c**	5-Me	63	94
4	**6d**	6-Me	69	99
5	**6e**	4-OMe	81	98
6	**6f**	6-OMe	54	95
7	**6g**	4-F	79	98
8	**6h**	4-Ph	65	97
9	**6i**	1-naphthol	67	97

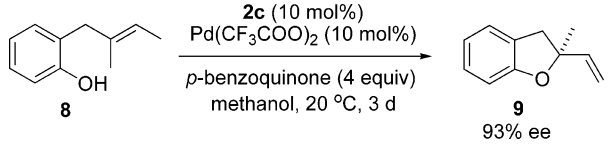
[a] The reactions were catalyzed by the Pd(II)−**2c** complex generated in situ by mixing $Pd(OCOCF_3)_2$ with tetraoxazoline **2c** (1:1 molar ratio) in the presence of 4 equiv of *p*-benzoquinone in methanol at 60 °C for 24 h. [b] Isolated yield by column chromatography. [c] The enantiomeric excesses were determined by chiral GC or HPLC. The absolute configurations were determined by comparing the sign of the optical rotation with that reported in ref 12a.

Very interestingly, it was found that the enantioselectivity in the cyclization largely depended on the ratios of palladium to ligand **2**. When the catalyst was made from $Pd(CF_3COO)_2$ and **2c** in a ratio of 1:0.75, which formed a mixture of (*S*,a*S*)-**4c**, (*S*,a*S*)-**3c** and **2c** with 1:0.5:0.4 ratio, the enantioselectivity was increased to 93% ee (entry 8). By increasing the ratio of ligand to palladium to 1:1, in which the catalytic system was composed of bimetallic complex (*S*,a*S*)-**4c**, monometallic complex (*S*,a*S*)-**3c**, and residual free ligand **2c** with the ratio of 1:1.4:1, the enantioselectivity was significantly improved to 96% ee (entry 9).[14] However, when the ratio of ligand to palladium was further increased to 2:1, only a slight influence was observed on the catalytic efficiency (entry 10). This result may suggest that monopalladium complex could play an important role in the enantioinduction. Unfortunately, all attempts in isolating a pure monopalladium complex were failed. Nevertheless, it should be noted here that the chelation-induced axially chiral catalytic system prepared from the axially achiral ligand **2c** and $Pd(CF_3COO)_2$ in 1:1 ratio is one of the most effective chiral catalytic systems for the Wacker-type cyclization.

The Wacker-type cyclization can be successfully applied to a series of *o*-allylphenols **6b**−**h** and *o*-allylnaphthols **6i**, giving the corresponding chiral 2,3-dihydrobenzofurans **7b**−**h** and dihydronaphtho[1,2-*b*]furan **7i** with $Pd(CF_3COO)_2$−**2c** (1:1 molar ratio) as catalyst. As shown in Table 2, a wide array of chiral dihydrobenzofurans was obtained with excellent enantioselectivities (94−99% ee), regardless of the steric or electronic properties of the phenyl group on the substrate **6** (entries 1−8). For 2-(2,3-dimethyl-2-butenyl)-1-naphthol (**6i**) derived from 1-naphthol, the cyclization reaction gave the corresponding dihydronaphtho[1,2-*b*]furan **7i** with good isolated yield and excellent enantioselectivity (97%, entry 9). It is noteworthy that the enantioseletivities obtained with Pd(II) complex with axially achiral tetraoxazoline **2c** are higher than or comparable to those obtained with other families of efficient chiral nitrogen-donor ligands.[11−13]

(14) Similar results have been found by Hayashi and Uozumi with Pd(II)−boxax catalyst. It was demonstrated that the higher ratio of ligand to palladium afforded higher enantioselectivity in Wacker-type cyclizations. See ref 12b,c.

SCHEME 3. Pd(II)-Catalyzed Asymmetric Wacker-Type Cyclization of Allylphenol 8



The effectiveness of this oxidative cyclization largely depended on the substituent circumstances of allyl group at a substrate according to previous reports by Hayashi and coworkers.[12c] For example, the cyclization of (*E*)-2-(2-methyl-2-butenyl)phenol (**8**), in which the allyl group possesses of three substituents, afforded dihydrobenzofuran **9** with only 9% ee using original Pd(II)-boxax as catalyst, even though the enantioselectivity was improved to 96% ee by ligand modification.[12c] Therefore, to further explore substrate scope, we examined the efficacy of our catalytic system for asymmetric Wacker-type cyclization of allylphenol **8**. Significantly, our catalytic system is also effective for cyclization of this substrate. Thus, the oxidative cyclization of allylphenol **8** in the present of 10 mol % of $Pd(CF_3COO)_2$−**2c** (1:1) at 20 °C for 3 days gave corresponding 2,3-dihydrobenzofuran **9** in 79% yield with 93% ee (Scheme 3).

Conclusions

In summary, we have developed a new family of chelation-induced axially chiral palladium complex systems by using tetraoxazoline ligands **2**. Although there is no any axial chirality in ligands **2** due to the molecular symmetry, it was demonstrated that only the (*S*)-axial configuration diastereomer was obtained upon the complexing process whether the monometallic or bimetallic palladium complexes were formed. The catalytic system, $Pd(CF_3COO)_2$−**2c** in a 1:1 molar ratio, showed excellent catalytic activities and enantioselectivities in the Wacker-type cyclization of various allylphenols **6** with up to 99% ee. Highly enantioselectivity was also obtained in Wacker-type cyclization of allylphenol **8** using our catalytic system. The concept demonstrated in our present work would lead to a new way for the development of novel axially chiral catalysts.

Experimental Section

General Procedure for Synthesis of Ligands 2a−c. 2,2′,6,6′-Tetra[(4′*S*)-*tert*-butyloxazolin-2′-yl]-1,1′-biphenyl (2a). Biphenyl-2,2′,6,6′-tetracarboxylic acid (**5**) (2.15 g, 6.51 mmol) was suspended in CH_2Cl_2 (30 mL) and cooled prior to the addition of thionyl chloride (10.0 mL, 0.14 mol) and DMF (two drops). The suspension was warmed to reflux for 8 h, concentrated to dryness, and then dissolved by dry CH_2Cl_2 (20 mL). This solution was added dropwise over 0.5 h to a solution of (*S*)-*tert*-leucinol (3.43 g, 29.3 mmol) and triethylamine (4.91 mL, 37.1 mmol) in dry CH_2Cl_2 (30 mL) with stirring at 0 °C. After being stirred for 20 h at room temperature, triethylamine (10.7 mL, 81.2 mol) was added to the reaction mixture and cooled to 0 °C, and then methanesulfonic chloride (2.53 mL, 32.2 mmol) was added dropwise. The mixture was stirred for 16 h at room temperature. The mixture was diluted with CH_2Cl_2 and washed with cold water and brine. The organic layer was dried over $MgSO_4$. After removal of the solvent in vacuo, the residue was chromatographed on silica gel to give tetraoxazoline **2a** (1.66 g, 39%) as a viscous liquid: $[\alpha]^{25}_D$ −73.44 (*c* 0.20,

$CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, $J = 8.0$ Hz, 4H), 7.31 (d, $J = 8.0$ Hz, 2H), 3.92 (dd, $J = 12.0$, 13.2 Hz, 4H), 3.74−3.68 (m, 8H), 0.67 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 140.4, 130.9, 129.2, 126.4, 76.3, 68.3, 33.8, 25.9; HRMS (Micromass LCT) calcd for $C_{40}H_{55}N_4O_4$ 655.4223, found 655.4221.

2,2′,6,6′-Tetra[(4′*S*)-isopropyloxazolin-2′-yl]-1,1′-biphenyl (2b). Product **2b** was obtained in 45% yield following the procedure for **2a**: $[\alpha]^{25}_D$ −125.65 (*c* 0.76, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, $J = 8.0$ Hz, 4 H, ArH), 7.34 (d, $J = 7.6$ Hz, 2H), 3.98 (t, $J = 7.6$ Hz, 4H), 3.76 (dd, $J = 8.0$, 14.8 Hz, 4H), 3.70 (dd, $J = 8.0$, 15.6 Hz, 4H), 1.52−1.60 (m, 4H), 0.76 (d, $J = 6.8$ Hz, 12H), 0.73 (d, $J = 6.4$ Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 139.9, 131.0, 129.2, 126.7, 72.7, 70.4, 32.8, 19.1, 18.4; HRMS (Micromass LCT) calcd for $C_{36}H_{47}N_4O_4$ 599.3597, found 599.3611.

2,2′,6,6′-Tetra[(4′*S*)-phenyloxazolin-2′-yl]-1,1′-biphenyl (2c). Product **2c** was obtained in 47% yield following the procedure for **2a**: $[\alpha]^{25}_D$ −143.43 (*c* 0.93, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, $J = 8.0$ Hz, 4H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.27−7.21 (m, 12H), 7.11 (dd, $J = 1.6$, 8.0 Hz, 8H), 5.18 (dd, $J = 8.4$, 10.4 Hz, 4H), 4.40 (dd, $J = 8.4$, 10.4 Hz, 4H), 3.91 (t, $J = 8.4$ Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 142.4, 139.5, 131.9, 129.2, 128.6, 127.4, 127.2, 126.9, 75.2, 69.9; HRMS (Micromass LCT) calcd for $C_{48}H_{39}N_4O_4$ 735.2971, found 735.2975.

General Procedure for Synthesis of Axial Chiral Bimetallic Palladium Complexes 4a−c. 2,2′,6,6′-Tetra[(4′*S*)-*tert*-butyloxazolin-2′-yl]-1,1′-biphenylpalladium(II) Triflate Complex [(*S*,a*S*)-4a]. To a solution of ligand **2a** (6.6 mg, 10 μmol) in acetone-d_6 was added 2 equiv of $Pd(OCOCF_3)_2$ (6.7 mg, 20 μmol), and the suspension was stirred at room temperature under nitrogen atmosphere until complete dissolution. The ^1H NMR of this solution showed only one set of signals: ^1H NMR (400 MHz, acetone-d_6) δ 8.32 (d, $J = 3.6$ Hz, 4H), 8.18 (dd, $J = 7.2$, 8.4 Hz, 2H), 4.53 (t, $J = 9.2$, 4H), 4.45 (dd, $J = 5.2$, 9.2 Hz, 4H), 3.95 (dd, $J = 5.6$, 10.0 Hz, 4H), 0.83 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 163.9, 140.5, 132.0, 129.7, 126.5, 116.2, 76.8, 68.4, 33.8, 26.0; HRMS (Micromass LCT) calcd for $C_{46}H_{54}F_9N_4O_{10}Pd_2$ 1205.1766, found 1205.1748.

2,2′,6,6′-Tetra[(4′*S*)-isopropyloxazolin-2′-yl]-1,1′-biphenylpalladium(II) triflate complex [(*S*,a*S*)-4b]: ^1H NMR (400 MHz, acetone-d_6) δ 8.33 (d, $J = 8.0$ Hz, 4H), 8.21 (dd, $J = 7.2$, 8.8 Hz, 2H), 4.57 (t, $J = 9.2$, 4H), 4.26 (dd, $J = 6.0$, 8.8 Hz, 4H), 3.65−3.71 (m, 4H), 1.32 (d, $J = 6.4$ Hz, 12H), 1.03−1.12 (m, 4H), 0.49 (d, $J = 6.8$ Hz, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 163.8, 134.0, 131.2, 129.1, 126.9, 116.2, 72.8, 70.7, 32.9, 19.3, 18.5; HRMS (Micromass LCT) calcd for $C_{42}H_{46}F_9N_4O_{10}Pd_2$ 1149.1140, found 1149.1152.

2,2′,6,6′-Tetra[(4′*S*)-phenyloxazolin-2′-yl]-1,1′-biphenylpalladium(II) triflate complex [(*S*,a*S*)-4c]: ^1H NMR (400 MHz, acetone-d_6) δ 7.90−8.00 (m, 6H), 7.35−7.39 (m, 12H), 7.01−7.04 (m, 8H), 5.11 (dd, $J = 7.2$, 10.8 Hz, 4H), 4.88 (dd, $J = 9.2$, 10.4 Hz, 4H), 4.49 (dd, $J = 6.4$, 9.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 163.9, 142.6, 139.3, 132.0, 129.9, 128.7, 127.6, 127.5, 127.0, 116.2, 75.4, 70.2; HRMS (Micromass LCT) calcd for $C_{54}H_{38}F_9N_4O_{10}Pd_2$ 1285.0514, found 1285.0500.

General Procedure for the Pd(II)-Catalyzed Asymmetric Wacker-Type Cyclization of *o*-Allylphenols. A typical procedure is given for the reaction of 2-(2,3-dimethyl-2-butenyl)phenol (**6a**) with a palladium(II) complex of **2a** forming (*S*)-2-isopropenyl-2-methyl-2,3-dihydrobenzofuran (**7a**). To a solution of palladium bis(trifluoroacetate) (14.0 mg, 0.04 mmol) and **2a** (13.8 mg, 0.02 mmol) in methanol (1.0 mL) was added *p*-benzoquinone (181.6 mg, 1.68 mmol) and 2-(2,3-dimethyl-2-butenyl)phenol (**6a**) (74.0 mg, 0.42 mmol) in methanol (0.5 mL) at room temperature. The reaction mixture was stirred at 60 °C for 24 h, concentrated in vacuo, and then chromatographed on silica gel (eluent: ethyl acetate and petroleum ether) to give (*S*)-2-isopropenyl-2-methyl-2,3-dihydrobenzofuran (**7a**) (31.5 mg, 43%, 38% ee) as a colorless oil: $[\alpha]_D^{26}$ −32.4 (*c* 1.45, chloroform); ^1H NMR (400 MHz, $CDCl_3$) δ 1.55 (s, 3H), 1.83 (dd, $J = 0.8$, 1.6 Hz, 3H), 3.02 (d, $J = 16.0$ Hz, 1H), 3.26 (d, $J = 15.2$ Hz, 1H), 4.84 (m, 1H), 5.09 (m, 1H), 6.79 (d, $J = 7.2$ Hz, 1H), 6.83 (m, 1H), 7.10−7.15 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 158.9, 147.7, 128.0, 126.5, 124.9, 120.0, 109.9, 109.4, 89.7, 41.3, 26.0, 18.7. The ee was determined by chiral GC on a Chirasil-DEX CB column (110 °C isothermal).

(*S*)-2-Isopropenyl-2,5-dimethyl-2,3-dihydrobenzofuran (7b): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 3H), 1.81 (br, 3H), 2.27 (s, 3H), 2.97 (d, $J = 16.0$ Hz, 1H), 3.22 (d, $J = 15.6$ Hz, 1H), 4.83 (m, 1H), 5.07−5.08 (m, 1H), 6.68 (d, $J = 8.4$ Hz, 1H), 6.89−6.96 (m, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 147.8, 129.3, 128.3, 126.5, 125.5, 109.8, 108.8, 89.6, 41.4, 26.0, 20.7, 18.9; HRMS (Micromass LCT) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1202. The ee was determined by chiral GC on a Chirasil-DEX CB column (110 °C isothermal).

(*S*)-2-Isopropenyl-2,6-dimethyl-2,3-dihydrobenzofuran (7c): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, $J = 7.2$ Hz, 1H), 6.67 (d, $J = 7.6$ Hz, 1H), 6.65 (s, 1H), 5.11 (br, 1H), 4.85 (br, 1H), 3.23 (d, $J = 15.2$ Hz, 1H), 2.98 (d, $J = 15.2$ Hz, 1H), 2.33 (s, 3H), 1.84 (br, 3H), 1.56 (br, 3H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 147.9, 138.2, 124.7, 123.6, 120.9, 110.3, 110.0, 90.1, 41.3, 29.8, 26.2, 18.9; HRMS (Micromass LCT) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1202. The ee was determined by chiral GC on a Chirasil-DEX CB column (110 °C isothermal).

(*S*)-2-Isopropenyl-2,7-dimethyl-2,3-dihydrobenzofuran (7d): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.57 (s, 3H), 1.83 (s, 3H), 2.24 (s, 3H), 3.03 (d, $J = 15.6$ Hz, 1H), 3.26 (d, $J = 15.6$ Hz, 1H), 4.84 (br, 1H), 5.10 (br, 1H), 6.75 (t, $J = 8.0$ Hz, 1H), 6.96 (t, $J = 7.2$ Hz, 2H), ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 147.9, 129.1, 125.7, 122.2, 119.9, 119.5, 109.7, 89.2, 41.7, 26.2, 18.7, 15.3; HRMS (Micromass LCT) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1202. The ee was determined by chiral GC on a Chirasil-DEX CB column (100 °C isothermal).

(*S*)-2-Isopropenyl-2-methyl-5-methoxy-2,3-dihydrobenzofuran (7e): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.65−6.73 (m, 3H), 5.08 (br, 1H), 4.84 (br, 1H), 3.75 (s, 3H), 3.23 (d, $J = 16.0$ Hz, 1H), 2.99 (d, $J = 15.6$ Hz, 1H), 1.82 (br, 3H), 1.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 153.3, 147.9, 127.7, 113.0, 111.5, 110.1, 109.4, 90.0, 56.2, 42.0, 26.2, 18.9; HRMS (Micromass LCT) calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1150. The ee was determined by chiral GC on a Chirasil-DEX CB column (125 °C isothermal).

(*S*)-2-Isopropenyl-2-methyl-7-methoxy-2,3-dihydrobenzofuran (7f): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.66−6.82 (m, 3H), 5.11 (br, 1H), 4.84 (br, 1H), 3.88 (s, 3H), 3.27 (d, $J = 15.6$ Hz, 1H), 3.03 (d, $J = 15.2$ Hz, 1H), 1.83 (br, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.54, 147.49, 144.7, 127.8, 120.7, 119.4, 117.3, 111.3, 110.2, 90.7, 42.0, 26.2, 18.9; HRMS (Micromass LCT) calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1150. The ee was determined by chiral GC on a Chirasil-DEX CB column (125 °C isothermal).

(*S*)-5-Fluoro-2-isopropenyl-2-methyl-2,3-dihydrobenzofuran (7g): colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 6.77−6.86 (m, 2H), 6.69 (dd, $J = 4.4$, 8.8 Hz, 1H), 5.09 (br, 1H), 4.86 (br, 1H), 3.24 (d, $J = 15.2$ Hz, 1H), 3.00 (d, $J = 15.6$ Hz, 1H), 1.83 (br, 3H), 1.55 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 156.3, 155.06, 155.05, 147.6, 128.0, 127.9, 114.3, 114.1, 112.3, 112.1, 110.3, 109.6, 109.5, 90.6, 41.71, 41.69, 26.1, 18.9; HRMS (Micromass LCT) calcd for $C_{12}H_{13}OF$ 192.0950, found 192.0950. The ee was determined by chiral GC on a Chirasil-DEX CB column (120 °C isothermal).

(*S*)-2-Isopropenyl-2-methyl-5-phenyl-2,3-dihydrobenzofuran (7h): colorless oil; $[\alpha]_D^{26}$ −5.99 (*c* 0.72, chloroform); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53−7.57 (m, 2H), 7.37−7.44 (m, 4H), 7.29−7.33 (m, 1H), 6.89 (dd, $J = 1.6$, 8.8 Hz, 1H), 5.15 (br, 1H), 4.90 (br, 1H), 3.34 (d, $J = 15.6$ Hz, 1H), 3.09 (d, $J = 15.2$ Hz, 1H), 1.88 (br, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 147.8, 141.5, 133.9, 128.8, 127.4, 127.3, 126.9, 126.6, 124.0, 110.2, 109.7, 90.5, 41.5, 26.3, 18.9; HRMS (Micromass LCT) calcd

for $C_{18}H_{18}O$ 250.1358, found 250.1358. The ee was determined by HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol = 99.7: 0.3, flow = 0.5 mL/min).

(*S*)-2-Isopropenyl-2-methyl-2,3-dihydronaphtho[1,2-*b*]furan (7i): colorless oil; $[\alpha]_D^{26}$ −31.94 (*c* 0.94, chloroform); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 9.2 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.49−7.53 (m, 1H), 7.33−7.37 (m, 1H), 7.20 (dd, J = 2.8, 11.6 Hz, 1H), 5.23 (br, 1H), 4.94 (br, 1H), 3.56 (d, J = 14.8 Hz, 1H), 3.33 (d, J = 15.2 Hz, 1H), 1.93 (br, 3H), 1.70 (br, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 148.0, 131.1, 129.23, 129.16, 128.9, 126.7, 122.8, 122.7, 117.9, 112.4, 110.1, 90.8, 40.5, 26.5, 18.8; HRMS (Micromass LCT) calcd for $C_{16}H_{16}O$ 224.1201, found 224.1204. The ee was determined by HPLC on a Daicel Chiralcel AD-H column (hexane/2-propanol = 99.9: 0.1, flow = 0.5 mL/min).

(*S*)-2-Ethenyl-2-methyl-2,3-dihydrobenzofuran (9): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11−7.16 (m, 2H), 6.76−6.88 (m, 2H), 6.05 (dd, J = 17.6, 11.2 Hz, 1H), 5.31 (dd, J = 17.2, 0.8 Hz, 1H), 5.10 (dd, J = 10.4, 0.8 Hz, 1H), 3.18 (d, J = 14.2 Hz, 1H), 3.06 (d, J = 15.6 Hz, 1H), 1.56 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.8, 141.8, 128.2, 126.6, 125.2, 120.4, 113.0, 109.6, 87.7, 42.2, 26.3. The ee was determined by HPLC on a Daicel Chiralcel OD-H column (hexane/2-propanol = 99.0: 1.0, flow = 0.5 mL/min).

Acknowledgment. This work was supported by the National Natural Science Foundation of China, the Ministry of Education of China, and Nippon Chemical Industrial Co., Ltd. We thank Qi Gao for part of the experimental work.

Supporting Information Available: Spectroscopic data (^{1}H NMR spectra and GC and HPLC chromatograms). This material is available free of charge via the Internet at http://pubs.acs.org.

JO701469Y