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Chiral 1,2-Cyclohexane-Bridged Bis-NHC Palladium Catalysts for Asymmetric Suzuki–Miyaura Coupling: Synthesis, Characterization, and Steric Effects on Enantiocontrol

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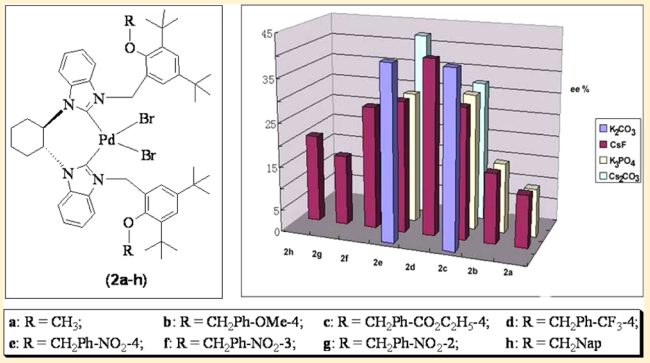
Supporting Information

ABSTRACT: The series of chiral 1,2-cyclohexane-bridged bis-N-heterocyclic carbene ligand precursors H_2[(1*R*,2*R*)-(**1a–i**)]Br with different substituent groups and their neutral and cationic diaqua palladium complexes, namely {Pd[(1*R*,2*R*)-(**1a–i**)]Br_2} (**2a–i**), {Pd[(1*R*,2*R*)-(**1a**)]X_2} (X = Cl (**3**), OAc (**4-OAc**), $OC(O)CF_3$ (**4-OCH(O)CF$_3$**)), and {Pd[(1*R*,2*R*)-(L^{OMe})]$(OH_2)_2$}X_2 (X = OTf (**5-OTf**), SbF_6 (**5-SbF$_6$**)) have been prepared in moderate to good yields. These chiral palladium complexes were fully characterized by elemental analysis, high-resolution mass spectra, ^{1}H and ^{13}C NMR, and optical rotation determinations. The crystal structures of the chiral complexes **2a** and **5-OTf** were further confirmed to adopt a distorted-square-planar coordination geometry around the palladium center. The obtained chiral NHC-Pd compounds were able to catalyze the asymmetric Suzuki–Miyaura couplings of aryl halides with arylboronic acids in good yields (up to 96%) and moderate enantioselectivities (up to 64% ee). The coligand and steric effects were studied carefully. The coligands, including Br^-, Cl^-, AcO^-, CF_3COO^-, and water molecules, have little influence on the catalytic results. However, a strong steric effect of the two aromatic substituents R on the enantiocontrol has been proved in the catalytic asymmetric Suzuki–Miyaura coupling reaction. The highest enantioselectivity of 64% ee could be achieved under the standard reaction conditions.



INTRODUCTION

Palladium-catalyzed asymmetric Suzuki–Miyaura coupling has recently emerged as an attractive alternative to standard methods for the controlled synthesis of axially chiral biaryls that are present in numerous natural products and are the core for many of the most effective chiral ligands.[1] To obtain good enantioselectivity, one of the challenges is to find suitable chiral ligands to support the catalysts. To date, several kinds of chiral ligands, including monophosphine,[2] kenphos,[3] bis-phosphine,[4] bis-hydrazones,[5] phosphino-hydrazones,[6] diene,[7] phosphoramite-oxazoline,[8] and phosphine-NHCs,[9] have been designed for palladium-catalyzed asymmetric Suzuki–Miyaura reactions, and some of them showed evident asymmetric induction activity. The studies also revealed the potential of chiral ligands applied in asymmetric cross-coupling reactions. The design of new and efficient chiral catalysts is still essential.

N-heterocyclic carbenes (NHCs) have proved to be a versatile class of spectator ligands in homogeneous catalysis.[10] In some cases, NHC ligands outperformed phosphine ligands in aspects such as the air and thermal stability of the resulting complexes and now are frequently encountered as ancillary ligands for different reactions. Although chiral NHCs have been applied to transition-metal-catalyzed reactions and delivered excellent catalytic properties,[11] using a chiral NHC as the ligand in palladium-catalyzed asymmetric cross-coupling transformations still remains a difficult problem. Quite recently, Labande and Poli reported the first example of asymmetric Suzuki–Miyaura coupling utilizing a palladium precatalyst with planar chiral ferrocenyl phosphine-NHC ligands (the ee value is less than 42%).[9] Snead et al. explored chiral acylic diaminocarbene–Pd catalyzed Suzuki-cross-coupling; unfortunately, only enantioselectivities of less than 4% ee were achieved.[10a] In general, the direct construction of chiral biaryls with chiral NHC-Pd precatalysts has provided some limited success; thus further improvement of the enantioselectivity is a challenging problem.

We have focused our attention on the synthesis of functionalized NHC ligands, with the aim of producing robust and highly active catalysts.[12] Late-transition-metal complexes bearing chiral bis-NHC ligands have proved to form higher stable catalysts capable of tolerating reaction conditions harsher than those for monodentate NHCs in asymmetric reactions.[13] Recently, we designed a series of chiral bis-N-heterocyclic

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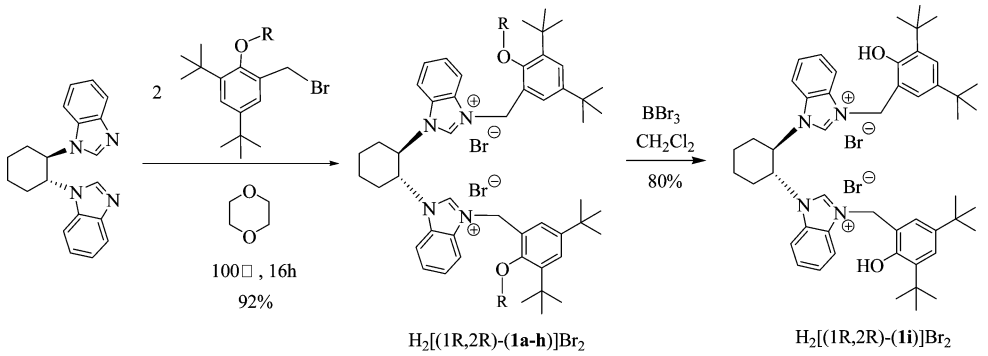
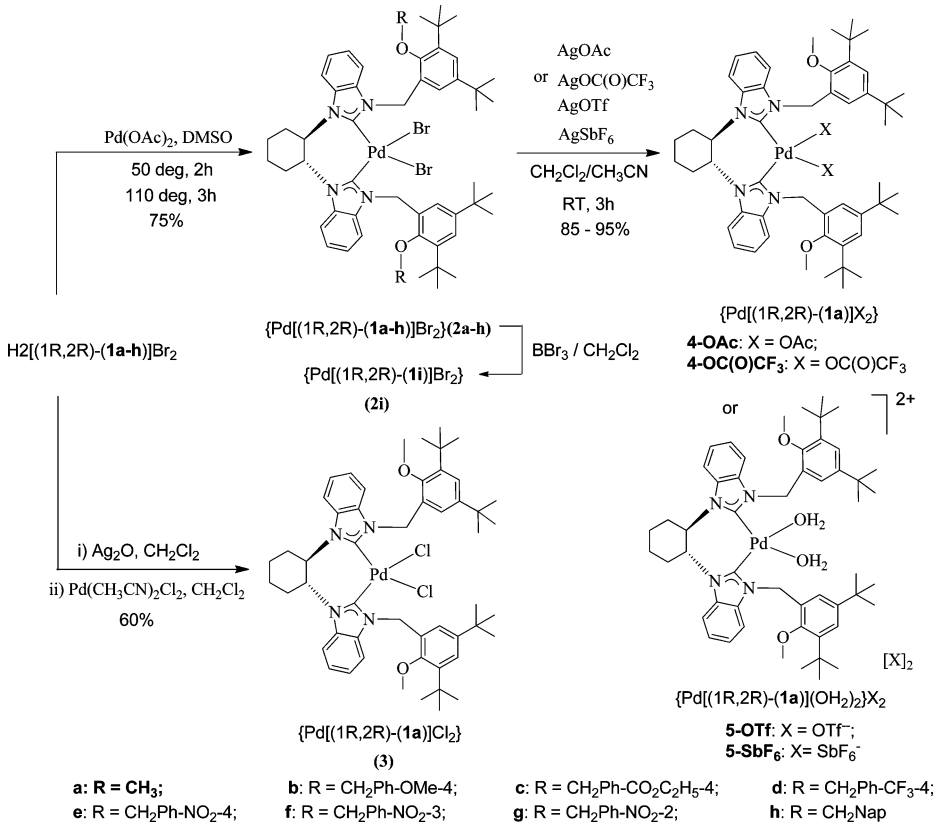
Scheme 1. Synthesis of Chiral Bis-N-Heterocyclic Carbene Precursors $H_2[(1R,2R)\text{-}(1a-i)]Br_2$

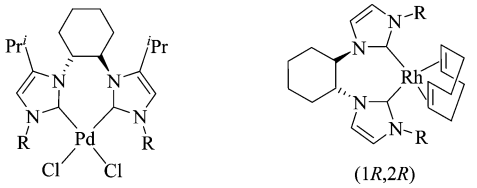


Scheme 2. Synthesis of Chiral Bis-NHC Palladium Complexes 2−5



carbene ligands (**1a−i**) derived from chiral 1,2-cyclohexanediamine (Scheme 1) and prepared their neutral and cationic diaqua palladium complexes (**2−5**) (Scheme 2). These chiral palladium compounds were able to catalyze the asymmetric Suzuki−Miyaura couplings of aryl bromides with arylboronic acids in good yields and moderate enantioselectivities (up to 64% ee). We herein describe the preparation and characterization of these bis-NHC Pd complexes and their coligand and steric effects in asymmetric Suzuki−Miyaura coupling reactions.

Chart 1



RESULTS AND DISCUSSION

Design and Synthesis of Chiral Bis-NHC Precursors and Palladium Complexes. Chart 1 gives two reported examples of metal complexes bearing chiral bis-NHC ligands derived from 1,2-cyclohexanediamine.[13] These chelating bidentate bis-NHC ligands are expected to form more highly stable catalysts capable of tolerating reaction conditions harsher than than those for monodentate NHCs. We proposed that the introduction of various coligands (Br^-, Cl^-, H_2O) and the

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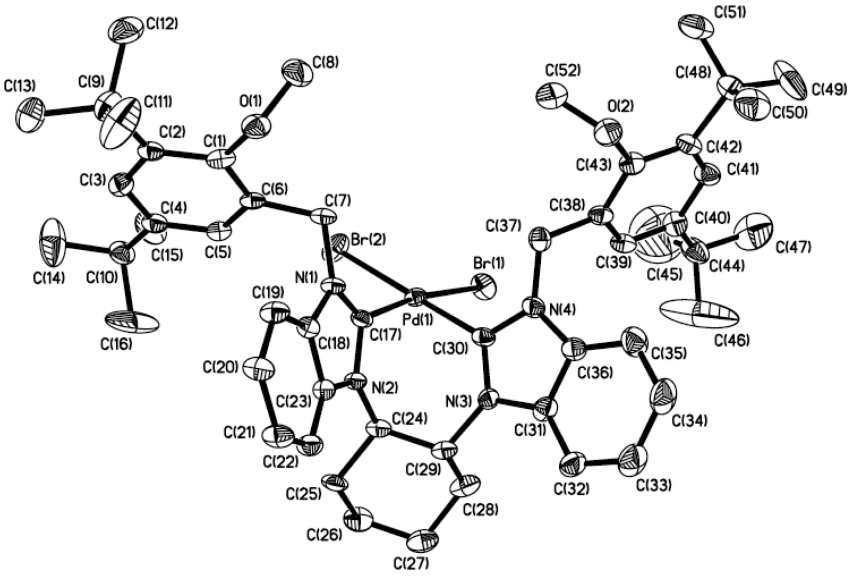

Figure 1. Molecular structure of the chiral palladium complex **2a**·2H_2O·$CHCl_3$. All hydrogen atoms and solvent molecules are omitted for clarity.

steric effect of the two aromatic substituents R would modulate the steric and electronic nature of the palladium reactive site, promoting the catalytic performance of the chiral bis-NHC palladium complexes **2**−**5** (as shown in Scheme 2) in asymmetric Suzuki−Miyaura coupling reactions. Moreover, the introduction of bulky *t*-Bu groups would improve the solubility of palladium complexes in common organic solvents.

Chiral Bis-NHC Precursor Synthesis. The required chiral bis-NHC precursor H_2[(1*R*,2*R*)-(**1a**−**h**)]Br_2 was prepared in a multistep sequence, as shown in Scheme 1. Chiral bis-imidazole, obtained from easily available (1*R*,2*R*)-(−)-diaminocyclohexene L-tartrate as the chiral starting material, reacted with 2-(alkyloxyl)-1-(bromomethyl)-3,5-di-*tert*-butylbenzene to afford the crude desired bis-imidazolium salts. After purification by silica gel column chromatography, the proligands H_2[(1*R*,2*R*)-(**1a**−**h**)]Br_2 were isolated as white solids in high yields. The hydroxy-substituted precursor H_2[(1*R*,2*R*)-(**1i**)]Br_2 was obtained in 80% yield by deprotection of the hydroxy group in H_2[(1*R*,2*R*)-(**1a**)]Br_2 using BBr_3 to cleave the methoxy groups.[14]

Bis-NHC-Pd Complex Synthesis. With the expected bis-NHC precursors in hand, the corresponding metalation reaction was attempted to prepare chiral palladium complexes. The synthetic route for chelating chiral bis-NHC palladium complexes **2**−**5** is depicted in Scheme 2. In general there are two reliable synthetic pathways for the synthesis of chelating NHC-Pd complexes.[10] One is the in situ deprotonation of imidazolium salts by $Pd(OAc)_2$;[15] the other is use of a silver-NHC complex as a transmetalating agent.[16] The proligands H_2[(1*R*,2*R*)-(**1a**−**h**)]Br_2 were combined directly with $Pd(OAc)_2$, and the chiral palladium complexes {Pd[(1*R*,2*R*)-(**1a**−**h**)]Br_2} (**2a**−**h**) were successfully obtained as white solids in 70−94% yield. The reaction of the bis(imidazolium) salt H_2[(1*R*,2*R*)-(**1a**)]Br_2 with Ag_2O afforded the silver-NHC complex, which was not isolated but continuously reacted as the carbene transfer reagent with $Pd(CH_3CN)_2Cl_2$ to give the complex {Pd[(1*R*,2*R*)-(**1a**)]Cl_2} (**3**) in 60% yield. Upon treatment of NHC-Pd^{II} complexes **2a** with the different silver salts AgX (X = OAc, $OC(O)CF_3$, OTf, SbF_6) in the mixed solvent $MeCN/CH_2Cl_2$ at room temperature for 3 h, the corresponding neutral complexes {Pd[(1*R*,2*R*)-(**1a**)]X_2} (X = OAc (**4-OAc**), $OC(O)CF_3$ (**4-OCH(O)CF$_3$**)), bearing weakly coordinating acetate counterions, and the cationic diaqua complexes {Pd[(1*R*,2*R*)-(**1a**)]$(OH_2)_2$}X_2 (X = OTf (**5-OTf**), SbF_6 (**5-SbF$_6$**)) were obtained in 85−95% yield.[17] Attempts to prepare 2-hydroxyphenyl-containing NHC-Pd complexes by direct reaction of the imidazolium salts H_2[(1*R*,2*R*)-(**1i**)]Br_2 with $Pd(OAc)_2$ proved unsuccessful; an insoluble palladium compound always formed, which prohibited us from further exploration. However, the complex {Pd[(1*R*,2*R*)-(**1i**)]Br_2} (**2i**) could be directly prepared in high yield (>90%) by deprotection of the hydroxy group in {Pd[(1*R*,2*R*)-(**1a**)]Br_2} (**2a**), using BBr_3 to cleave the methoxy groups.[14]

Characterization of Palladium Complexes. All chiral palladium complexes **2**−**5** are air- and moisture-stable in the solid state and even in solution. Their structures were confirmed by elemental analysis, high-resolution mass spectra (HRMS), ^1H and ^{13}C NMR, and optical rotation determinations. All palladium complexes were in good agreement with the results by HRMS. For the neutral complexes **2a**−**i**, **3** and **4**, although no peak was observed at the position corresponding to the parent molecule M, there was a dominant fragment ion $[M - X]^+$ (X = Br^-, Cl^-, AcO^-, CF_3COO^-, Br^-) (see the Supporting Information) that showed the most dominant intensity (100%) as the base peak in their mass spectra. For the cationic diaqua complexes **5-OTf** and **5-SbF$_6$**, in addition to the presence of the fragment ion $[M - 2H_2O - X]$ at *m*/*z* 1035.3945 (X = $CF_3SO_3^-$), and 1123.3351 (X = SbF_6^-), the fragment ion at *m*/*z* 653.2498 (100%) showed the most dominant intensity as the base peak. It was formed by bond cleavage between the alkyl carbon and nitrogen in the fragment ion $[M - 2H_2O - 2X]^{2+}$ to lose the {2-CH_3O-3,5-*t*-$Bu_2C_6H_2CH_2^+$} (for short, RCH_2^+) moiety.

The formation of the NHC-Pd(II) complexes was conformed by the loss of the C*H* proton resonance of the imidazolium salt and the presence of a carbene carbon (Pd-*C*) at 176.4−168.0 ppm, which is a characteristic peak for metal carbene complexes.[10,17] Notably, from their ^{13}C NMR spectra there existed two types of NHC carbenes in these cyclometalated palladium(II) complexes. For example, the signals for the carbene carbon atom of compounds **2a** and **3** appear at 176.4 and 171.0 ppm and at 175.3 and 169.2 ppm, respectively.

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Moreover, the resonance of weakly coordinating water molecules in the cationic diaqua complexes **5-OTf** and **5-SbF_6** was observed at around 2.2 ppm, which is downshifted in comparison with that of free residual water at 1.56 ppm in deuterated chloroform.

A single crystal of the neutral complex **2a**·$2H_2O$·$CHCl_3$ was obtained from hexane/chloroform. Its crystal structure (Figure 1) exhibited that the synthesis of such a chiral palladium(II) complex did not lead to appreciable racemization; the absolute configuration at each chiral center was assigned to be 1*R*,2*R*, which was in accordance with the absolute configuration of the primarily employed chiral 1,2-cyclohexanediamine. Moreover, the cationic diaqua complex **5-OTf**·CH_2Cl_2 was crystallized from hexane/dichloromethane solution and its structure also undoubtedly confirmed by X-ray crystallography (Figure 2). The selected bond lengths and angles of these two complexes are given in Table 1.

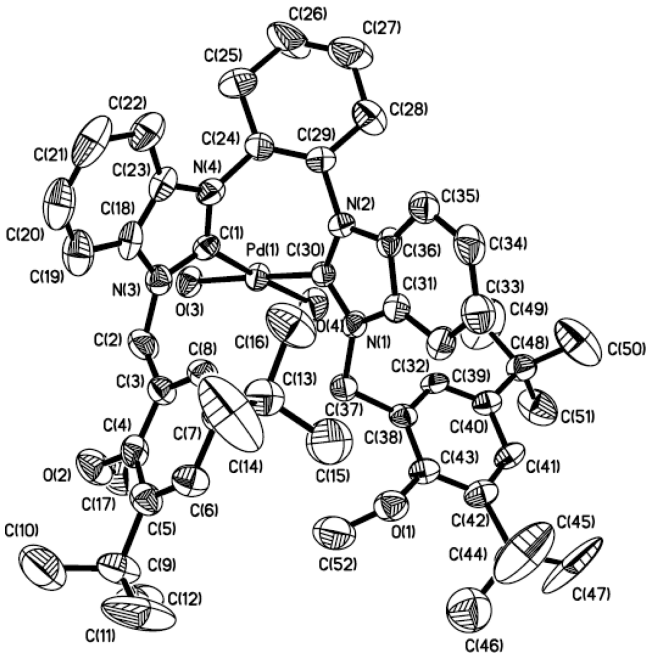

Figure 2. Molecular structure of the complex **5-OTf**·CH_2Cl_2. All hydrogen atoms, triflate counterions, and solvent molecules are omitted for clarity.

Table 1. Selected Bond Distances (Å) and Angles (deg) for 2a and 5-OTf

Complex **2a**			
Pd(1)−C(17)	1.982(10)	Pd(1)−C(30)	2.003(10)
Pd(1)−Br(1)	2.4800(12)	Pd(1)−Br(2)	2.4637(13)
C(17)−Pd(1)−C(30)	84.3(3)	C(17)−Pd(1)−Br(1)	171.6(2)
C(30)−Pd(1)−Br(1)	89.7(2)	C(17)−Pd(1)−Br(2)	93.6(2)
C(30)−Pd(1)−Br(2)	177.2(2)	Br(1)−Pd(1)−Br(2)	92.51(4)
Complex **5-OTf**			
Pd(1)−C(1)	1.960(7)	Pd(1)−C(30)	1.947(6)
Pd(1)−O(3)	2.090(4)	Pd(1)−O(4)	2.085(5)
C(1)−Pd(1)−C(30)	83.0(3)	C(1)−Pd(1)−O(4)	175.9(2)
C(30)−Pd(1)−O(4)	93.1(2)	C(1)−Pd(1)−O(3)	96.2(2)
C(30)−Pd(1)−O(3)	178.1(2)	O(4)−Pd(1)−O(3)	87.7(2)

Complexes **2a** and **5-OTf** showed similar crystal structures with a distorted square planar coordinated palladium center. The bis-carbene ligand chelated the Pd(II) center in a *cis* arrangement, and the two remaining coordination sites were occupied by bromo anions or water molecules. The seven-membered palladacycle adopted a pseudo-boatlike conformation, and the bis-NHC C−Pd−C bite angles were 84.3(3) and 83.0(3)°, respectively. The Pd−C distances (1.982(10) and 2.003(10) Å for **2a**; 1.960(7) and 1.947(6) Å for **5-OTf**) fall comfortably within the range found for the neutral chiral chelating bis(carbene)palladium(II) complexes (1.987(5) and 2.003(5) Å)[13b] and dibromo{1,1′-bis[(*R*)-1″-phenylethyl]-3,3-methylenediimidazolin-2,2′-diylidene}palladium(II) (1.992(3) and 1.974(3) Å)[18] and the axially chiral bis-NHC-Pd(II) complex (1.997(7) and 1.984(3) Å) as well as with those reported for the related nonchiral neutral and dicationic bis-NHC palladium complex *cis*-$CH_2\{NC(H)=C(H)N(CH_3)-C\}_2PdI_2$ (1.990(3) and 1.997(3) Å)[19] and *cis*-$CH_2\{NC(H)=C(H)N(CH_3)C\}_2Pd(NCCH_3)_2]^{2-}[BF_4^-]_2$ (1.966(2) and 1.972(3) Å).[20]

Suzuki−Miyaura Cross-Coupling. We chose complex **2a** to catalyze the Suzuki−Miyaura coupling between 1-bromo-2-methoxynaphthalene (**6**) and naphthylboronic acid (**7**) to optimize the reaction conditions, including primarily palladium catalyst, base, and solvent. As shown in Table S1 (Supporting Information), THF and Cs_2CO_3 proved to be the best solvent and base, respectively. The coligands, including Br^-, Cl^-, AcO^-, CF_3COO^-, and water, have little influence on the catalytic results (Table S2, Supporting Information). The neutral complexes **2a** and **3** with halide coligands (Br, Cl) were found to give the best results, with 92% yield and 14−16% ee values (entries 1 and 2, Table S2). Complex **2i** revealed no activity for this model reaction (entry 7, Table S2). A possible reason for this is that the two hydroxyl groups were deprotonated with cesium carbonate, leading to the formation of a stable palladium complex bearing a tetracoordinated bis-phenol-bis-NHC ligand.[21]

Noncovalent interactions involving aromatic rings are myriad areas of chemistry, materials science, and molecular biology.[22] We envisioned that the aromatic interactions between the two R groups in the chiral bis-NHC ligand might modulate the steric and electronic nature of Pd(0)/Pd(II) reactive sites during the oxidative addition/reductive elimination process, promoting the enantioselectivity of Suzuki−Miyaura coupling reactions. On the basis of this concept, we synthesized complexes **2b−h** (Scheme 2) for comparison. Table S3 (Supporting Information) and Figure 3 give the catalytic results of model Suzuki−Miyaura coupling reactions between **6** and **7** using **2b−h** as procatalysts.

When a 4-methoxybenzyl group was introdced, the yield was 75−95% with an ee value of 11−17% (complex **2b**; entries 1−4, Table S3). This result is similar to that of complex **2a** with methyl group (entries 4−6, Table S1). Notably, complexes **2c−e** bearing ester or nitro groups promoted the reaction, providing the biaryl product in 50−88% yield with 30−45% ee values (entries 9−17, Table S3; see also Figure 3). This result suggested a strong steric effect of the R groups of the NHC ligand on the enantiocontrol in the catalytic asymmetric Suzuki−Miyaura coupling reactions. Complex **2h** with more bulky naphthylmethyl groups also gave a poor result of 10% yield and 20% ee (entry 20, Table S3). Further investigation showed that the position of a weakly coordinating substituent on the aryl group influenced the catalytic results. For example, complexes **2e** with 4-nitro, **2f** with 3-nitro, and **2g** with 2-nitro gave almost similar yields of 83−85%, but quite different ee %

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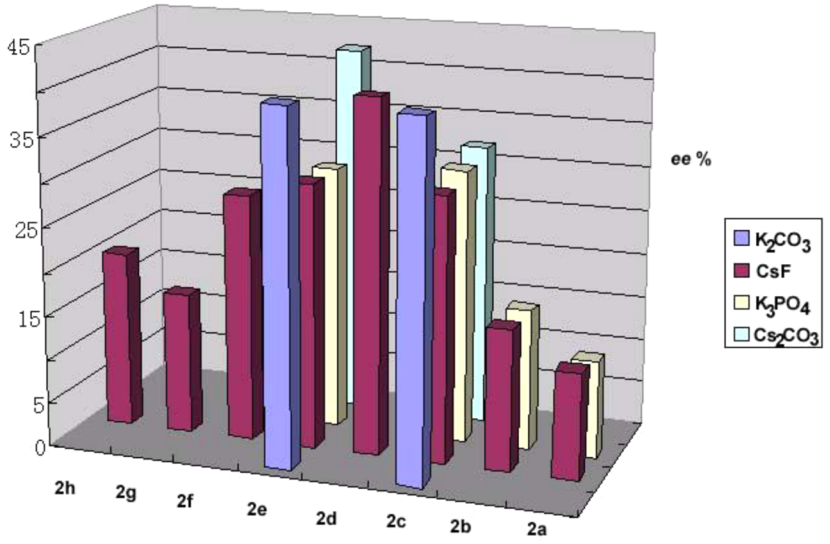
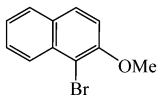
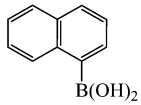
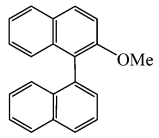
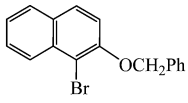
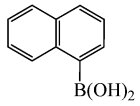
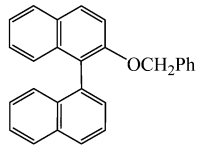
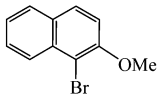
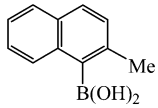
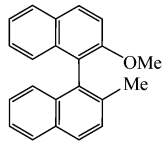
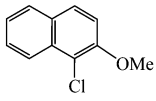
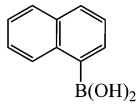
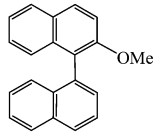


Figure 3. Steric effects on the ee values of Suzuki–Miyaura coupling.

Table 2. Typical Substrate Scope of Suzuki–Miyaura Coupling Using 2e[a]

entry	Ar^1-X	$(HO)_2$-Ar^2	Ar^1-Ar^2	yield (%)[b]	ee %[c]
1				83	45
2				45	57
3				N. R.[d]	-
4				52	64

[a]Reagents and conditions: aryl halide (1.0 equiv), arylboronic acid (1.5 equiv), Pd cat. **2e** (3 mol %), CsF (2.5 equiv), THF, 65 °C, 24 h. [b]Isolated yields after column chromatography. [c]The ee value was determined by HPLC, using a Chirlcel OJ-H column. [d]No reaction.

values (45% for **2e**, 28% for **2f**, 16% for **2g**) were achieved under the same conditions (entries 16, 18, and 19, Table S3).

Previously we conducted DFT calculations to explore the energy difference between the *cis*- and *trans*-dihalido-bis(NHC) nickel(II) complexes.[23] We used a similar DFT method to study the substituent effect of the bis-NHC-Pd catalysts. Complexes **2e** (R = CH_2Ph-NO_2-4) and **2g** (R = CH_2Ph-NO_2-2) were chosen as model compounds. The minimized energy values of the two complexes are 18.6244 kcal/mol (for **2e**) and 22.3492 kcal/mol (for **2g**), respectively. From the optimized structures of **2e**,**g** (see the Supporting Information, Figure S0), we found that aromatic interactions[22] exist between the two R groups. Also in **2e**, hydrogen bonding (N–O–H) could be found. The observed high ee value of **2e** is due to the combined effect of the noncovalent interaction and hydrogen bonding between the two substituted aromatic groups.

A typical substrate scope screening test of the Suzuki–Miyaura reaction with **2e** as the catalyst was performed. These results are summarized in Table 2. Under the representative conditions (CsF, THF, 65 °C, 24 h), several naphthyl halides and arylboronic acids with different steric substituents were investigated for coupling with each other (Table 2). We did observe an obvious improvement in coupling enantioselectivity (from 45% to 57% ee) with a decrease of product yield (from 83% to 45%) when a more bulky substituent was introduced to the bromide substrate (entry 2 vs 1, Table 2). We failed to obtain the polysubstituted biary compounds by Suzuki coupling using the above palladium catalyst (entry 3, Table 2). Interestingly, aryl chloride was also successfully coupled to

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arylboronic acid with a moderate yield of ca. 50%. The Suzuki–Miyaura coupling between 1-chloro-2-methoxynaphthalene and naphthylboronic acid provided the highest enantioselectivity of 64% ee (entry 4, Table 2).

CONCLUSIONS

In summary, a series of new neutral and cationic palladium(II) complexes bearing chiral-bridged bis-NHC ligands have been synthesized and fully characterized. These palladium complexes showed good activities in Suzuki–Miyaura reactions of naphthyl halides with naphthylboronic acids. The coligands, including Br^-, Cl^-, AcO^-, CF_3COO^-, and water, have little influence on the catalytic results. However, a strong steric effect of the aromatic interactions between the two R groups in the chiral bis-NHC ligand on the enantiocontrol has been proved in the catalytic asymmetric Suzuki–Miyaura coupling reaction. A moderate enantioselectivity of 64% ee could be achieved under the standard reaction conditions. This protocol provides a promising method for the synthesis of bis-aryl products.

EXPERIMENTAL SECTION

General Considerations. All manipulations were performed under an inert atmosphere of dry argon by using vacuum line and Schlenk tube techniques. All chemical reagents were purchased from commercial sources (Acros, Aldrich, Alfa Aesar, or Fluka) and used as received unless otherwise indicated. The solvents were dried and distilled prior to use by literature methods. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on JEOL ECA-400 and Bruker AV500 spectrometers. ^1H and ^{13}C chemical shifts (δ) are given in ppm (the residual peak of deuterated solvents was used as reference). Elemental and high-resolution mass spectral (HRMS) analyses were carried out by the Analysis Center, Fudan University. Optical rotations were measured in a 100 mm cell with a Perkin-Elmer 241 photopolarimeter. Flash column chromatography was performed on silica gel (300–400 mesh). GC chromatograms were recorded on a HP 4890A GC equipped with a DB-5 MS UI capillary column, and the products were identified by comparison with authentic samples. HPLC chromatograms were recorded on a Shimadzu LC-2010A (HT) equipped with a Chiralcel OJ-H column.

X-ray Crystallographic Studies. Single crystals of **2a** and **5-OTf** suitable for X-ray analysis were sealed into a glass capillary, and the intensity data of the single crystals were collected on the CCD Bruker Smart APEX system. Data obtained with the ω–2θ scan mode were collected on a Bruker SMART 1000 CCD diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) at 293 K. The structures were solved using direct methods, while further refinement with full-matrix least squares on F^2 was obtained with the SHELXTL program package.[24] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were introduced in calculated positions with the displacement factors of the host carbon atoms.

Crystal Data for ***1a***$\cdot 2H_2O\cdot CHCl_3$*:* $C_{53}H_{73}Br_2Cl_3N_4O_4Pd$, M_r = 1202.72, colorless block, 0.18 × 0.15 × 0.13 mm, triclinic, space group $P1$, a = 9.141(3) Å, b = 10.484(4) Å, c = 15.961(6) Å, α = 91.789(5)°, β = 104.749(4)°, γ = 96.057(4)°, V = 1468.2(9) Å^3, Z = 1, ρ_{calcd} = 1.360 g cm^{-3}, μ = 1.857 mm^{-1}, $F(000)$ = 618, T = 293(2) K; all data, R1 = 0.0591 and wR2 = 0.1569; $I > 2\sigma(I)$, R1 = 0.0554 and wR2 = 0.1503; GOF 1.034, 6090 independent reflections ($2\theta \leq 50.04°$) and 595 parameters, 3 restraints.

Crystal Data for ***5-OTf***$\cdot CH_2Cl_2$*:* $C_{55}H_{72}Cl_2F_6N_4O_{10}PdS_2$, M_r = 1304.59, colorless prism, 0.51 × 0.23 × 0.20 mm, monoclinic, space group $P2_1/c$, a = 22.615(7) Å, b = 15.136(5) Å, c = 18.857(6) Å, β = 95.865(5)°, V = 6421(3) Å^3, Z = 4, ρ_{calcd} = 1.350 g cm^{-3}, μ = 0.509 mm^{-1}, $F(000)$ = 2704, T = 293(2) K; all data, R1 = 0.1381 and wR2 = 0.2654; $I > 2\sigma(I)$, R1 = 0.0831 and wR2 = 0.2409; GOF 1.015, 11291 independent reflections ($2\theta \leq 50.02°$) and 708 parameters, 6 restraints.

The X-ray crystallographic files, in CIF format, are available from the Cambridge Crystallographic Data Centre on quoting the deposition numbers CCDC 909112 for **2a**$\cdot 2H_2O\cdot CHCl_3$ and CCDC 909113 for **5-OTf**$\cdot CH_2Cl_2$. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2IEZ, U.K. (fax, +44-1223-336033; e-mail, deposit@ccdc.cam.ac.uk; web, http://www.ccdc.cam.ac.uk). X-ray crystallographic data and refinement details for **2a** and **5-OTf** are given in the Supporting Information, and selected bond lengths and angles are given in Table 1.

Synthesis of {Pd[(1*R*,2*R*)-(1a)]Br$_2$} (2a). A mixture of H_2[(1*R*,2*R*)-(**1a**)]Br_2 (188 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure while heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford a brown crude product. The crude product was then washed with toluene to afford the pure palladium complex **2a** as a white solid. Yield: 188 mg (90%). Anal. Calcd for $C_{52}H_{68}Br_2N_4O_2Pd$ [1047.35 g/mol]: C, 59.63; H, 6.54; N, 5.35. Found: C, 59.44; H, 6.66; N, 5.57. HRMS (positive ions): m/z 967.3609 (calcd for $[M - Br^-]^+$ 967.36). $[\alpha]_D^{20}$ = 26.89° (c = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 7.65–7.67 (d, J = 8.86 Hz, 1H), 7.55 (t, J = 12.80 Hz, 1H), 7.34 (d, J = 10.00 Hz, 1H), 7.12–7.24 (m, 4H), 7.03 (t, J = 9.60 Hz, 1H), 6.93 (t, J = 9.60 Hz, 1H), 6.68–6.80 (d, J = 7.80 Hz, 2H), 6.56 (d, J = 7.80 Hz, 1H), 5.94–6.17 (m, 4H), 5.45 (s, 1H), 4.68–4.74 (t, J = 10.42 Hz, 1H), 3.85 (s, 3H), 3.40 (s, 3H), 2.97–3.00 (d, J = 11.92 Hz, 1H), 2.77–2.79 (m, 1H), 2.62–2.64 (d, J = 11.92 Hz, 1H), 2.15–2.34 (m, 3H),1.99–2.03 (m, 1H), 1.83 (m, 1H), 1.24–1.37 (d, J = 9.64 Hz, 18H, *t*-Bu), 0.94 (s, 9H, *t*-Bu), 0.77 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.4, 171.0 ($C^{carbene}$), 155.5, 155.2 ($C^{Ar\text{-}O}$), 146.4, 145.9, 142.0, 141.4 ($C^{Ar\text{-}t\text{-}Bu}$), 134.2, 134.0($C^{Ar}$), 131.8, 129.1, 128.3, 127.2, 125.0, 126.8, 124.1, 123.8, 123.3, 113.1, 111.4, 109.8 (CH^{Ar}), 63.3, 62.8 (OCH_3), 62.4, 61.1 ($CH^{cyclohexyl}$), 50.2, 47.6 (CH_2–N), 35.3, 34.4, 34.3 ($C^{t\text{-}Bu}$), 31.1, 31.0 ($CH_3^{t\text{-}Bu}$), 25.8, 25.1. 21.0 ($CH_2^{cyclohexyl}$).

Synthesis of {Pd[(1*R*,2*R*)-(1b)]Br$_2$} (2b). A mixture of H_2[(1*R*,2*R*)-(**1b**)]Br_2 (231 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2b** as a white solid. Yield: 201 mg (80%). HRMS (positive ions): m/z 1179.4392 (calcd for $[M - Br^-]^+$ 1179.4402). ^1H NMR (400 MHz, $CDCl_3$): δ 7.50–7.65 (m, 4H), 7.29–9.31 (d, J = 8.00 Hz, 3H), 7.21 (s, 2H), 7.08–7.14 (q, J = 16.00 Hz, 2H), 6.87–6.96 (dt, J = 20.80, 8.00 Hz, 2H), 6.76 (m, 4H), 6.49–6.54 (m, 2H), 4.49 (m, 2H), 4.71 (m, 2H), 3.71 (s, 3H), 3.57 (s, 3H), 2.91 (m, 1H), 2.79 (m, 1H), 2.58 (m, 1H), 2.12–2.25 (m, 3H), 1.84–1.99 (m, 1H), 1.60–1.72 (m, 4H), 1.44–1.46 (d, J = 9.60 Hz, 18H), 0.89 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 169.8, 159.1, 159.0, 154.1, 153.7, 146.5, 145.7, 141.6, 134.6, 134.0, 133.4, 132.3, 129.7, 129.2, 129.0, 127.7, 127.4, 123.7, 123.7, 123.5, 123.3, 123.1, 113.8, 113.7, 113.0, 112.6, 111.6, 109.9, 76.3, 63.0, 60.6, 55.1, 54.8, 50.1, 47.7, 35.3, 34.1, 33.8, 31.0, 30.9, 30.6, 29.6, 25.5, 24.7.

Synthesis of {Pd[(1*R*,2*R*)-(1c)]Br$_2$} (2c). A mixture of H_2[(1*R*,2*R*)-(**1c**)]Br_2 (248 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2c** as a white solid. Yield: 252 mg (94%). HRMS (positive ions): m/z 1263.4642 (calcd for $[M - Br^-]^+$ 1263.4613). ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 4H), 7.69–7.71 (d, J = 8.24 Hz, 1H), 7.55 (s, 3H), 7.37–7.39 (d, J = 8.24 Hz, 3H), 7.09–7.18 (m, 4H), 6.90–6.92 (m, 2H), 6.51–6.53 (d, J = 7.80 Hz, 2H), 6.45–6.47 (d, J = 7.80 Hz, 2H), 4.98 (s, 2H), 4.79–4.82 (m, 2H), 4.64 (s, 1H), 4.31–4.34 (q, J = 12.36 Hz, 4H), 2.81 (s, 2H), 2.55–2.58 (d, J = 12.84 Hz, 1H), 2.29 (s, 2H), 2.06 (s, 2H), 1.91 (s, 2H), 1.33–1.36 (d, J = 11.80 Hz, 18H), 0.80–0.81 (d, J = 3.68 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7, 169.8, 166.4, 153.5, 153.4, 146.5, 146.4, 142.1,

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141.9, 134.6, 134.0, 133.8, 132.2, 129.8, 127.3, 126.9, 124.1, 123.9, 112.9, 112.7, 111.8, 110.2, 75.8, 63.2, 60.9, 35.4, 35.3, 31.1, 30.9, 30.8, 25.8, 25.2, 14.4.

Synthesis of {Pd[(1*R*,2*R*)-(1d)]Br_2} (2d). A mixture of H_2[(1*R*,2*R*)-(**1d**)]Br_2 (246 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/10 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2d** as a white solid. Yield: 187 mg (70%). HRMS (positive ions): *m*/*z* 1255.39 (calcd for [M − Br^-]$^+$ 1255.39). $[\alpha]_D^{20}$ = 27.15° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67−7.69 (d, *J* = 8.40 Hz, 3H), 7.52 (s, 7H), 7.33−7.35 (d, *J* = 8.40 Hz, 1H), 7.13−7.22 (m, 4H), 6.92−6.98 (m, 2H), 6.51−6.56 (m, 2H), 4.99−5.01 (m, 2H), 4.88 (m, 1H), 4.71−4.77 (m, 1H), 2.81 (m, 2H), 2.57−2.60 (d, *J* = 12.40 Hz, 1H), 2.22−2.25 (d, *J* = 12.40 Hz, 2H), 2.13−2.16 (d, *J* = 13.20 Hz, 1H), 1.96 (m, 1H), 1.82−1.86 (d, *J* = 13.20 Hz, 1H), 1.39−1.43 (d, *J* = 17.20 Hz, 18H), 0.86 (m, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.9, 170.0, 153.47, 153.3, 146.9, 141.8, 140.9, 134.8, 133.6, 132.4, 128.0, 127.8, 127.4, 127.0, 125.4, 124.1, 123.9, 123.8, 123.7, 123.4, 122.7, 113.0, 112.8, 111.6, 109.9, 77.4, 77.0, 76.7, 75.5, 63.0, 60.8, 35.4, 34.3, 33.9, 31.0, 30.8, 25.6, 25.0.

Synthesis of {Pd[(1*R*,2*R*)-(1e)]Br_2} (2e). A mixture of H_2[(1*R*,2*R*)-(**1e**)]Br_2 (236.8 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2e** as a white solid. Yield: 219 mg (85%). HRMS (positive ions): *m*/*z* 1209.3929 (calcd for [M − Br^-]$^+$ 1209.3892). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06−8.09 (dd, *J* = 14.64 Hz, 8.68 Hz, 4H), 7.75 (s, 2H), 7.68−7.71 (d, *J* = 8.24 Hz, 1H), 7.53 (m, 3H), 7.35 (d, *J* = 8.24 Hz, 1H), 7.19−7.21 (d, *J* = 7.32 Hz, 2H), 7.12−7.16 (t, *J* = 7.32 Hz, 2H), 6.94−6.98 (m, 2H), 5.17 (s, 1H), 5.04−5.07 (d, *J* = 12.84 Hz, 1H), 4.91−4.94 (d, *J* = 10.08 Hz, 1H), 4.68−4.79 (m, 2H), 2.79 (s, 2H), 2.55−2.58 (d, *J* = 12.36 Hz, 1H), 2.16−2.22 (t, *J* = 10.48 Hz, 1H), 2.09−2.13 (d, *J* = 13.76 Hz, 1H), 1.79−1.95 (m, 3H), 1.41 (s, 9H), 1.34 (s, 9H), 0.82−0.83 (d, *J* = 4.12 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 169.8, 153.1, 147.4, 146.7, 144.3, 142.0, 135.2, 134.2, 134.0, 132.8, 128.2, 127.6, 126.8, 124.1, 124.0, 123.8, 112.7, 111.8, 110.2, 74.5, 63.1, 60.8, 50.2, 47.8, 35.4, 34.4, 34.2, 31.1, 30.9, 24.9.

Synthesis of {Pd[(1*R*,2*R*)-(1f)]Br_2} (2f). A mixture of H_2[(1*R*,2*R*)-(**1f**)]Br_2 (240 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (45 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/10 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2f** as a white solid. Yield: 190 mg (73%). HRMS (positive ions): *m*/*z* 1209.39 (calcd for [M − Br^-]$^+$ 1209.39). $[\alpha]_D^{20}$ = 25.03° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 2H), 8.07−8.09 (d, *J* = 7.60 Hz, 1H), 8.03 (s, 1H), 7.914 (s, 1H), 7.66−7.73 (m, 2H), 7.45−7.53 (m, 3H), 7.35−7.37 (d, *J* = 8.00 Hz, 1H), 7.13−7.20 (m, 4H), 6.93−7.02 (m, 2H), 6.51−6.55 (t, *J* = 7.60 Hz, 3H), 6.15 (m, 1H), 5.14 (m, 1H), 4.99−5.02 (d, *J* = 12.80 Hz, 2H), 4.72−4.78 (m, 2H), 2.78 (s, 2H), 2.56 (d, 1H), 2.14−2.21 (m, 3H), 1.85−1.94 (m, 2H), 1.34−1.36 (d, *J* = 9.60 Hz, 18H), 0.85−0.86 (t, *J* = 3.40 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.6, 169.7, 153.1, 153.0, 148.3, 148.2, 147.0, 146.7, 141.9, 139.2, 134.8, 133.9, 133.7, 133.5, 132.9, 132.3, 129.5, 127.8, 127.0, 124.1, 124.0, 123.9, 123.8, 123.5, 122.6, 121.6, 121.4,112.9, 112.7, 111.6, 110.0, 77.4, 77.1, 76.8, 74.4, 63.0, 60.7, 35.3, 34.3, 33.8, 31.0, 30.9, 25.6, 24.9.

Synthesis of {Pd[(1*R*,2*R*)-(1g)]Br_2} (2g). A mixture of H_2[(1*R*,2*R*)-(**1g**)]Br_2 (240 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (45 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2g** as a white solid. Yield: 189 mg (73%). HRMS (positive ions): *m*/*z* 1209.39 (calcd for [M − Br^-]$^+$ 1209.39). $[\alpha]_D^{20}$ = 26.05° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−8.06 (m, 5H), 7.66−7.74 (m, 4H), 7.36- 7.46 (m, 3H), 7.10−7.18 (m, 4H), 6.93−7.00 (m, 2H), 6.76−6.78 (d, *J* = 8.00 Hz, 1H), 6.56−6.58 (d, *J* = 8.40 Hz, 1H), 5.98 (m, 2H), 5.16−5.42 (m, 4H), 4.77−4.82 (m, 1H), 2.83 (s, 2H), 2.54−2.56 (d, *J* = 11.60 Hz, 1H), 2.20 (s, 2H), 2.08−2.11 (m, 1H), 1.85−1.91 (m, 2H), 1.28 (s, 18H), 0.83 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.0, 170.0, 153.3, 153.1, 147.2, 147.1, 146.6, 146.4, 141.6, 134.9, 134.2, 134.1, 134.0, 133.6, 133.4, 133.0, 132.5, 129.7, 129.0, 128.4, 128.3, 128.0, 127.4, 124.9, 124.7, 124.2, 123.9, 123.8, 123.7, 123.3, 113.0, 112.7, 111. 8, 110.0, 73.5, 73.3, 63.0, 60.7, 35.2, 34.3, 33.8, 31.0, 25.6, 24.9.

Synthesis of {Pd[(1*R*,2*R*)-(1h)]Br_2} (2h). A mixture of H_2[(1*R*,2*R*)-(**1h**)]Br_2 (238.8 mg, 0.2 mmol) and 98% $Pd(OAc)_2$ (44.8 mg, 0.2 mmol) in DMSO (3.0 mL) was stirred at 50 °C for 2 h and then at 110 °C for 3 h. After the solvent was removed by reduced pressure with heating, the residue was purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford the pure palladium complex **2h** as a white solid. Yield: 187 mg (72%). HRMS (positive ions): *m*/*z* 1219.4545 (calcd for [M − Br^-]$^+$ 1219.4479). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.85 (s, 3H), 7.40−7.65 (m, 8H), 7.10−7.28 (m, 8H), 7.00 (s, 3H), 6.79 (s, 2H), 6.47 (d, *J* = 8.24 Hz, 1H), 6.28 (s, 1H), 5.13 (s, 2H), 4.52 (s, 1H), 2.86 (s, 1H), 2.64 (m, 1H), 2.47 (m, 1H), 1.93−2.15 (m, 5H), 1.33−1.45 (m, 18H), 1.18 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2, 170.5, 154.0, 153.6, 146.8, 145.6, 141.5, 134.9, 134.6, 133.9, 133.7, 133.5, 133.2, 133.0, 132.8, 132.4, 128.5, 128.2, 128.0, 127.8, 127.5, 127.3, 126.8, 125.9, 125.7, 124.9, 123.7, 123.5, 123.3, 123.2, 113.3, 112.9, 111.1, 109.5, 62.9, 60.9, 51.0, 47.5, 35.5, 35.4, 33.8, 31.4, 31.0, 29.7, 29.4, 25.6, 25.0, 14.1.

Synthesis of {Pd[(1*R*,2*R*)-(1i)]Br_2} (2i). Boron tribromide (0.30 mL, 3.13 mmol) was added dropwise to a stirred solution of the palladium complex {Pd[(1*R*,2*R*)-(**2a**)]Br_2} (105 mg, 0.1 mmol) in DCM (15 mL) previously cooled in an acetone/liquid nitrogen slush bath (−80 °C). The mixture was kept at this temperature for 1 h and then warmed to room temperature and stirred overnight. The mixture was cooled again in an acetone/liquid nitrogen slush bath, and methanol (30 mL) was added slowly. The solvent was then removed under vacuum to give a brown-orange solid, which was recrystallized from methanol to yield a white solid. Yield: 96 mg (95%). Anal. Calcd for $C_{50}H_{64}Br_2N_4O_2Pd$ [1019.3 g/mol]: C, 58.92; H, 6.33; N, 5.50. Found: C, 58.81; H, 6.42; N, 5.71. HRMS (positive ions): *m*/*z* 939.3427 (calcd for [M − Br^-]$^+$ 939.33), 639.2320 (calcd for [M − 2Br^- − RCH_2^+]$^+$ (RCH_2^+ = [2-HO-3,5-(*t*-Bu)$_2$(C_6H_2)CH_2^+]) 639.23). ^{1}H NMR (400 MHz, CD_3SOCD_3): δ 7.99−7.79 (m, 6H), 7.40−7.10 (m, 4H), 6.88 (m, 2H), 6.47 (m, 2H), 6.25 (m, 1H), 5.79 (m, 2H), 5.06 (s, 1H), 3.06 (s, 4H), 2.72 (s, 2H), 2.22 (s, 2H), 2.02−1.80 (m, 4H), 1.36 (s, 18H), 0.97 (s, 9H), 0.91 (s, 9H). No satisfactory ^{13}C NMR could be obtained due to the low solubility of **2i** in organic solvent.

Synthesis of {Pd[(1*R*,2*R*)-(1a)]Cl_2} (3). Ag_2O (23.2 mg, 0.1 mmol) was added to a dichloromethane solution (10 mL) of H_2[(1*R*,2*R*)-(**1a**)]Br_2 (94 mg, 0.1 mmol). The suspension became clear after it was stirred for 2 h at room temperature. $Pd(CH_3CN)_2Cl_2$ was then added, and the resultant solution was stirred for an additional 2 h. After the precipitate was filtered, the solvent was removed by reduced pressure with heating and the residue was further purified by silica gel column chromatography (eluent 1/9 EtOAc/CH_2Cl_2) to afford a brown crude product. The crude product was washed with toluene to afford the pure palladium complex **3** as a white solid. Yield: 57.5 mg (60%). Anal. Calcd for $C_{52}H_{68}Cl_2N_4O_2Pd$ [958.45 g/mol]: C, 65.16; H, 7.15; N, 5.85. Found: C, 64.99; H, 7.26; N, 5.95. HRMS (positive ions): *m*/*z* 921.4104 (calcd for [M − Cl^-]$^+$ 921.41). $[\alpha]_D^{20}$ = 21.52° (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64−7.67 (d, *J* = 11.72 Hz, 1H), 7.55 (t, *J* = 14.00 Hz, 1H), 7.30 (d, *J* = 9.20 Hz, 1H), 7.15−7.24 (m, 3H), 7.05 (t, *J* = 9.60 Hz, 1H), 6.95 (t, *J* = 9.60 Hz, 1H), 6.80 (s, 1H), 6.77 (d, *J* = 9.60 Hz, 1H), 6.69 (d, *J* = 10.04 Hz, 1H), 6.60 (s, 1H), 5.94−6.07 (m, 4H), 5.46 (s, 1H), 4.68−4.74 (t, *J* = 9.60 Hz, 1H), 3.83 (s, 3H), 3.44 (s, 3H), 2.96−2.99 (d, *J* = 11.00 Hz, 1H), 2.80 (m, 1H), 2.1−2.64 (d, *J* = 11.92 Hz, 1H), 2.15−2.26 (m, 2H), 2.03 (m, 1H), 1.84 (m, 1H), 1.59 (m, 1H), 1.37−1.39 (d, *J* =

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8.24 Hz, 18H, *t*-Bu), 0.84 (s, 9H, *t*-Bu), 0.76 (s, 9H, *t*-Bu). ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.3, 169.2 ($C^{carbene}$), 155.5, 155.2 ($C^{Ar\text{-}O}$), 146.5, 145.8, 142.0, 141.4 ($Ar^{C\text{-}t\text{-}Bu}$), 134.8, 134.0, 132.4($C^{Ar}$), 128.0 ($CH^{Ar}$), 127.0, 124.1, 123.8, 123.4, 113.0, 111.4, 109.8 (CH^{Ar}), 63.3, 62.6 (OCH_3), 61.1($CH^{cyclohexyl}$), 49.7, 47.3 (CH_2-N), 35.3, 34.2 ($C^{t\text{-}Bu}$), 31.1, 31.0 ($CH_3^{t\text{-}Bu}$), 30.2, 25.7, 25.0 ($CH_2^{cyclohexyl}$).

Synthesis of {Pd[(1*R*,2*R*)-(1a)](OAc$_2$} (4-OAc). Complex **2a** (104.8 mg, 0.1 mmol) was suspended in a mixture of CH_2Cl_2 (7.5 mL) and CH_3CN (2.5 mL). AgOAc (35 mg, 0.21 mmol) was added, and the mixture was stirred at room temperature for 3 h. The resulting suspension was filtered from the precipitated AgBr through Celite, and the solvent was removed under reduced pressure to give complex **4-OAc** as a white powder. Yield: 90.4 mg (90%). Anal. Calcd for $C_{56}H_{74}N_4O_6Pd$ [1005.63 g/mol]: C, 66.88; H, 7.42; N, 5.57. Found: C, 66.65; H, 7.31; N, 5.71. HRMS (positive ions): *m*/*z* 945.4545 (calcd for $[M - AcO^-]^+$ 945.45). $[\alpha]_D^{20}$ = 7.84° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (m, 1H), 7.66−7.68 (d, *J* = 6.88 Hz, 1H), 7.15−7.31 (m, 6H), 6.92−6.97 (m, 2H), 6.53−6.55 (m, 2H), 5.92−6.18 (m, 4H), 5.56 (m, 1H), 4.72 (m, 1H), 3.88 (s, 3H), 3.59 (s, 3H), 3.01−3.03 (d, *J* = 10.52 Hz, 1H), 2.77 (m, 2H), 2.55 (m, 1H), 2.19 (s, 2H), 1.97 (s, 2H), 1.82 (s, 6H), 1.39−1.42 (d, *J* = 12.36 Hz, 18H), 0.77 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.6, 175.3 ($C^{carbene}$), 168.0 (C^{AcO}), 154.4, 154.3 ($C^{Ar\text{-}O}$), 145.2, 144.9, 141.2, 141.0 ($Ar^{C\text{-}t\text{-}Bu}$), 133.7, 133.2, 132.8, 131.8 (C^{Ar}), 126.0, 125.4, 122.7, 122.6, 122.0, 121.3, 120.9, 111.8, 111.7, 110.8, 109.2 (CH^{Ar}), 61.8, 61.6 (OCH_3), 60.7 ($CH^{cyclohexyl}$), 48.0, 46.4 (CH_2-N), 34.5, 33.3 ($C^{t\text{-}Bu}$), 31.2 ($CH_3^{t\text{-}Bu}$), 30.3, 30.2, 24.7, 24.5 ($CH_2^{cyclohexyl}$), 22.8, 22.7 (CH_3^{AcO}).

Synthesis of {Pd[(1*R*,2*R*)-(1a)](OC(O)CF$_3$} (4-OCH(O)CF$_3$). Complex **2a** (104.8 mg, 0.1 mmol) was suspended in a mixture of CH_2Cl_2 (7.5 mL) and CH_3CN (2.5 mL). $AgOC(O)CF_3$ (46 mg, 0.21 mmol) was added, and the mixture was stirred at room temperature for 3 h. The resulting suspension was filtered from the precipitated AgBr through Celite, and the solvent was removed under reduced pressure to give **4-OCH(O)CF$_3$** as a white powder. Yield: 102.3 mg (92%). Anal. Calcd for $C_{56}H_{68}F_6N_4O_6Pd$ [1113.57 g/mol]: C, 60.40; H, 6.15; N, 5.03. Found: C, 60.33; H, 6.22; N, 5.14. HRMS (positive ions): *m*/*z* 999.4289 (calcd for $[M - CF_3COO^-]^+$ 999.42). $[\alpha]_D^{20}$ = 11.68° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81−7.84 (t, *J* = 11.00 Hz, 1H), 7.71−7.73 (d, *J* = 8.28 Hz, 1H), 7.36 (d, *J* = 8.28 Hz, 1H), 7.17−7.25 (m, 5H), 7.05 (t, *J* = 8.80 Hz, 1H), 6.98 (t, *J* = 9.60 Hz, 1H), 6.65 (d, *J* = 11.80 Hz, 1H), 6.51−6.53 (d, *J* = 11.80 Hz, 1H), 6.27−6.31 (d, *J* = 16.04 Hz, 1H), 6.03−6.10 (m, 2H), 5.79 (s, 1H), 5.47−5.51 (d, *J* = 16.00 Hz, 1H), 4.77−4.78 (m, 1H), 3.89 (s, 3H), 3.51 (s, 3H), 3.05−3.07 (d, *J* = 9.16 Hz, 1H), 2.82−2.85 (m, 1H), 2.62 (m, 2H), 2.16−2.24 (m, 3H), 1.77−1.84 (m, 1H), 1.38−1.42 (d, *J* = 17.88 Hz, 18H), 0.75−0.77 (d, *J* = 6.84 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6 ($C^{carbene}$), 162.1 (C^{CF_3COO}), 154.3, 154.1 ($C^{Ar\text{-}O}$), 145.2, 144.8, 141.4, 140.9($Ar^{C\text{-}t\text{-}Bu}$), 133.5, 132.9, 132.5, 131.0 (C^{Ar}), 126.2, 125.4, 123.2, 123.0, 122.5, 120.8, 120.1, 111.9, 110.8, 109.2 (CH^{Ar} + $CF_3^{CF_3COO}$), 62.2, 61.5 (OCH_3), 61.0, 60.4 ($CH^{cyclohexyl}$), 48.1, 46.5 (CH_2-N), 34.3, 33.0 ($C^{t\text{-}Bu}$), 31.8 ($CH_3^{t\text{-}Bu}$), 30.1, 29.9, 24.6, 24.1 ($CH_2^{cyclohexyl}$).

Synthesis of {Pd[(1*R*,2*R*)-(1a)] (OH$_2$)$_2$}[OTf]$_2$ (5-OTf). Complex **2a** (104.8 mg, 0.1 mmol) was suspended in a mixture of CH_2Cl_2 (7.5 mL) and CH_3CN (2.5 mL). AgOTf (54 mg, 0.21 mmol) was added, and the mixture was stirred at room temperature for 3 h. The resulting suspension was filtered from the precipitated AgBr through Celite, and the solvent was removed under reduced pressure to give complex **5-OTf** as a white powder. Yield: 111.6 mg (94%). Anal. Calcd for $C_{54}H_{72}F_6N_4O_{10}PdS_2$ [1221.71 g/mol]: C, 53.09; H, 5.94; N, 4.59. Found: C, 53.07; H, 6.00; N, 4.65. HRMS (positive ions): *m*/*z* 1035.3945 (calcd for $[M - 2H_2O - CF_3SO_3^-]^+$ 1035.39), 653.2498 (calcd for $[M - 2H_2O - 2CF_3SO_3^- - RCH_2^+]^+$ (RCH_2^+ = [2-PhCH$_2$O-3,5-(*t*-Bu)$_2$(C_6H_2)CH_2^+]) 653.25). $[\alpha]_D^{20}$ = −7.00° (*c* = 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77−7.79 (d, *J* = 8.28 Hz, 1H), 7.50 (m, 1H), 7.42−7.44 (d, *J* = 8.72 Hz, 1H), 7.25 (m, 5H), 7.05 (m, 2H), 6.70 (m, 2H), 6.82 (s, 1H), 6.11−6.20 (m, 2H), 5.90 (d, *J* = 16.04 Hz, 1H), 5.65 (d, *J* = 18.80 Hz, 1H), 4.80−4.82 (d, *J* = 9.16 Hz, 1H), 3.79 (s, 3H), 3.55 (s, 3H), 3.09−3.41 (m, 4H), 2.83 (m, 1H), 2.65−2.69 (d, *J* = 15.60 Hz, 1H), 2.42 (m, 1H), 2.25 (br, <4H, H_2O-Pd), 1.80 (m, 1H), 1.39−1.41 (d, *J* = 7.80 Hz, 18H), 0.78−0.81 (d, *J* = 11.44 Hz, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3 ($C^{carbene}$), 155.5, 155.4 ($C^{Ar\text{-}OMe}$), 146.5, 142.8 ($C^{Ar\text{-}t\text{-}Bu}$), 134.8, 134.2, 133.7, 132.6, 125.0, 125.8, 124.9, 124.5, 124.4, 124.3, 121.9, 119.8, 117.0, 113.3, 112.9, 112.8 (CH^{Ar} + $CF_3^{CF_3SO_3}$), 65.0, 63.2 (OCH_3), 62.7, 62.6, 61.3($CH^{cyclohexyl}$), 49.4, 47.7 (CH_2-N), 35.5, 34.8 ($C^{t\text{-}Bu}$), 31.1, 31.0 ($CH_3^{t\text{-}Bu}$), 30.9, 24.9, 24.6 ($CH_2^{cyclohexyl}$).

Synthesis of {Pd[(1*R*,2*R*)-(1a)] (OH$_2$)$_2$}[SbF$_6$]$_2$ (5-SbF$_6$). Complex **2a** (104.8 mg, 0.1 mmol) was suspended in a mixture of CH_2Cl_2 (7.5 mL) and CH_3CN (2.5 mL). $AgSb_6$ (54 mg, 0.21 mmol) was added, and the mixture was stirred at room temperature for 3 h. The resulting suspension was filtered from the precipitated AgBr through Celite, and the solvent was removed under reduced pressure to give complex **5-SbF$_6$** as a white powder. Yield: 132.4 mg (95%). Anal. Calcd for $C_{52}H_{72}F_{12}N_4O_4PdSb_2$ [1395.07 g/mol]: C, 44.77; H, 5.20; N, 4.02. Found: C, 44.89; H, 5.22; N, 4.11. HRMS (positive ions): *m*/*z* 1123.3351 (calcd for $[M - 2H_2O - SbF_6^-]^+$ 1123.33), 653.2498 (calcd for $[M - 2H_2O - 2SbF_6^- - RCH_2^+]^+$ (RCH_2^+ = [2-PhCH$_2$O-3,5-(*t*-Bu)$_2$(C_6H_2)CH_2^+]) 653.25). $[\alpha]_D^{20}$ = −16.65° (*c* 0.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94−7.96 (d, *J* = 6.44 Hz, 1H), 7.60 (s, 1H), 7.25 (m, 7H), 7.05 (m, 1H), 6.80−6.82 (m, 2H), 6.20−6.24 (d, *J* = 16.04 Hz, 1H), 5.86−5.90 (m, 3H), 5.73−5.77 (d, *J* = 15.12 Hz, 1H), 5.02 (s, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 3.45−3.47 (d, *J* = 6.88 Hz, 1H), 2.94 (s, 1H), 2.64 (s, 1H), 1.96−2.19 (m, 9H, CH_2 of cyclohexyl + H_2O-Pd), 1.42 (s, 18H), 0.84 (s, 9H), 0.74 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5 ($C^{carbene}$), 155.5, 153.7 ($C^{Ar\text{-}O}$), 146.4, 143.1, 142.9 ($Ar^{C\text{-}t\text{-}Bu}$), 134.0, 133.5, 133.0, 132.4 (C^{Ar}), 126.8. 126.0, 125.6, 124.9, 124.6, 124.5, 121.1, 113.0, 112.9, 112.0 (CH^{Ar}), 66.0, 63.4 (OCH_3), 62.6, 60.9 ($CH^{cyclohexyl}$), 49.3, 47.9 (CH_2-N), 35.5, 34.2, 34.1($C^{t\text{-}Bu}$), 31.1($CH_3^{t\text{-}Bu}$), 30.9, 22.8, 22.0 ($CH_2^{cyclohexyl}$).

General Procedure for Asymmetric Suzuki−Miyaura Coupling Reactions. The desired aryl bromides (0.2 mmol), the corresponding palladium complex (0.006 mmol), the corresponding boronic acid (0.3 mmol), and base (0.50 mmol) were introduced into an oven-dried Schlenk tube (25 mL). Deoxygenated solvent (2 mL) was added, the flask was sealed, and the mixture was stirred and heated at the indicated temperature. After the reaction mixture was heated to reflux (when THF was used as a reaction solvent) or maintained at 70 °C for 24 h, it was treated with distilled water (10 mL), extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), and purified by flash chromatography (1/50 EtOAc/hexane) to give the corresponding product.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, tables, and CIF files giving X-ray crystal data, experimental syntheses of the chiral bis-NHC precursors H_2[(1*R*,2*R*)-(**1a−i**)]Br_2, ^{1}H and ^{13}C NMR spectra and complete HRMS spectra of NHC palladium compounds, and typical chiral HPLC spectra of biaryl products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Kozlowski, M. C.; Morgan, B. J.; Linton, E. C. *Chem. Soc. Rev.* **2009**, *38*, 3193−3207. (b) Bringmann, G.; Mortimer, A. J. P.; Keller,

P. A.; Gresser, M. J.; Garner, J.; Breuning, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5384−5427. (c) Baudoin, O. *Eur. J. Org. Chem.* **2005**, 4223−4229.
(2) (a) Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723−1724. (b) Wang, S.; Li, J.; Miao, T.; Wu, W.; Li, Q.; Zhuang, Y.; Zhou, Z.; Qiu, L. *Org. Lett.* **2012**, *14*, 1966−1969. (c) Wu, W.; Wang, S.; Zhou, Y.; He, Y.; Zhuang, Y.; Li, L.; Wan, P.; Wang, L.; Zhou, Z.; Qiu, L. *Adv. Synth. Catal.* **2012**, *354*, 2395−2402. (d) Jensen, J. F.; Johannsen, M. *Org. Lett.* **2003**, *5*, 3025−5028. (e) Herrbach, A.; Marinetti, A.; Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2003**, *68*, 4897−4905. (f) Bronger, R. P. J.; Guiry, P. J. *Tetrahedron: Asymmetry* **2007**, *18*, 1094−1102. (g) Uozumi, Y.; Matsuura, Y.; Arakawa, T.; Yamada, Y. M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2708−2710. (h) Tang, W.; Patel, N.; Xu, G.; Xu, X.; Savole, J.; Ma, S.; Hao, M.-H.; Keshipeddy, S.; Capacci, A. G.; Wei, X.; Zhang, Y.; Gao, J.; Li, W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayaka, C. H. *Org. Lett.* **2012**, *14*, 2258−2261.
(3) (a) Shen, X.; Jones, G. O.; Waston, D. A.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 112781−11287. (b) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051−12052.
(4) (a) Genov, M.; Almorín, A.; Espinet, P. *Chem. Eur. J.* **2006**, *12*, 9346−9352. (b) Genov, M.; AlmorÍn, A.; Espinet, P. *Tetrahedron: Asymmetry* **2007**, *18*, 625−627. (c) Castanet, A.-S.; Colobert, F.; Broutin, P.-E.; Obringer, M. *Tetrahedron: Asymmetry* **2002**, *13*, 659−665. (d) Colobert, F.; Valdivia, V.; Choppin, S.; Leroux, F. R.; Fernández, I.; Alvarez, E.; Khiar, N. *Org. Lett.* **2009**, *22*, 5130−5133. (e) Mikami, K.; Miyamoto, T.; Hatano, M. *Chem. Commun.* **2004**, 2082−2083. (f) Sawai, K.; Tatumi, R.; Nakahodo, T.; Fujihara, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6917−6919.
(5) Bermejo, A.; Ros, A.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15798−15799.
(6) Ros, A.; Estepa, B.; Bermejo, A.; Álvarez, R.; Fernández, R.; Lassaletta, J. M. *J. Org. Chem.* **2012**, *77*, 4740−4750.
(7) (a) Zhang, S.; Wang, Z.; Xu, M.; Lin, G. *Org. Lett.* **2010**, *23*, 5546−5549. (b) He, X.; Zhang, S.; Guo, Y.; Wang, H.; Lin, G. *Organometallics* **2012**, *31*, 2945−2948.
(8) Bronger, R. P. J.; Guiry, P. J. *Tetrahedron: Asymmetry* **2007**, *18*, 1094−1102.
(9) Debono, N.; Labande, A.; Manoury, E.; Daran, J.-C.; Poli, R. *Organometallics* **2010**, *29*, 1879−1882.
(10) (a) Snead, D. R.; Inagaki, S.; Abboud, K. A.; Hong, S. *Organometallics* **2010**, *29*, 1729−1739. (b) Nolan, S. P. In *N-Heterocyclic Carbenes in Synthesis*; Nolan, S. P., Ed.; Wiley-VCH: Weinheim, Germany, 2006. (c) Glorius, F. In *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Glorius, F., Ed.; Springer-Verlag: Heidelberg, Germany, 2007. (d) Bourissou, D.; Guerret, O.; Gabbaï, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39−91. (e) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290−1309. (f) Würtz, S.; Glorius, F. *Acc. Chem. Res.* **2008**, *41*, 1523−1533. (g) Díez-Gonzalez, S.; Marion, N.; Nolan, S. P. *Chem. Rev.* **2009**, *109*, 3612−3676. (h) Normand, A. T.; Cavell, K. J. *Eur. J. Inorg. Chem.* **2008**, 2781−2800. (i) Snead, D. R.; Seo, H.; Hong, S. *Curr. Org. Chem.* **2008**, *12*, 1370−1387.
(11) (a) Wang, F.; Liu, L.; Wang, C.; Shi, M. *Coord. Chem. Rev.* **2012**, *256*, 804−853. (b) César, V.; Bellemin-Laponnaz, S.; Gade, L. H. *Chem. Soc. Rev.* **2004**, *33*, 619−636.
(12) (a) Zhang, D.; Liu, N. *Organometallics* **2009**, *28*, 499−505. (b) Zhang, D.; Kawaguchi, H. *Organometallics* **2006**, *25*, 5506−5509. (c) Shigeng, G.; Tang, J.; Zhang, D.; Wang, Q.; Chen, Z.; Weng, L. *J. Organomet. Chem.* **2012**, *700*, 223−229.
(13) (a) Gigler, P.; Bechlars, B.; Herrmann, W. A.; Kuhn, F. E. *J. Am. Chem. Soc.* **2011**, *133*, 1589−1595. (b) Bonnet, L. G.; Douthwaite, R. E.; Hodgson, R. *Organometallics* **2003**, *22*, 4384−4386.
(14) Berben, L. A.; Craig, D. C.; Gimbert-Surinach, C.; Robinson, A.; Sugiyarto, K. H.; Colbran, S. B. *Inorg. Chim. Acta* **2011**, *370*, 374−381.
(15) Herrmann, W. A.; Reisinger, C.-P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93−96.
(16) Wang, H. M. J; Lin, I. J. B. *Organometallics* **1998**, *17*, 972−975.
(17) (a) Wang, W.; Zhang, T.; Shi, M. *Organometallics* **2009**, *28*, 2640−2642. (b) Liu, Z.; Shi, M. *Organometallics* **2010**, *29*, 2831−2834.
(18) Scherg, T.; Schneider, S. K.; Frey, G. D.; Schwarz, J.; Herdtweck, E.; Herrmann, W. A. *Synlett* **2006**, 2894−2897.
(19) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2371−2374.
(20) Schwarz, J.; Böhm, V. P. W.; Gardiner, M. G.; Grosche, M.; Herrmann, W. A.; Hieringer, W.; Raudaschl-Sieber, G. *Chem. Eur. J.* **2000**, *6*, 1773−1780.
(21) (a) Li, K.; Guan, X.; Ma, C.-W.; Lu, W.; Chen, Y.; Che, C.-M. *Chem. Commun.* **2011**, *47*, 9075−9077. (b) Meyer, A.; Unger, Y.; Poethig, A.; Strassner, T. *Organometallics* **2011**, *30*, 2980−2985. (c) Yagyu, T.; Yano, K.; Kimata, T.; Jitsukawa, K. *Organometallics* **2009**, *28*, 2342−2344.
(22) (a) Sinnokrot, M. O.; Sherrill, C. D. *J. Phys. Chem. A* **2006**, *110*, 10656−10668. Sonoda, Y.; Tsuzuki, S.; Goto, M.; Tohnai, N.; Yoshida, M. *J. Phys. Chem. A* **2010**, *114*, 172−182. (c) Dey, S. K.; Das, G. *Cryst. Growth Des.* **2010**, *10*, 754−760. (d) Wheeler, S. E. *J. Am. Chem. Soc.* **2011**, *133*, 10262−10274. (e) Wheeler, S. E. *Acc. Chem. Res.* **2013**, *46*, 1029−1038.
(23) Zhang, D.; Zhou, S.; Li, Z.; Wang, Q.; Weng, L. *Dalton Trans.* **2013**, *42*, 12020−12030.
(24) Sheldrick, G. M. *SHELXL-97 Program for the Refinement of Crystal Structures*; Universität Göttingen, Göttingen, Germany, 1997.