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N-Heterocyclic Pyridylmethylamines: Synthesis, Complexation, Molecular Structure, and Application to Asymmetric Suzuki−Miyaura and Oxidative Coupling Reactions

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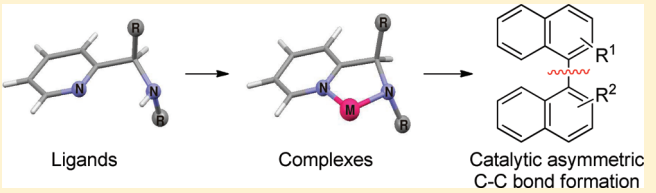
Supporting Information

ABSTRACT: The synthesis of N,N-bidentate ligands based on a π-deficient N-heterocyclic pyridylmethylamine core is described. The preparation and characterization of the corresponding N,N-ligand−palladium complexes in solution and the solid state are illustrated. Pd complexes showed a good yield and moderate catalytic activity (up to 40% ee) in the asymmetric Suzuki−Miyaura coupling reaction, leading to methoxybinaphthyl derivatives. The combination of *N,N*-pyridylmethylamines with cuprous iodide revealed effective catalytic systems in oxidative naphthol derivative coupling reactions, affording the corresponding binaphthyls in high yields and with enantioselectivities of up to 61%.



INTRODUCTION

Pyridines bearing one methylamine pendant arm constitute an appealing subclass of vicinal diamines that serve as efficient pentadentate ligands. Especially valuable is the (2-pyridyl) methylamine motif, which forms an ideal 1,2-N,N-bidentate ligand. The association of several of such frameworks can be found in bioinspired tetra- or pentadentate ligands that enable the stabilization of metastable metallic species[1] or mimic P-450 in vivo oxidations.[2] Tripodal ligands related to tris(pyridylmethyl)amine (TPA), tris(pyridyl)methylamine (tpm), or bis(pyridylmethyl) pyridine-2-carboxamide have recently received a great deal of attention. Indeed, Cu, Re, Fe, and Zn complexes have been obtained, characterized, and studied.[3] Moreover, the (2-pyridyl)-methylamine scaffold associated with a camphor substituent has been recently used in efficient Cu-promoted Henry reactions.[4]

Despite increasing reports of both stoichiometric and catalytic issues related to such ligands, there is a steady demand for original, easily accessible, and flexible 1,2-N,N-bidentate ligands capable of generating a large number of selective chemical transformations. According to this general statement, we recently reported the synthesis of new simple *N,N*-pyridylpiperidines and *N,N*-pyridylalkylamines.[5−8] Associated with Pd[5] or Yb,[6] such ligands were shown to be efficient in the preparation of various biphenyls and 3-substituted indoles through Suzuki−Miyaura couplings and Friedel−Crafts alkylations, respectively (Figure 1).

In the present paper, we describe the synthesis and characterization of the six new enantiopure N,N-bidentate ligands **L10**−**L14** based on our previous *N,N*-pyridylalkylamine design (Figures 2 and 3) and their palladium complexes. Various aspects of the preparation and properties of racemic N,N-bidentate ligands (**L1**−**L9**) and their metal complexes, previously synthesized by us (Figure 3),[5−8] are also included in the paper for comparison and summarization. We have studied the coordination chemistry of all these ligands in solution and the molecular structures in the solid state for **C4**−**C6**, **C8**, **C9**, and **C14**. In addition, we describe the use of both ligands and complexes in the stereoselective preparation of binaphthyl derivatives through asymmetric Cu-promoted oxidative naphthol coupling and Pd-assisted Suzuki−Miyaura coupling reactions, respectively (Figure 2).

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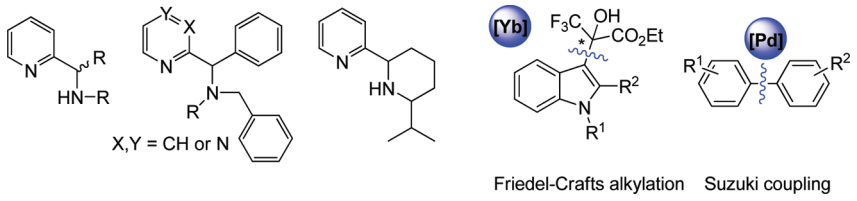

Figure 1. N,N-bidentate pyridylamine and pyridylpiperidine ligands.

RESULTS AND DISCUSSION

Synthesis of Ligands. We first focused on the preparation of a large panel of ligands. As illustrated in Figure 3, the multiple modulation sites of the pyridylmethylamine central core are one of the clear advantages of this ligand family. Indeed, substitutions at the pyridine heterocycle, of the pendant methylene arm, and of the second nitrogen atom account for the strong steric and electronic modulations that may arise from the installation of various additional groups at the ligand skeleton in order to finely tune the ligand characteristics. As shown below, positions α to the pendant arm nitrogen atom were assigned to as 1 and 1′.

Most N-heterocyclic pyridylmethylamine ligands presented in Figure 3 were easily obtained from common reactants in one or two steps. Several strategies have been developed to obtain ligands **L1**−**L14** depending on the commercial availability of the reactants and their intrinsic reactivity, the targeted substituent, and the substitution pattern as well as the stereochemical outcome in the preparation of nonracemic ligands.

As detailed in Schemes 1−4, ligands **L1**−**L9** have been previously reported. This section intends to gather all preparation methods. Thus, ligands **L2**−**L4** were synthesized in two steps according to previous studies (Scheme 1).[5a,7] This strategy allowed easy access to pyrimidine and pyrazine analogues. Ligand **L5**, comprising a trialkylated nitrogen atom in the pendant arm, was obtained through additional alkylation of **L2**.

Moving from a phenyl ring at the pendant arm to a larger substituent was also examined. In this context, installation of a large carboranyl cluster in ligand **L6** required the modification of the preparation sequence. Indeed, the joint presence of an aminomethyl-*o*-carborane cluster and a pyridine heterocycle was not trivial, and **L6** was efficiently prepared by a two-step procedure involving mesylation of the corresponding carboranyl alcohol prior to nucleophilic amination, as shown in Scheme 2.[8]

We next focused on ligands that display any substitution at the pseudobenzylic position of the pendant arm. Ligands **L1** and enantiopure **L7** were thus prepared in one step by reductive amination of pyridine-2-carboxaldehyde with the corresponding amines in quantitative yields (Scheme 3).[6,5]

Pyridine-based ligands **L8**−**L14** are more complex structures than the former **L1**−**L7**, as they simultaneously bear various substituents at the pseudobenzylic position (Me, Ph, ferrocenyl) and at the second nitrogen atom. Since all these ligands have been obtained through formal addition of a nucleophile to an aldimine or ketimine, several strategies were developed in order to obtain nonracemic ligands and evaluate the influence of stereogenic centers on asymmetric catalytic transformations (vide infra).

Ligands **L9**[6] and **L13** were obtained in 90 and 92% overall yields, respectively, by reduction of the corresponding ketimines with sodium borohydride (Scheme 4). The addition of methylmagnesium bromide or phenyllithium to the corresponding

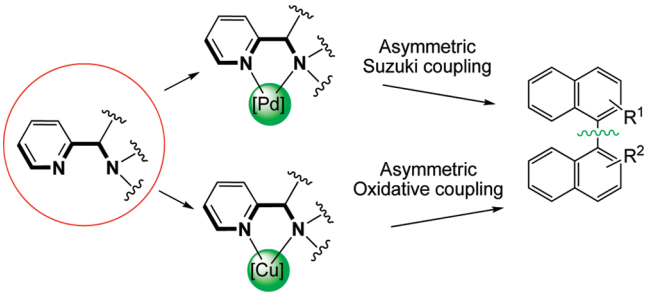

Figure 2. Asymmetric C−C bond formation using N-heterocyclic pyridylmethylamine-based Cu and Pd complexes.

intermediate aldimines afforded the ligands **L8**,[6] **L11**,[6] and **L12** with yields ranging from 49 to 74%. This reaction has proved to be highly diastereoselective in the case of **L14**, thus leading to (1*S*,1′*S*)-**L14** as the almost unique diastereomer (dr = 98/2). Furthermore, to synthesize both the next diastereomer of **L14** and ligand **L10**, we have used an in situ quenching (ISQ) procedure,[9] which involved the addition of *n*-BuLi to a mixture of the corresponding imine and aryl bromide. The generated aryllithium derivative is further directly trapped by the imine in the reaction medium. This method led to (1*R*,1′*S*)-**L14** in 65% yield (dr = 92/8), whereas ligand **L10** was obtained in 33% yield.

All these methodologies allowed us to prepare a variously substituted N,N-bidentate ligand family based on a pyridylalkylamine core. Diastereomeric ligands **L12** and **L13** are inseparable, and in the case of ligand **L10** only one diastereomer could be isolated. Fortunately, diastereomeric ligands **L8**, **L9**, and **L11** could be separated and isolated by column chromatography on silica gel. The absolute configuration of each diastereomer of **L8** was determined by comparison of their optical activity and NMR spectra with literature data.[10] In addition, the 1*S*,1′*R* absolute configuration of the second eluted diastereomer of **L8** was confirmed by X-ray diffraction analysis of the corresponding Pd(II) complex (vide infra). Configuration of the newly formed tertiary carbon center in **L11** was assigned according to **L8** analytical data. The X-ray diffraction analysis of the corresponding Pd(II) complexes allowed us to unambiguously establish the absolute configuration of the 1*R*,1′*R* and 1*S*,1′*R* diastereomers of **L9**. Finally, the 1*R*,1′*S* absolute configuration of **L14** was again determined by X-ray diffraction analysis of the corresponding Pd(II) complex.

Complexation. In order to illustrate the potential of this family of ligands in coordination chemistry, we next turned our attention to the synthesis of palladium complexes. Analysis both in solution and in the solid state may allow us not only to confirm privileged conformations and configurations of ligands and complexes but also to gain additional structural information in the catalysis context of this paper. Thus, ligands **L1**−**L14** were treated with Na_2PdCl_4 in freshly distilled methanol at room temperature according to standard conditions[11] to give the

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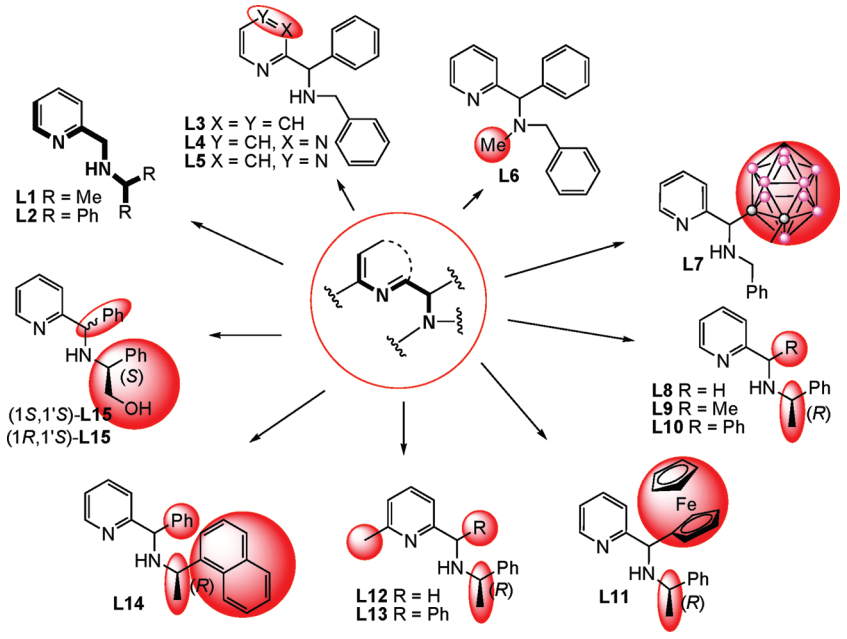
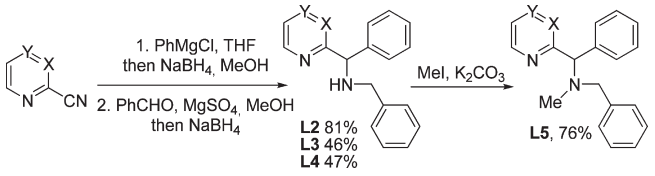
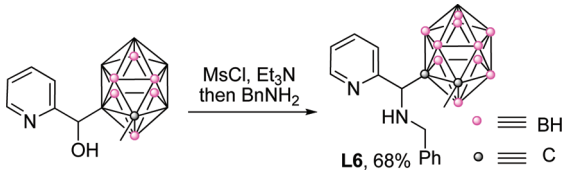


Figure 3. N-Heterocyclic pyridylmethylamine ligands **L1**−**L14**.

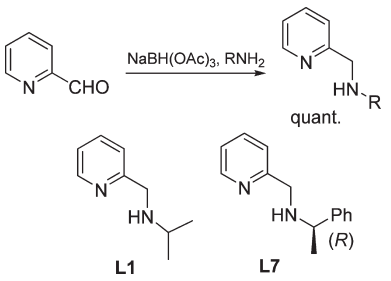
Scheme 1. Hetero-Biarylmethylamine Ligands L2−L5[5a,7]



Scheme 2. 2-Aminomethylpyridine−Carborane Ligand L6[8]

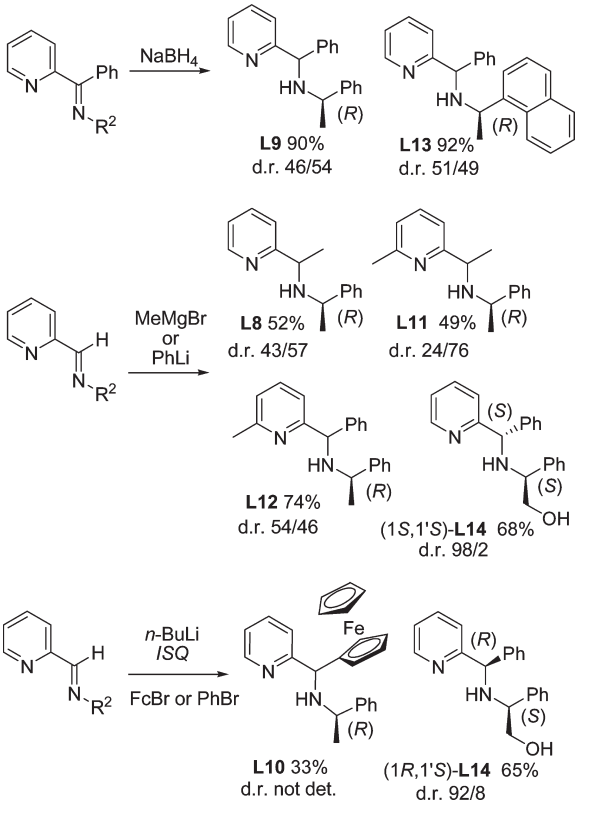


Scheme 3. Preparation of Pyridylamine Ligands L1 and L7[5c,6]



expected Pd(II) complexes in yields ranging from 71% to quantitative yields (Scheme 5). As shown in Scheme 5, complexes **C2**−**C6** have been previously reported.

Scheme 4. Preparation of Pyridylamine Ligands L8−L14[6]



It is noteworthy that the substituents installed at the pyridylmethylamine core did not affect the complexation yields. In all cases, the desired complexes were easily purified by simple filtration through a silica gel pad and were perfectly air-stable, both in the solid state and in solution. The complexation has resulted in the creation of a chiral center on the pendant arm

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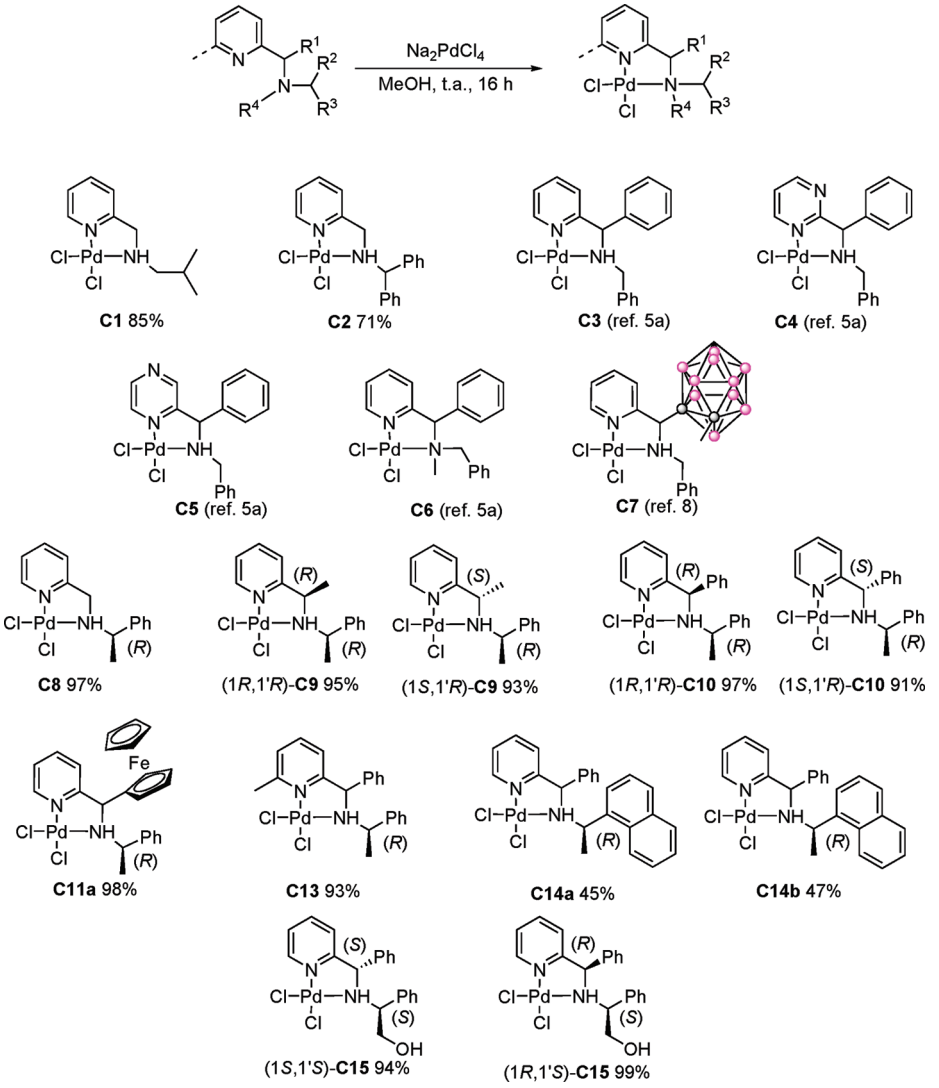
Scheme 5. Preparation of Palladium Complexes



nitrogen atom that could adopt *R* and *S* configurations (see the Supporting Information for an illustration). Depending on the nature of the R^1 substituent on the ligand, the complexation reaction may occur selectively or not. When there is no chiral center at the pseudo-benzylic position (R^1 = H), there is no control of the chirality on the nitrogen atom and consequently the complexation reaction occurs in a nonselective way. Indeed, in the case of achiral ligand **L1** the complexation process afforded a racemic mixture of two palladium complex enantiomers **C1**. For chiral ligand **L7**, two enantiopure diastereomers **C7** were obtained after complexation, evidenced by the presence of two sets of signals (dr = 50/50) in the ^{1}H NMR spectra.

On the other hand, the presence of a stereocenter at a pseudobenzylic position ($R^1 \neq$ H) seems to control the central chirality on the nitrogen atom. The complexation reaction then occurred in a diastereoselective way. Thus, complexes **C2**−**C6**, prepared from racemic ligands **L2**−**L6**, were obtained as single *rac* diastereomers, since only one set of signals was found in the ^{1}H NMR spectra. Furthermore, the complexation reaction involving the enantiopure ligands (1*R*,1′*R*)-**L8**, (1*S*,1′*R*)-**L8** (see the Supporting Information), (1*R*,1′*R*)-**L9**, (1*S*,1′*R*)-**L9**, **L10a**, (1*S*,1′*S*)-**L14**, and (1*R*,1′*S*)-**L14** apparently afforded only one enantiopure diastereomer complex in each case. Interestingly, diatereomeric ligands **L12** and **L13** were inseparable and the reaction with Na_2PdCl_4 led to the corresponding complexes **C12** and **C13** as a mixture of two enantiopure diastereomers. Fortunately, diatereomeric complexes **C13** could be separated by column chromatography on silica gel; the **C13a** and **C13b** notations are relative to the first and second eluted diastereomers. All complexes have been fully characterized by NMR spectroscopy, the spectroscopic data being in agreement with their respective structures.

Coordination of both nitrogen atoms of the ligand has been confirmed by a characteristic positive shielding observed between the aforementioned probe protons of ligands **L** and those of their corresponding complexes **C**, regardless of the heterocycle core and the presence of additional substituents on the methylamine fragment.

Molecular Structures. As mentioned above, there are three sources of chirality in complexes **C2**−**C6** that could lead, in principle,

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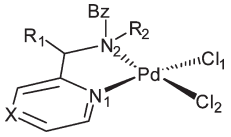
Table 1. Selected Bond Distances (Å), Bond Angles (deg), and Torsion Angles (deg) for Complexes C2 and C4−C6[a]



			bond distance				bond angle	
compd	R_1	R_2	N_1−Pd	N_2−Pd	Cl_1−Pd	Cl_2−Pd	N_1PdN_2	$N_1CC(R_1)N_2$[b]
C2	Ph	H	2.021(2)	2.031(2)	2.2819(6)	2.303(6)	81.49(8)	±23.1(2)
C4[c]	Ph	H	2.024(7)	2.043(7)	2.281(2)	2.289(2)	82.0(3)	±34.9(9)
			2.027(5)	2.022(8)	2.278(2)	2.294(3)	82.3(3)	±27.9(9)
C5	Ph	Me	2.020(2)	2.083(2)	2.2931(7)	2.301(7)	82.12(8)	±29.4(3)
C6	Carb.	H	2.030(2)	2.049(3)	2.2887(8)	2.288(8)	81.1(1)	±37.0(3)

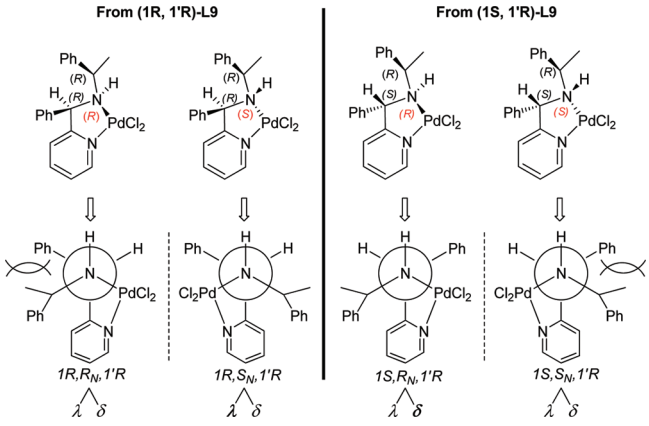
[a] See structure given above the table for nomenclature. [b] Positive (+) and negative (−) torsion angles correspond to the λ and δ isomers, respectively. [c] There are two independent molecules in the asymmetric unit.

to eight different diateroisomers. The pseudo-benzylic carbon and coordinated amine nitrogen atom are chiral centers that can adopt *R* and *S* configurations, giving rise to four possible diastereomeric pairs (R_CR_N, R_CS_N, S_CR_N, and S_CS_N; Supporting Information). Formation of enantiomeric pairs of the same configuration (R_CR_N and S_CS_N) are disfavored due to the steric hindrance of the substituents at both the pseudo-benzylic carbon and the benzyl substituent at nitrogen (Supporting Information). The other source of chirality is the nonplanar chelating ring that adopts two conformations: δ and λ (Supporting Information). In fact, crystal structures for complexes **C2** and **C4**−**C6** contain racemic mixtures of $R_CS_N\lambda$ and $S_CR_N\delta$ diastereoisomers, exclusively. Although these structures have been reported separately over several papers,[5a,7,8] no discussion on the configuration of the chiral centers was given, nor was a comparison between them provided. Thus, we will compare and discuss all structures in this paper. The molecular structures for the latter complexes are included in the Supporting Information, and selected bond lengths and angles are given in Table 1.

As previously reported,[5a] the chelating ligands in complexes **C2** and **C4**−**C6** bind to the Pd through a pyridyl donor N1 and a secondary amine donor N2, giving a puckered five-membered ring. The coordination sphere at Pd is close to square planar, and the Pd−N(pyridine) bond distances are significantly shorter than the Pd−N(secondary amine) distances. The torsion angles $N_1CC(R_1)N_2$ (Table 1) clearly show the coexistence of both the λ and δ isomers for these complexes. Interestingly, the fact that only the racemic mixtures of $R_CR_N\lambda$ and $S_CS_N\delta$ diastereoisomers are found in the solid state suggests that these are the most stable diastereomers in complexes **C2** and **C4**−**C6**.

In complexes **C8**−**C10** and **C12**−**C14** there are 4 sources of chirality that could lead, in principle, to 16 different diastereoisomers. These complexes contain two chiral carbons, the coordinated amine nitrogen atom, and the two possible conformations (δ and λ). However, since both carbon stereocenters have been fixed in ligands **L8**, **L9**, and **L14**, the number of diastereoisomers are greatly reduced in their metal complexes **C8**, **C9**, and **C14**. Let us consider as an example complex **C9** (Scheme 6), for which X-ray structures for two pure diastereoisomers have been determined (vide infra). Complexation of (1*R*,1′*R*)-**L9** to Pd could afford, in principle, four enantiomers ($R_CR_NR_N\delta$, $R_CR_NR_C\lambda$, $R_CS_NR_C\delta$, and $R_CS_NR_C\lambda$). An examination of Scheme 6 clearly shows that the same configuration at the benzylic and contiguous nitrogen is not favored due to the aforementioned steric interactions. Therefore, only configurations $R_CS_NR_C\delta$ and $R_CS_NR_C\lambda$ are expected to be stable. From a similar reasoning for complexation of (1*S*,1′*R*)-**L9** to Pd, we could expect the formation of the most stable $S_CR_NR_C\delta$ and $S_CR_NR_C\lambda$ diastereoisomers. Very interestingly, crystal structures for complexes **C9**, derived from (1*R*,1′*R*)-**L9** or (1*S*,1′*R*)-**L9**, contains exclusively the pure $R_CS_NR_C\lambda$ and $S_CR_NR_C\delta$ diastereoisomers, respectively (vide infra).

Scheme 6. Possible Configurations for Complex C9



The molecular structures of complexes (1*S*,1′*R*)-**C8**, (1*R*,1′*R*)-**C9**, and (1*S*,1′*R*)-**C14** have been now determined by X-ray diffraction studies (Figure 4). Crystal data and details of the structure determination for the new compounds are given in the Supporting Information, and selected bond lengths and angles for all related complexes are given in Table 2. For comparison, the crystal structure for (1*S*,1′*R*)-**C9**, previously reported by us,[6] is also included in Figure 4, Table 2, and the discussion below.

Complexes (1*S*,1′*R*)-**C8**, (1*R*,1′*R*)-**C9**, and (1*S*,1′*R*)-**C14** all crystallized in the noncentrosymmetric $P2_12_12_1$ space group and are diastereomerically pure, as shown by the nearly zero Flack parameter (Supporting Information). The previously reported (1*S*,1′*R*)-**C9**[6] crystallized in the noncentrosymmetric $P6_1$ space group and showed a Flack parameter of 0.08(4). As in the related complexes **C2** and **C4**−**C6**, the chelating ligands in **C8**, **C9**, and **C14** bind to the Pd through a pyridyl donor N1 and a secondary amine donor N2, giving a puckered five-membered ring.

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The coordination sphere at Pd is close to square planar, the largest deviation of Cl_1, Cl_2, N_1, and N_2 from their mean plane being 0.058 Å. As in the previous complexes, the Pd−N(pyridine) bond distances are significantly shorter than the Pd−N(secondary amine) distances. The torsion angles $N_1CC(R_1)N_2$ (Table 2) clearly show that only one of the two possible λ or δ isomers is found in these complexes. Thus, the solid-state configurations for these complexes are as follows: $(S_CR_NR_C\delta)$-**C8**, $(R_CS_NR_C\lambda)$-**C9**, $(S_CR_NR_C\delta)$-**C9**, and $(R_CR_NS_C\lambda)$-**C14**.

Another interesting feature of the molecular structures for these complexes is that all, except that for **C6**, show intramolecular $\pi-\pi$ interactions between the azaheterocycle and the pendant arm substituent of the secondary amine (Figure 4, Table 3, and the Supporting Information). It is noteworthy that whereas most of the complexes show centroid-to-centroid distances between 3.8 and 4.0 Å and interplanar angles of 28−34°, those for $(R_CS_NR_C\lambda)$-**C9** are 3.6 Å and 21.0°, respectively. Although solid state−liquid state conformations may differ, the presence of intramolecular $\pi-\pi$ interactions in most of the solid-state structures suggests that this is an energetically favored conformation and thus it could be also present in solution.

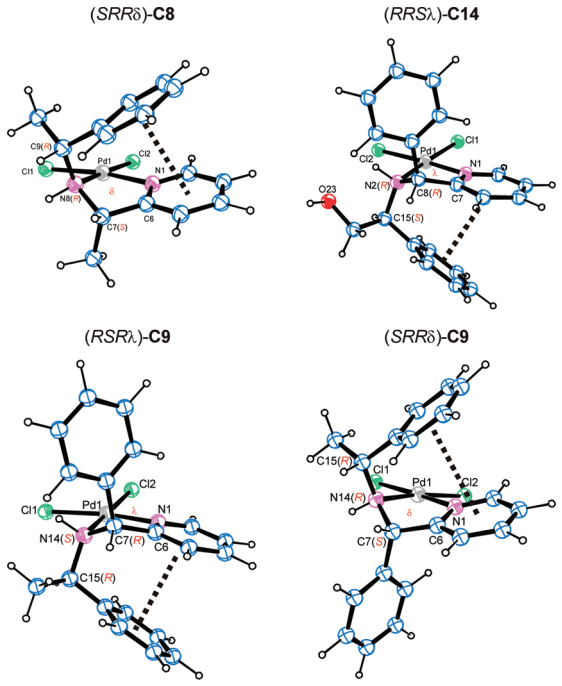
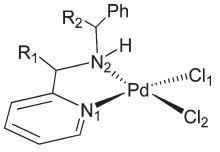


Figure 4. Molecular structures of **C8**, **C9**, and **C14** showing the intramolecular $\pi-\pi$ interactions, with thermal ellipsoids set at the 50% probability level. No other isomers are present in the crystals (see text).

Catalytic Studies. *Asymmetric Suzuki−Miyaura Coupling.* Transition-metal-catalyzed bond formation has become a powerful chemical tool over the last decades. Among these catalyzed transformations, the Suzuki−Miyaura reaction can be considered as one of the most popular and general ways to create carbon−carbon bonds and thus has found widespread applications in organic synthesis.[12] We previously reported the efficient combination of **L1** or racemic ligands **L2**−**L6** and Na_2PdCl_4 for Suzuki−Miyaura couplings, allowing us to prepare biaryl products in good yields.[5a,4b,8] Although axially chiral biaryls are present in numerous natural products and constitute an important class of ligands for asymmetric catalysis, there are few reports to date dealing with asymmetric biaryl syntheses involving Suzuki−Miyaura cross-coupling reactions. Most of the examples leading to axially chiral biaryl compounds,[13] with enantiomeric excesses from moderate to high, concern the use of chiral palladium−phosphine complexes as catalysts.[14,15] Recent noteworthy examples have been reported separately by Fujihara[16] and Uozumi,[17] who showed that palladium nanoparticles stabilized by a chiral phosphine and a recyclable palladium complex of a polymer-supported chiral imidazoindole phosphine ligand can effectively catalyze the asymmetric Suzuki−Miyaura reaction with excellent selectivities in some cases. The most recent studies described the use of NHCs (N-heterocyclic carbenes)[18] and ADCs (acyclic diainocarbenes)[19] as chiral ligands and also the use of unsymmetrical chiral PCN pincer palladium complexes,[20] but in all cases the enantiomeric excess remained modest (<39%). In this context, there is a steady demand for alternative, new, easy to prepare, stable, and efficient catalytic systems. The determination of a robust ligand arises from an overall compromise between several significant criteria. If the whole efficiency of the catalytic system (catalyst loading, yields, conversion, etc.) is a key parameter, rapid access to the ligand, stability of both ligand and transition-metal complex, a common starting material, and ease of purification should also be taken into account. According to these guidelines, we wish to report the first example of asymmetric Suzuki coupling catalyzed by chiral, air-stable, easy to prepare and handle palladium N-heterocyclic pyridylmethylamine complexes.

Table 2. Selected Bond Distances (Å), Bond Angles (deg), and Torsion Angles (deg) for Complexes (1*S*,1′*R*)-C8, (1*R*,1′*R*)-C9, (1*S*,1′*R*)-C9, and (1*S*,1′*R*)-C14[a]



	bond distance				bond angle		
compd	N_1-Pd	N_2-Pd	Cl_1-Pd	Cl_2-Pd	N_1PdN_2	$N_1CC(R_1)N_2$[b]	config
C8	2.025(2)	2.043(2)	2.2822(6)	2.3103(6)	81.99(7)	−32.6(2)	$S_CR_NR_C\delta$
C9	2.020(2)	2.038(1)	2.2851(5)	2.3090(5)	82.47(6)	+35.5(2)	$R_CS_NR_C\lambda$
C9	2.031(3)	2.066(2)	2.279(1)	2.3092(7)	81.86(9)	−27.6(4)	$S_CR_NR_C\delta$
C14	2.020(1)	2.043(1)	2.2986(7)	2.3031(6)	82.30(5)	+31.0(2)	$R_CR_NS_C\lambda$

[a] See the structure given above the table for nomenclature. [b] Positive (+) and negative (−) torsion angles correspond to the λ and δ isomers, respectively.

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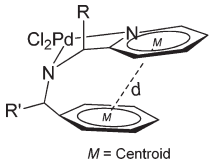
Table 3. Intramolecular Arene−Arene Packing Geometries (Distances in Å and Angles in deg), Involved in Complexes C2, C4−C6, ($S_CR_NR_C\delta$)-C8, ($R_CS_NR_C\lambda$)-C9, ($S_CR_NR_C\delta$)-C9, and ($R_CR_NS_C\lambda$)-C14[a]

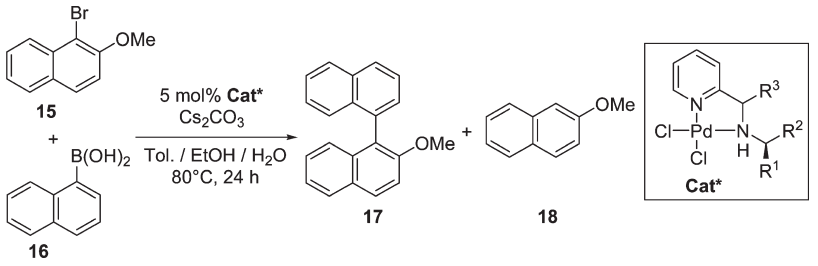


M = Centroid

	C2	C4	C5	C6	C8 (*SRRδ*)	C9 (*RSRλ*)	C9 (*SRRδ*)	C14 (*RRSλ*)
d[b]	3.956	3.714	3.797	5.900	3.762	3.614	3.811	3.795
		3.875						
interplanar angle[c]	32.25	27.71	33.91		27.97	21.08	30.17	33.59
		31.43						

[a] See structure at the top of the table for nomenclature. [b] Ring centroid to ring centroid distance. [c] Angle between planes containing the aromatic rings.

Table 4. Asymmetric Suzuki Coupling Reaction[a]



entry	R^1	R^2	R^3	cat.	conversn (%)[b]	**17**/**18**[b]	yield of **17** (%)[c]	ee of **17** (%)[d]
1	Me	Ph	Me	(1*R*,1′*R*)-**C8**	60	53/47	25	11 (*S*)
2	Me	Ph	Me	(1*S*,1′*R*)-**C8**	86	79/21	57	11 (*R*)
3	Me	Ph	Ph	(1*R*,1′*R*)-**C9**	100	77/23	75	40 (*S*)
4	Me	Ph	Ph	(1*S*,1′*R*)-**C9**	100	74/26	70	20 (*R*)
5	Me	Ph	Fc	**C10a**	76	67/33	45	33 (*S*)
6	Me	1-Np	Ph	**C13a**	100	80/20	70	35 (*S*)
7[e]	Me	1-Np	Ph	**C13b**	77	88/12	58	8 (*R*)
8[f]	CH_2OH	Ph	Ph	(1*S*,1′*S*)-**C14**	87	9/91		36 (*S*)
9[f]	CH_2OH	Ph	Ph	(1*R*,1′*S*)-**C14**	76	12/88		27 (*R*)

[a] Reactions were carried out with 5 mol % palladium complex, **15** (0.226 mmol), **16** (0.452 mmol), and Cs_2CO_3 (0.904 mmol) in 2.5 mL of solvent (toluene/EtOH/H_2O = 1/1/0.5) at 80 °C for 24 h. [b] The conversion was determined by ^{1}H NMR on the crude product. [c] Isolated yield. [d] Determined by chiral HPLC analysis (see the Supporting Information). [e] The reaction time was 48 h. [f] The pure product was not isolated.

We focused our study on chiral palladium catalysts bearing two stereocenters such as **C8**−**C10**, **C13**, and **C14.** The reaction of 1-bromo-2-methoxynaphthalene (**15**) with 1-naphthaleneboronic acid (**16**) was chosen as the model system. The experiments were performed in a toluene/ethanol/water mixture at 80 °C, using Cs_2CO_3 as base and 5 mol % of the [$PdCl_2$-pyridylmethylamine] species **C8**−**C10**, **C13**, and **C14** as catalysts, as is shown in Table 4. It should be noted that both diastereomers of **C8** provided the binaphthyl product **18** with the same level of enantioselectivity but with the opposite configuration, showing the importance of the stereocenter bearing the R^3 substituent to the enantioselectivity. Complete conversions were observed with both diastereomer complexes (1*R*,1′*R*)-**C9** and (1*S*,1′*R*)-**C9** (entries 4 and 5), the binaphthyl compound **17** being isolated in good yield. The first diastereomer (1*R*,1′*R*)-**C9** allowed us to reach a promising 40% ee in favor of the *S* enantiomer (entry 3), while the second diastereomer (1*S*,1′*R*)-**C9** provided an enantioselectivity of 20% in favor of the opposite enantiomer. These results clearly demonstrate the crucial role played by the pseudo-benzylic stereocenter and the pendant arm nitrogen atom in the enantiomer-discriminating step. Further screening involving the use of catalysts (1*S*,1′*S*)-**C14** and (1*R*,1′*S*)-**C14** bearing a tridentate ligand led to the desired product **17** with moderate selectivities of 36 and 27%, respectively, albeit in poor yields (entries 8 and 9). Although we have no clear explanation for the loss of stereoselectivity, intervention by the additional hydroxyl group during the catalytic process seems likely detrimental to the overall catalytic efficiency of **C14**.

Although the formation of side product **18** during the catalytic sequence could not be avoided, reactions conducted at 80 °C afforded the target **17** in each case as the major product. However, the presence of the protodehalogenation side product **18** appears detrimental to a high catalytic compromise in the asymmetric Suzuki coupling context. The stereochemical outcome of the catalytic process seems to be influenced by the configuration of the pseudo-benzylic center. The presence of a

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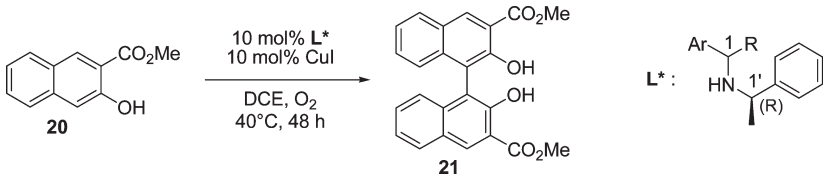
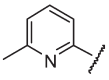
Table 5. Oxidative Biaryl Coupling



Entry	Ar	R	Ligand	Conversion (%)[a]	Yield (%)[b]	ee (%)[c]
1		H	(1'*R*)-**L7**	100	80	7
2		Me	(1*R*,1'*R*)-**L8**	100	84	42
3		Me	(1*S*,1'*R*)-**L8**	100	78	-25
4		Ph	(*1R,1'R*)-**L9**	100	95	37
5		Ph	(*1S,1'R*)-**L9**	100	99	6
6		Fc	**L10a**	51	50	61
7[d]		H	(1*R*,1'*S*)-**L14**	0	-	-
8		Me	(1*R*,1'*R*)-**L11**	83	81	19

[a] Determined by ^{1}H NMR. [b] Isolated yield. [c] Determined by chiral HPLC analysis (see the Supporting Information). [d] No conversion was observed at 40 °C after 48 h. The reaction was carried out at 70 °C for 4 days.

phenyl or naphthyl group seems crucial, as best results in both yields and ee's were obtained using the **C13** and **C9** catalytic systems. In addition, it is worth noting that complex **C9**, showing the shortest intramolecular $\pi-\pi$ stacking interaction (Table 3) with centroid-to-centroid distance (3.6 Å) and the shortest interplanar angle (21.0°), exhibited the highest ee in the asymmetric Suzuki coupling reactions tested in this work.

Oxydative Biaryl Coupling. We next turned our attention to the naphthol oxidative coupling reaction, which represents an elegant alternative to Suzuki coupling for the synthesis of symmetrical binaphthyl compounds. Moreover, the asymmetric oxidative coupling of naphthols is particularly adapted to the synthesis of chiral biaryl natural products that incorporate a binaphthyl unit such as hypocrellin, nigerone, calphostine D, cercosporin, and phleichrome as well as numerous analogues.[21] Current catalysts for asymmetric oxidative naphthol coupling are copper−amine complexes.[22] An enantioselective study was initially reported in the presence of stoichiometric copper(II) complexes of chiral amines, such as sparteine and α-methylbenzylamine.[23] Further development was made by using catalytic amounts of proline-derived diamines and copper(I), but the enantioselectivity still remained moderate.[24] Better results were obtained using 1,5-diaa-*cis*-decalin[21] and mono-N-alkylated octahydrobinaphthyl-2,2′-diaine (H_8-BINAM)[25] as chiral diaine ligands. In the context of N-heterocyclic pyridylmethylamines, we started to examine the Cu-catalyzed enantioselective oxidative coupling of 3-hydroxy-2-naphthoate ester **20** to binaphthol **21** in the presence of chiral N-heterocyclic pyridylmethylamines **L7**−**L9**, **L10a**, and **L11**. The chiral catalytic systems were prepared in situ from CuI (10 mol %) and pyridylmethylamines (10 mol %) in dichloroethane (DCE). The experiments were performed at 40 °C under an oxygen atmosphere. Reaction times were not optimized and were extended to 48 h to maximize conversions (Table 5).

Disappointingly, binaphthol **21** was obtained in good yield but with a very low ee using ligand **L7** (entry 1). The enantiopure diastereomeric ligands (1*S*,1′*R*)-**L8** and (1*R*,1′*R*)-**L8** showed improved results, affording the expected binaphthyl product in both good yields (78−84%) and ee's (25−42%). As already observed, moving from (1*S*,1′*R*)-**L8** to (1*R*,1′*R*)-**L8** generated the opposite senses of induction (entries 2 and 3), clearly confirming that the pseudo-benzylic stereogenic center plays a crucial role in the chiral information transfer. The diastereomeric ligands (*1S,1′R*)-**L9** and (*1R,1′R*)-**L9** both led to excellent or quantitative yields but were almost ineffective or only provided a moderate ee of 37% (entries 4 and 5). Using ligand **L10a**, bearing a ferrocenyl substituent, afforded fair results, providing 50% isolated yield for 51% conversion and an encouraging 61% selectivity. In contrast, no traces of binaphthol **21** could be observed using **L14**, even after a prolonged reaction course (entry 7). This might be attributed to the presence of an additional coordinating hydroxyl group detrimental to the optimal coordination mode invoked by Kozlowsky some years ago.[21] Finally, attempts to improve the selectivity by using (1*S*,1′*R*)-**L11** or (1*R*,1′*R*)-**L11**, based on a 6-methylpyridine core or phenylglycinol fragment, respectively, failed. In the case of **L11**, binaphthol **21** could be isolated in 81% yield (entry 8), but the presence of an additional methyl group at the pyridine heterocycle proved detrimental to the enantioselectivity.

CONCLUSION

In conclusion, we have described the synthesis of N,N-bidentate ligands based on a π-deficient N-heterocyclic pyridylmethylamine core. NMR analysis in solution and X-ray in the solid state revealed the favored combination of configurations due to the selective complexation process. Moreover, the presence of privileged conformations λ and δ were confirmed by

X-ray data in the solid state. Starting from two fixed configurations at both carbon atoms, the selective complexation induces the absolute configuration of the nitrogen atom and the chiral conformation (λ or δ) of the metallacycle. The use of Pd complexes in asymmetric Suzuki−Miyaura reactions afforded binaphthyls in 40 ee's. In addition, the combination of *N*,*N*-pyridylmethylamines and Cu proved efficient in the oxidative coupling reactions of binaphthols, leading to binaphthyls in high enantioselectivities (61%). Results disclosed in this paper highlight the crucial role played by the pendant arm nitrogen atom and the substituent of the pseudo-benzylic position in asymmetric C−C bond formation. In addition, they evidence the beneficial contribution of the presence of aromatic groups in the Pd complexes, in which centroid-to-centroid distances and interplanar angles are minimized.

EXPERIMENTAL SECTION

General Comments. All manipulations were carried out under an atmosphere of argon in round-bottomed flasks equipped with magnetic stirring. DCM, DCE, and toluene were distilled over CaH_2. THF and Et_2O were distilled over sodium metal, and MeOH was distilled over Mg/I_2. 2-Pyridyl-*o*-carboranylmethanol[26] and ligands **L1**,[5c] **L2**−**L5**,[5a] **L6**,[8] **L7**−**L9**[6], and **L11**[6] as well as complexes **C2**−**C5**[5a] and **C6**[8] were prepared according to our previously described procedures. The crude products were purified by column chromatography using Merck Kieselgel 60 silica gel. ^1H and ^{13}C NMR spectra were recorded on Bruker AM 300 and DPX 200 spectrometers and referenced to $CDCl_3$ or $[D_6]$DMSO, unless otherwise noted. FT-IR spectra were recorder with a Perkin-Elmer Spectrum BX spectrometer. High-resolution mass spectra were measured with a Perkin-Elmer Finnigan MAT 95 S spectrometer. Optical rotations were measured by using a Perkin-Elmer 241 polarimeter at room temperature in a 1 dm cell at the sodium D radiation (λ 589 nm) and are reported as follows: $[\alpha]_D^{rt}$ (*c* in g/100 mL, solvent). HPLC analyses were performed on a Thermo Separation Product Pump P100 instrument with a UV detector and a chiral stationary-phase column (Chiralpak OJ-H or AD).

Synthesis of *N*-[(Pyridin-2-yl)(ferrocenyl)methyl]-*N*-[(1′*R*)-1′-phenylethyl]amine (L10). A solution of ferrocenecarboxaldehyde (500 mg, 2.34 mmol) and (*R*)-1-phenylethylamine (283 mg, 2.34 mmol) in dry THF (10 mL) was stirred at room temperature over anhydrous $MgSO_4$ for 24 h. The reaction mixture was filtered through a pad of Celite and washed with DCM, and the solvents were removed under vacuum to yield the corresponding imine (100%, 743 mg).

To a stirred solution of the crude imine (250 mg, 0.79 mmol) and 2-bromopyridine (162 mg, 1.03 mmol) in dry THF (7 mL) at −78 °C was added dropwise *n*-BuLi (0.67 mL, 1.06 mmol, 1.6 M solution in hexane). The mixture was stirred for 5 min at −78 °C and then for 20 h at room temperature. The reaction was quenched by adding a saturated solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel, using petroleum ether/ethyl acetate (85/15) as eluent, to afford one of the desired diastereomers (33%, 104 mg).

The first diastereomer eluted, **L10a**, was isolated as an orange oil (104 mg). $[\alpha]_D^{20}$ = +56.2° (*c* 0.376, $CHCl_3$). ^1H NMR ($CDCl_3$, 300 MHz): δ 8.53 (ddd, *J* = 4.8, 1.7, 0.8 Hz, 1H, Ar), 7.57 (td, *J* = 7.6, 1.8 Hz, 1H, Ar), 7.33−7.15 (m, 6H), 7.09 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H, Ar), 4.28 (s, 1H, CH−N), 4.10−4.04 (m, 2H, Cp), 4.00−3.94 (m, 2H, Cp), 3.84 (s, 5H, Cp), 3.41 (q, *J* = 6.6 Hz, 1H, CH−N), 2.29 (br s, 1H, NH), 1.25 (d, *J* = 6.6 Hz, 3H, Me). ^1H NMR ($[D_6]$DMSO, 300 MHz) δ 8.52 (ddd, *J* = 4.8, 1.7, 0.8 Hz, 1H, Ar), 7.77 (td, *J* = 7.6, 1.8 Hz, 1H, Ar), 7.48 (d, *J* = 7.8 Hz, 1H, Ar), 7.39−7.20 (m, 6H, Ar), 4.25 (d, *J* = 7.5 Hz, 1H, CH−N), 4.10 (dd, *J* = 2.4, 1.2 Hz, 1H. Cp), 4.07−3.98 (m, 3H, Cp), 3.94 (s, 5H, Cp), 3.43−3.31 (m, 1H, CH−N), 2.66 (dd, *J* = 7.2, 5.7 Hz, 1H, NH), 1.26 (d, *J* = 6.6 Hz, 3H, Me). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 163.31 (C_{quat}, Ar), 149.18 (Ar), 145.50 (C_{quat}, Ar), 136.11 (Ar), 128.53 (2C, Ar), 127.03 (Ar), 126.88 (2C, Ar), 122.45 (Ar), 121.97 (Ar), 91.89 (C_{quat}, Cp), 68.51 (5C, Cp), 67.85 (Cp), 67.33 (Cp), 67.11 (Cp), 66.67 (Cp), 60.64 (CH−N), 55.77 (CH−N), 24.67 (Me). HRMS (ESI): calcd for $C_{24}H_{25}N_2Fe$ (MH^+) 397.1367, found 397.1349.

The second diastereomer was obtained as a mixture with several unidentified byproducts.

Synthesis of *N*-[(6-Methylpyridin-2-yl)(phenyl)methyl]-*N*-[(1′*R*)-1′-phenylethyl]amine (L12). A solution of 6-methylpyridine-2-carboxaldehyde (600 mg, 4.95 mmol) and (*R*)-1-phenylethylamine (600 mg, 4.95 mmol) in dry THF (25 mL) was stirred at room temperature over anhydrous $MgSO_4$ for 24 h. The reaction mixture was filtered through a pad of Celite and washed with DCM, and the solvents were removed under vacuum to yield the corresponding imine (100%, 1.13 g).

To a stirred solution of the crude imine (400 mg, 1.78 mmol) in dry Et_2O (14 mL) at 0 °C was added dropwise PhLi (2.08 mL, 3.74 mmol, 1.8 M solution in dibutyl ether). The mixture was stirred at room temperature for 20 h, and the reaction was quenched by adding water. The aqueous layer was extracted with Et_2O, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel, using petroleum ether/ethyl acetate (95/5) as eluent, to afford an inseparable mixture of the two desired diastereomers (dr = 54/46, 74%, 397 mg) as a yellow solid. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.37 (t, *J* = 7.6 Hz, 1H, Ar major), 7.30−7.03 (m, 21H, Ar major and minor), 6.97 (d, *J* = 7.7 Hz, 1H, Ar minor), 6.88 (d, *J* = 7.6 Hz, 1H, Ar minor), 6.81 (d, *J* = 7.6 Hz, 1H, Ar major), 6.72 (d, *J* = 7.7 Hz, 1H, Ar major), 4.66 (s, 1H, CH−N minor), 4.57 (s, 1H, CH−N major), 3.56 (q, *J* = 6.7 Hz, 1H, CH−N major or minor), 3.55 (q, *J* = 6.6 Hz, 1H, CH−N major or minor), 2.85 (br s, 2H, NH major and minor), 2.45 (s, 3H, Me major), 2.44 (s, 3H, Me minor), 1.31 (d, *J* = 6.7 Hz, 3H, Me major), 1.28 (d, *J* = 6.6 Hz, 3H, Me minor). ^1H NMR ($[D_6]$DMSO, 300 MHz) δ 7.64 (t, *J* = 7.6 Hz, 1H, Ar minor), 7.55 (t, *J* = 7.7 Hz, 1H, Ar major), 7.39−7.12 (m, 22H, Ar major and minor), 7.08 (d, *J* = 7.5 Hz, 1H, Ar minor), 7.03 (d, *J* = 7.5 Hz, 1H, Ar major), 4.61 (s, 1H, CH−N minor), 4.56 (s, 1H, CH−N major), 3.60−3.44 (m, 2H, CH−N major and minor), 3.20 (br s, 2H, NH major and minor), 2.40 (s, 3H, Me minor), 2.40 (s, 3H, Me major), 1.29 (d, *J* = 6.6 Hz, 3H, Me major), 1.28 (d, *J* = 6.6 Hz, 3H, Me minor). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.69 (C_{quat}, Ar), 161.47 (C_{quat}, Ar), 158.14 (C_{quat}, Ar), 157.70 (C_{quat}, Ar), 145.76 (C_{quat}, Ar), 145.49 (C_{quat}, Ar), 143.47 (C_{quat}, Ar), 142.86 (C_{quat}, Ar), 136.52 (Ar), 128.46 (Ar), 128.44 (Ar), 128.38 (Ar), 128.22 (Ar), 127.68 (Ar), 127.17 (Ar), 126.97 (Ar), 126.94 (Ar), 126.84 (Ar), 121.47 (Ar), 121.29 (Ar), 119.62 (Ar), 119.00 (Ar), 65.06 (CH−N), 64.79 (CH−N), 55.74 (CH−N), 54.89 (CH−N), 24.76 (Me), 24.70 (Me), 24.68 (Me), 24.34 (Me). HRMS (ESI): calcd for $C_{21}H_{23}N_2$ (MH^+) 303.1861, found 303.1850.

Synthesis of *N*-[(Pyridin-2-yl)(phenyl)methyl]-*N*-[(1′*R*)-1′-phenylethyl]amine (L13). A solution of 2-benzoylpyridine (1.00 g, 5.46 mmol), (*R*)-1-(naphthalen-1-yl)ethylamine (0.935 g, 5.46 mmol), and 4-methylbenzenesulfonic acid (104 mg, 0.546 mmol) in toluene (25 mL) was refluxed for 40 h using a Dean−Stark apparatus. After the mixture was cooled, the solvent was removed and the residue was dried under vacuum. The crude imine was dissolved in MeOH (30 mL), and sodium borohydride (207 mg, 5.46 mmol) was added portionwise at 0 °C. The mixture was stirred overnight at room temperature, and the reaction was quenched by adding saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc. The combined organic layers were washed with a saturated aqueous NaCl solution, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was

purified by flash chromatography on silica gel, using petroleum ether/ethyl acetate (90/10) as eluent, to afford an inseparable mixture of the two desired diastereomers (dr = 51/49, 95%, 397 mg) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.54−8.47 (m, 2H, Ar 2 dia (dia = diastereomer)), 7.86−7.61 (m, 8H, Ar 2 dia, 7.52−6.91 (m, 22H, Ar 2 dia, 4.77 (s, 1H, CH−N 1 dia, 4.74 (s, 1H, CH−N 1 dia), 4.47 (q, J = 6.6 Hz, 1H, CH−N 1 dia), 4.43 (q, J = 6.7 Hz, 1H, CH−N 1 dia), 2.88 (br s, 2H, NH 2 dia), 1.43 (d, J = 6.6 Hz, 3H, Me 1 dia), 1.43 (d, J = 6.7 Hz, 3H, Me 1 dia). ^{1}H NMR ([D_6]DMSO, 200 MHz) δ 8.46 (t, J = 4.4 Hz, 2H, Ar 2 dia), 7.99−7.59 (m, 10H, Ar 2 dia), 7.58−7.02 (m, 20H, Ar 2 dia), 4.76 (s, 2H, CH−N 2 dia), 4.54−4.27 (m, 2H, CH−N 2 dia), 3.46 (br s, 2H, NH 2 dia), 1.42 (d, J = 6.5 Hz, 6H, Me 2 dia). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.65 (C_{quat}, Ar), 162.29 (C_{quat}, Ar), 149.61 (Ar), 149.08 (Ar), 143.25 (C_{quat}, Ar), 142.96 (C_{quat}, Ar), 141.25 (C_{quat}, Ar), 141.17 (C_{quat}, Ar), 136.35 (Ar), 136.34 (Ar), 134.01 (C_{quat}, Ar), 133.97 (C_{quat}, Ar), 131.47 (C_{quat}, Ar), 131.46 (C_{quat}, Ar), 128.88 (Ar), 128.82 (Ar), 128.50 (Ar), 128.48 (Ar), 128.16 (Ar), 127.62 (Ar), 127.26 (Ar), 127.12 (Ar), 127.07 (Ar), 125.85 (Ar), 125.82 (Ar), 125.56 (Ar), 125.26 (Ar), 123.44 (Ar), 123.10 (Ar), 123.02 (Ar), 122.96 (Ar), 122.29 (Ar), 121.97 (Ar), 121.81 (Ar), 65.10 (CH−N), 64.87 (CH−N), 51.31 (CH−N), 50.26 (CH−N), 24.48 (Me), 23.81(Me). HRMS (ESI): calcd for $C_{24}H_{23}N_2$ (MH^+) 339.1861, found 339.1848.

Synthesis of (2*S*)-2-Phenyl-2-(phenyl(pyridin-2-yl)methylamino)ethanol ((1*S*,1′*S*)-L14). A solution of pyridine-2-carboxaldehyde (300 mg, 2.80 mmol) and (*S*)-2-phenylglycinol (384 mg, 2.80 mmol) in dry THF (14 mL) was stirred at room temperature over anhydrous $MgSO_4$ for 24 h. The reaction mixture was filtered through a pad of Celite and washed with DCM, and the solvents were removed under vacuum to yield the corresponding imine (100%, 632 mg).

To a stirred solution of the crude imine (300 mg, 1.33 mmol) in dry THF (15 mL) at −78 °C was added dropwise PhLi (2.28 mL, 4.11 mmol, 1.8 M solution in dibutyl ether). The mixture was stirred at room temperature for 20 h, and the reaction was quenched by adding a saturated solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel, using dichloromethane/methanol (98/2) as eluent, to afford an inseparable mixture (dr = 92/8) of the two desired diastereomers (68%, 274 mg) as an orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.61 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H, Ar major), 7.55 (td, J = 7.7, 1.8 Hz, 1H, Ar major), 7.4−7.29 (m, 10H, Ar major), 7.15 (ddd, J = 7.5, 4.9, 0.8 Hz, 1H, Ar major), 7.02 (d, J = 7.9 Hz, 1H, Ar major), 4.95 (s, 1H, CH−N minor), 4.84 (s, 1H, CH−N major), 3.88−3.62 (m, 3H, CH−N and CH_2−O major), 3.12 (br s, 2H, NH and OH major). ^{1}H NMR ([D_6]DMSO, 300 MHz): δ 8.47 (ddd, J = 4.8, 1.7, 0.8 Hz, 1H, Ar major), 7.65 (td, J = 7.7, 1.8 Hz, 1H, Ar major), 7.38−7.14 (m, 12H, Ar major), 4.99 (t, J = 5.4 Hz, 1H, OH major), 4.65 (s, 1H, CH−N major), 3.61 (br s, 1H, NH major), 3.58−3.38 (m, 3H, CH−N and CH_2−O major). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.94 (C_{quat}, Ar), 148.83 (Ar), 142.05 (C_{quat}, Ar), 140.38 (C_{quat}, Ar), 136.44 (Ar), 128.75 (2C, Ar), 128.70 (2C, Ar), 128.46 (2C, Ar), 127.64 (Ar), 127.61 (Ar), 127.47 (2C, Ar), 122.27 (Ar), 121.94 (Ar), 67.07 (CH_2−O), 64.25 (CH−N), 61.42 (CH−N). HRMS (ESI): calcd for $C_{20}H_{21}N_2O$ (MH^+) 305.1654, found 316.1636.

Synthesis of (2*S*)-2-Phenyl-2-(phenyl(pyridin-2-yl)methylamino)ethanol ((1*R*,1′*S*)-L14). A solution of benzaldehyde (297 mg, 2.80 mmol) and (*S*)-2-phenylglycinol (384 mg, 2.80 mmol) in dry THF (14 mL) was stirred at room temperature over anhydrous $MgSO_4$ for 24 h. The reaction mixture was filtered through a pad of Celite and washed with DCM, and the solvents were removed under vacuum to yield the corresponding imine (100%, 629 mg).

To a stirred solution of the crude imine (300 mg, 1.33 mmol) and 2-bromopyridine (421 mg, 2.66 mmol) in dry THF (15 mL) at −78 °C was added dropwise *n*-BuLi (1.83 mL, 2.93 mmol, 1.6 M solution in hexane). The mixture was stirred for 5 min at −78 °C and then 20 h at room temperature. The reaction was quenched by adding a saturated solution of NH_4Cl. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel, using dichloromethane/methanol (98/2) as eluent, to afford selectively one of the desired diastereomers (65%, 262 mg) as an orange oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.65 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H, Ar), 7.68 (td, J = 7.7, 1.8 Hz, 1H, Ar), 7.46−7.15 (m, 12H, Ar), 4.95 (s, 1H, CH−N), 3.88−3.61 (m, 3H, CH−N and CH_2−O), 3.07 (br s, 2H, NH and OH). ^{1}H NMR ([D_6]DMSO, 300 MHz): δ 8.51 (ddd, J = 4.8, 1.7, 0.7 Hz, 1H, Ar), 7.76 (td, J = 7.6, 1.8 Hz, 1H, Ar), 7.43 (d, J = 7.8 Hz, 1H, Ar), 7.36−7.11 (m, 11H, Ar), 4.91 (t, J = 5.5 Hz, 1H, OH), 4.63 (s, 1H, CH−N), 3.50 (q, J = 5.7 Hz, 1H, CH−N), 3.46 (br s, 1H, NH), 3.43 (dd, J = 8.4, 3.0 Hz, 2H, CH_2−O). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.99 (C_{quat}, Ar), 149.45 (Ar), 143.01 (C_{quat}, Ar), 140.74 (C_{quat}, Ar), 136.77 (Ar), 128.67 (2C, Ar), 128.61 (2C, Ar), 127.64 (Ar), 127.57 (2C, Ar), 127.48 (2C, Ar), 127.35 (Ar), 122.87 (Ar), 122.24 (Ar), 67.15 (CH_2−O), 64.94 (CH−N), 62.45 (CH−N). HRMS (ESI): calcd for $C_{20}H_{21}N_2O$ (MH^+) 305.1654, found 316.1660.

General Procedure for the Synthesis of the Palladium Complexes C1−C14. To a stirred solution of ligand (1 equiv) in freshly distilled MeOH (10 mL for 0.5 mmol of ligand) was added Na_2PdCl_4 (1 equiv). The mixture was stirred at room temperature for 16 h, and the solvent was removed by evaporation under vacuum. The residue was then filtered through a pad of silica gel (first with EtOAc/petroleum ether (4/6) as eluent to remove traces of ligand and then with EtOAc) to afford the corresponding palladium complex.

Complex ***C1***. The reaction was performed with 100 mg (0.61 mmol) of **L1** and 180 mg (0.61 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (176 mg, 85%). ^{1}H NMR ([D_6]DMSO, 300 MHz): δ 8.73 (d, J = 5.4 Hz, 1H, Ar), 8.08 (t, J = 7.5 Hz, 1H, Ar), 7.66 (t, J = 7.7 Hz, 1H, Ar), 7.53 (t, J = 6.4 Hz, 1H, Ar), 6.10 (br s, 1H, NH), 4.50 (dd, J = 11.4, 5.4 Hz, 1H, CH_2−N), 3.99 (d, J = 16.5 Hz, 1H, CH_2−N), 2.75 (m, 1H, CH_2−N), 2.50 (m, 1H, CH_2−N), 0.88 (d, J = 4.6 Hz, 6H, 2 Me). ^{13}C NMR ([D_6]DMSO, 75 MHz): δ 164.42 (C_{quat}, Ar), 149.96 (C, Ar), 141.08 (C, Ar), 125.03 (C, Ar), 123.75 (C, Ar), 62.14 (CH_2−N), 59.87 (CH_2−N), 26.28 (CH), 21.80 (Me), 21.02 (Me). HRMS (ESI): calcd for $C_{10}H_{16}N_2{}^{35}Cl_2{}^{104}Pd$ (M + Na) 362.9618, found 362.9616.

Complex ***C7***. The reaction was performed with 100 mg (0.47 mmol) of **L7** and 139 mg (0.47 mmol) of Na_2PdCl_4. The palladium complex (inseparable mixture of two diastereomers, dr = 50/50) was obtained as a yellow powder (178 mg, 97%). ^{1}H NMR ([D_6]DMSO, 300 MHz): δ 8.57 (dd, J = 5.8, 0.9 Hz, 1H, Ar), 8.44 (dd, J = 5.8, 0.9 Hz, 1H, Ar), 7.99−7.80 (m, 2H, Ar), 7.70 (dd, J = 8.0, 1.4 Hz, 2H, Ar), 7.60 (dd, J = 8.0, 1.4 Hz, 2H, Ar), 7.45 (d, J = 8.0 Hz, 1H, Ar), 7.39−7.10 (m, 9H, Ar), 6.88 (br s, J = 2.5 Hz, 1H, NH), 6.81 (t, J = 5.0 Hz, 1H, NH), 4.50−4.34 (m, 2H, 1H CH_2−N and 1H CH−N), 4.34−4.18 (m, 2H, 1H CH_2−N and 1H CH−N), 4.02 (d, J = 17.5 Hz, 1H, CH_2−N), 3.96 (d, J = 17.5 Hz, 1H, CH_2−N), 1.68 (d, J = 7.0 Hz, 3H, Me), 1.64 (d, J = 7.0 Hz, 3H, Me). ^{13}C NMR ([D_6]DMSO, 75 MHz): δ 164.36 (C_{quat}, Ar), 164.06 (C_{quat}, Ar), 148.42 (Ar), 148.34 (Ar), 139.53 (Ar), 139.38 (Ar), 138.16 (C_{quat}, Ar), 138.09 (C_{quat}, Ar), 128.85 (2C, Ar), 128.81 (2C, Ar), 128.22 (2C, Ar), 128.18 (2C, Ar), 123.32 (Ar), 123.13 (Ar), 121.89 (Ar), 121.70 (Ar), 60.95 (CH−N), 60.01 (CH−N), 55.95 (CH_2−N), 54.30 (CH_2−N), 19.07 (Me), 18.57 (Me). HRMS (ESI−, MeOH): calcd for $C_{14}H_{16}N_2{}^{35}Cl_3{}^{104}Pd$ [M + Cl] 422.9412, found 422.9414.

*Complex (1R,1′R)-****C8***. The reaction was performed with 34 mg (0.15 mmol) of (1*R*,1′*R*)-**L8** and 44 mg (0.15 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (57 mg, 95%). ^{1}H NMR ([D_6]DMSO, 300 MHz): δ 8.46 (dd, J = 5.8, 0.9 Hz, 1H, Ar), 7.92 (td, J = 7.7, 1.5 Hz, 1H, Ar), 7.61 (dd, J = 7.8, 1.6 Hz, 2H, Ar), 7.41

(d, J = 7.4 Hz, 1H, Ar), 7.33 (ddd, J = 7.4, 5.8, 1.4 Hz, 1H, Ar), 7.27−7.14 (m, 3H, Ar), 6.41 (d, J = 6.3 Hz, 1H, NH), 4.32−4.10 (m, 2H, 2 CH−N), 1.80 (d, J = 6.7 Hz, 3H, Me), 1.73 (d, J = 7.0 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 167.55 (C$_{quat}$, Ar), 148.81 (Ar), 139.90 (Ar), 138.96 (C$_{quat}$, Ar), 128.51 (2C, Ar), 128.26 (2C, Ar), 128.11 (Ar), 123.45 (Ar), 121.84 (Ar), 61.29 (CH−N), 61.19 (CH−N), 23.28 (Me), 20.14 (Me). HRMS (ESI−, MeOH): calcd for $C_{15}H_{18}N_2{}^{35}Cl_3{}^{104}Pd$ [M + Cl] 436.9569, found 436.9570.

*Complex (1S,1′R)-**C8***. The reaction was performed on 36 mg (0.16 mmol) of (1*S*,1′*R*)-**L8** and 47 mg (0.16 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (56 mg, 93%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.32 (d, J = 5.7 Hz, 1H, Ar), 7.86−7.62 (m, 3H, Ar), 7.29−6.91 (m, 5H, Ar), 6.36 (br s, 1H, NH), 4.28 (q, J = 6.5 Hz, 1H, CN−N), 3.87 (qd, J = 6.5, 2.1 Hz, 1H, CH−N), 1.83 (d, J = 6.7 Hz, 3H, Me), 1.66 (d, J = 6.9 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 167.79 (C$_{quat}$, Ar), 148.35 (Ar), 139.47 (Ar), 138.51 (C$_{quat}$, Ar), 129.30 (2C, Ar), 128.04 (Ar), 127.80 (2C, Ar), 123.03 (Ar), 121.39 (Ar), 66.04 (CH−N), 63.54 (CH−N), 23.31 (Me), 21.34 (Me). HRMS (ESI−, MeOH): calcd for $C_{15}H_{18}N_2{}^{35}Cl_3{}^{104}Pd$ [M + Cl] 436.9569, found 436.9570.

*Complex (1R,1′R)-**C9***. The reaction was performed on 100 mg (0.35 mmol) of (1*R*,1′*R*)-**L9** and 102 mg (0.35 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (157 mg, 97%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.47 (d, J = 5.2 Hz, 1H, Ar), 7.86 (d, J = 6.8 Hz, 5H, Ar), 7.57−7.36 (m, 4H, Ar), 7.30 (t, J = 6.7 Hz, 1H, Ar), 7.26−7.13 (m, 3H, Ar), 6.65 (d, J = 4.8 Hz, 1H, NH), 5.47 (s, 1H, CH−N), 4.68−4.39 (m, 1H, CH−N), 1.82 (d, J = 6.9 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 165.83 (C$_{quat}$, Ar), 148.41 (Ar), 139.93 (Ar), 138.75 (C$_{quat}$, Ar), 137.57 (C$_{quat}$, Ar), 129.10 (2C, Ar), 128.92 (Ar), 128.88 (2C, Ar), 128.64 (2C, Ar), 128.29 (Ar), 128.20 (2C, Ar), 123.56 (Ar), 123.00 (Ar), 67.93 (CH−N), 61.83 (CH−N), 18.75 (Me). HRMS (ESI−, MeOH): calcd for $C_{20}H_{19}N_2{}^{35}Cl_2{}^{104}Pd$ (M − H) 460.9966, found 460.9965.

*Complex (1S,1′R)-**C9***. The reaction was performed on 50 mg (0.17 mmol) of (1*S*,1′*R*)-**L9** and 51 mg (0.17 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (72 mg, 91%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.42 (d, J = 4.9 Hz, 1H, Ar), 8.09 (d, J = 7.0 Hz, 2H, Ar), 7.94 (d, J = 6.7 Hz, 2H, Ar), 7.71 (td, J = 7.7, 1.4 Hz, 1H, Ar), 7.54−7.37 (m, 3H, Ar), 7.28−7.04 (m, 5H, Ar), 6.55 (br s, 1H, NH), 5.44 (s, 1H, CH−N), 4.16−4.05 (m, 1H, CH−N), 1.74 (d, J = 6.8 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 165.68 (C$_{quat}$, Ar), 148.23 (Ar), 139.76 (Ar), 138.44 (C$_{quat}$, Ar), 137.79 (C$_{quat}$, Ar), 129.57 (2C, Ar), 128.96 (Ar), 128.85 (2C, Ar), 128.53 (2C, Ar), 128.29 (Ar), 127.94 (2C, Ar), 123.38 (Ar), 122.69 (Ar), 73.53 (CH−N), 64.75 (CH−N), 21.39 (Me). HRMS (ESI−, MeOH): calcd for $C_{20}H_{19}N_2{}^{35}Cl_2{}^{104}Pd$ (M − H) 460.9966, found 460.9968.

*Complex **C10a***. The reaction was performed on 30 mg (0.076 mmol) of **L10a** and 22 mg (0.076 mmol) of Na_2PdCl_4. The palladium complex was obtained as an orange powder (43 mg, 98%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.51 (d, J = 5.5 Hz, 1H, Ar), 8.03 (t, J = 7.2 Hz, 1H, Ar), 7.69 (d, J = 7.3 Hz, 3H, Ar), 7.43 (t, J = 6.3 Hz, 1H, Ar), 7.36−7.21 (m, 3H, Ar), 5.39 (d, J = 6.8 Hz, 1H, NH), 5.03 (s, 1H, Cp), 4.91 (s, 1H, CH−N), 4.39 (s, 1H, Cp), 4.35 (s, 2H, Cp), 4.30−4.16 (m, 1H, CH−N), 1.90 (d, J = 6.9 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 164.39 (C$_{quat}$, Ar), 148.74 (Ar), 139.91 (Ar), 138.78 (C$_{quat}$, Ar), 128.60 (2C, Ar), 128.51 (Ar), 128.44 (2C, Ar), 124.02 (Ar), 123.62 (Ar), 87.25 (C$_{quat}$, Cp), 68.92 (5C, Cp), 68.48 (2C, Cp), 68.10 (Cp), 67.45 (Cp), 65.26 (CH−N), 61.91 (CH−N), 21.19 (Me). HRMS (ESI−, MeOH): calcd for $C_{24}H_{24}N_2{}^{35}Cl_3{}^{56}Fe{}^{104}Pd$ [M + Cl] 606.9394, found 606.9389.

*Complex **C12***. The reaction was performed on 60 mg (0.20 mmol) of **L12** (mixture of two diastereomers) and 59 mg (0.20 mmol) of Na_2PdCl_4. The two desired diastereomers were obtained as a yellow powder (dr = 55/45, 88 mg, 93%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.43 (d, J = 7.2 Hz, 2H, Ar major), 7.98 (d, J = 7.0 Hz, 2H, Ar minor), 7.87−7.75 (m, 3H, Ar major and minor), 7.63−7.42 (m, 9H, Ar major and minor), 7.33−7.00 (m, 9H, Ar major and minor), 6.92 (d, J = 7.3 Hz, 1H, Ar major), 6.24 (s, 1H, NH major), 6.11 (d, J = 7.2 Hz, 1H, NH minor), 5.57 (s, 1H, CH−N major), 5.19 (s, 1H, CH−N minor), 4.06 (p, J = 6.6 Hz, 1H, CH−N minor), 3.94−3.79 (m, 1H, CH−N major), 2.71 (s, 3H, Me minor), 2.57 (s, 3H, Me major), 1.83 (d, J = 6.9 Hz, 3H, Me minor), 1.68 (d, J = 6.7 Hz, 3H, Me major). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 164.59 (C$_{quat}$, Ar), 163.89 (C$_{quat}$, Ar), 162.41 (C$_{quat}$, Ar), 161.53 (C$_{quat}$, Ar), 140.19 (Ar), 139.64 (C$_{quat}$, Ar), 139.58 (Ar), 139.52 (C$_{quat}$, Ar), 138.68 (C$_{quat}$, Ar), 138.18 (C$_{quat}$, Ar), 130.12, 129.89, 129.43, 129.32, 129.18, 129.01, 128.80 (Ar), 128.53, 128.26, 125.96 (Ar), 125.22 (Ar), 121.27 (Ar), 120.47 (Ar), 75.96 (CH−N), 70.41 (CH−N), 64.91 (CH−N), 62.43 (CH−N), 26.83 (Me), 26.65 (Me), 21.63 (Me), 20.77 (Me). HRMS (ESI+, CH$_3$CN): calcd for $C_{23}H_{25}N_3{}^{35}Cl{}^{104}Pd$ (M + CH$_3$CN − Cl) 484.0772, found 484.0764.

*Complexes **C13a,b***. The reaction was performed on 117 mg (0.35 mmol) of **L13** (mixture of two diastereomers) and 102 mg (0.35 mmol) of Na_2PdCl_4. The two desired diastereomers (dr = 51/49) were obtained in 92% overall yield and were separated by flash chromatography on silica gel, using petroleum ether/ethyl acetate (90/10) as eluent.

The first eluted diastereomer **C13a** was isolated as a yellow powder (81 mg). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.89 (d, J = 7.9 Hz, 1H, Ar), 8.21 (d, J = 5.5 Hz, 1H, Ar), 8.02 (d, J = 7.2 Hz, 1H, Ar), 7.95−7.82 (m, 3H, Ar), 7.81−7.66 (m, 2H, Ar), 7.64−7.30 (m, 6H, Ar), 7.25−7.09 (m, 2H, Ar), 6.58 (s, 1H, NH), 5.34 (s, 1H, CH−N), 5.30−5.18 (m, 1H, CH−N), 1.98 (d, J = 6.7 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 164.60 (C$_{quat}$, Ar), 148.33 (Ar), 139.73 (Ar), 137.18 (C$_{quat}$, Ar), 134.35 (C$_{quat}$, Ar), 133.17 (C$_{quat}$, Ar), 130.88 (C$_{quat}$, Ar), 128.97, 128.87, 128.83, 128.51, 126.70, 126.00, 125.80, 125.05, 123.85, 123.52, 122.94, 68.96 (CH−N), 56.26 (CH−N), 21.10 (Me). HRMS (ESI+, CH$_3$CN): calcd for $C_{26}H_{25}N_3{}^{35}Cl{}^{104}Pd$ (M + CH$_3$CN − Cl): 520.0772, found 520.0751.

The second diastereomer **C13b** was isolated as a yellow powder (85 mg). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.61−8.50 (m, 2H, Ar), 8.47 (d, J = 7.2 Hz, 1H, Ar), 7.95−7.83 (m, 2H, Ar), 7.72 (t, J = 7.7 Hz, 1H, Ar), 7.64−7.45 (m, 3H, Ar), 7.39−7.24 (m, 6H, Ar), 7.20 (d, J = 7.8 Hz, 1H, Ar), 5.64 (s, 1H, NH), 5.46−5.30 (m, 1H, CH−N), 5.38 (s, 1H, CH−N), 1.92 (d, J = 6.7 Hz, 3H, Me). ^{13}C NMR ([D$_6$]DMSO, 75 MHz) δ 164.87 (C$_{quat}$, Ar), 148.23 (Ar), 139.73 (Ar), 137.66 (C$_{quat}$, Ar), 133.54 (C$_{quat}$, Ar), 133.24 (C$_{quat}$, Ar), 130.73 (C$_{quat}$, Ar), 129.44 (Ar), 129.11 (Ar), 129.00 (3C, Ar), 127.83 (2C, Ar), 127.09 (Ar), 126.99 (Ar), 125.91 (Ar), 125.05 (Ar), 124.04 (Ar), 122.72 (Ar), 122.24 (Ar), 70.52 (CH−N), 57.44 (CH−N), 19.31 (Me). HRMS (ESI+, CH$_3$CN): calcd for $C_{26}H_{25}N_3{}^{35}Cl{}^{104}Pd$ (M + CH$_3$CN − Cl) 520.0772, found 520.0752.

*Complex (1S,1′S)-**C14***. The reaction was performed on 51 mg (0.17 mmol) of (1*S*,1′*S*)-**L14** and 50 mg (0.17 mmol) of Na_2PdCl_4. The palladium complex was obtained as a yellow powder (75 mg, 94%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.42 (d, J = 5.3 Hz, 1H, Ar minor), 8.28 (d, J = 5.4 Hz, 1H, Ar major), 8.09−7.88 (m, 4H, Ar major), 7.86−7.71 (m, 1H, Ar major), 7.65−7.42 (m, 3H, Ar major), 7.36 (d, J = 7.6 Hz, 1H, Ar major), 7.27−7.09 (m, 4H, Ar major), 5.97 (s, 1H, NH major), 5.76 (s, 1H, CH−N minor), 5.66 (s, 1H, CH−N major), 5.13 (t, J = 4.7 Hz, 1H, OH major), 4.42−4.25 (m, 1H, CH$_2$−O), 4.04 (t, J = 6.7 Hz, 1H, CH−N major), 3.92−3.79 (m, 1H, CH$_2$−O major). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 164.74 (C$_{quat}$, Ar), 148.34 (Ar), 139.80 (Ar), 137.79 (C$_{quat}$, Ar), 135.85 (C$_{quat}$, Ar), 130.10 (2C, Ar), 129.22 (3C, Ar), 128.52 (Ar), 128.15 (2C, Ar), 127.92 (2C, Ar), 123.55 (Ar), 122.78 (Ar), 74.58 (CH−N), 71.42 (CH−N), 61.77 (CH$_2$−O). HRMS (ESI−, MeOH): calcd for $C_{20}H_{19}N_2O{}^{35}Cl_2{}^{104}Pd$ (M − H) 476.9915, found 476.9902.

*Complex (1R,1′S)-**C14***. The reaction was performed on 57 mg (0.19 mmol) of (1*R*,1′*S*)-**L14** and 55 mg (0.19 mmol) of Na_2PdCl_4.

The palladium complex was obtained as a yellow powder (89 mg, 99%). ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ 8.42 (dd, J = 5.8, 0.9 Hz, 1H, Ar), 7.90 (d, J = 7.5 Hz, 2H, Ar), 7.84 (td, J = 7.8, 1.5 Hz, 1H, Ar), 7.76 (d, J = 7.0 Hz, 2H, Ar), 7.59−7.43 (m, 3H, Ar), 7.35 (d, J = 7.8 Hz, 1H, Ar), 7.28 (ddd, J = 7.3, 6.0, 1.3 Hz, 1H, Ar), 7.25−7.12 (m, 3H, Ar), 5.77 (s, 1H, CH−N), 5.57 (t, J = 4.7 Hz, 1H, OH), 5.44 (d, J = 2.4 Hz, 1H, NH), 4.65−4.42 (m, 2H, CH$_2$−O and CH−N), 3.80 (dt, J = 10.3, 4.3 Hz, 1H, CH$_2$−O). ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ 165.26 (C$_{quat}$, Ar), 148.29 (Ar), 139.90 (Ar), 137.97 (C$_{quat}$, Ar), 133.96 (C$_{quat}$, Ar), 130.18 (2C, Ar), 129.34 (2C, Ar), 129.29 (Ar), 128.83 (Ar), 128.21 (2C, Ar), 128.14 (2C, Ar), 123.70 (Ar), 123.06 (Ar), 67.31, 66.76, 58.37. HRMS (ESI−, MeOH): calcd for $C_{20}H_{19}N_2O^{35}Cl_2{}^{104}Pd$ (M − H) 476.9915, found 476.9914.

General Procedure for the Suzuki−Miyaura Coupling Reaction. To a stirred suspension of 1-bromo-2-methoxynaphthalene (54 mg, 0.226 mmol, 1 equiv), naphthalen-1-ylboronic acid (78 mg, 0.452 mmol, 2 equiv), and Cs_2CO_3 (294 mg, 0.904 mmol, 4 equiv) in a degassed mixture of toluene (1 mL), absolute ethanol (1 mL), and water (0.5 mL) was added the palladium complex (5 mol %). The mixture was stirred at 80 °C for 24 h under argon. Water was then added, and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel (petroleum ether/EtOAc 98/2) to give the desired binaphthyl compound **17**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.96 (t, J = 8.4 Hz, 2H), 7.95 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 6.3 Hz, 1H), 7.65−7.60 (m, 3H), 7.37−7.15 (m, 5H), 3.77 (s, 3H). HPLC (Chiralpak OJ-H, hexane/2-propanol 95/5, 1.0 mL/min, λ 254 nm): t_R = 12.75 min (major) and 23.70 min (minor), ee = 40% in favor of the S enantiomer.[27]

General Procedure for Oxidative Naphthol Coupling. To a solution of 3-hydroxynaphth-2-yl carboxylic acid methyl ester (50.5 mg, 0.25 mmol) dissolved in DCE was added CuI (4.8 mg, 0.1 equiv) and **L10** (9.9 mg, 0.1 equiv) to yield a greenish solution which was actively purged with air for 1 min and then placed under an air atmosphere at 40 °C. After 48 h, the reaction mixture was diluted with CH_2Cl_2 and was washed with 1 N HCl. The aqueous phase was back-extracted with CH_2Cl_2, and the combined organic solutions were dried over Na_2SO_4. Filtration and concentration afforded the crude product, which was purified by flash chromatography on silica gel (petroleum ether/EtOAc 98/2) to give the desired binaphthyl compound **21**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.76 (s, 2H), 8.71 (s, 2H), 7.95−7.92 (m, 2H), 7.39−7.16 (m, 6H), 4.06 (s, 3H). HPLC (Chiralpak AD, hexane/2-propanol 90/10, 1.0 mL/min, λ 254 nm): t_R = 13.98 min (major) and 25.23 min (minor), ee = 61% in favor of the S enantiomer.[28]

■ ASSOCIATED CONTENT

Supporting Information. Text, tables, figures, and CIF files giving ^{1}H and ^{13}C NMR data for ligands and complexes as well as crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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