JOC The Journal of Organic Chemistry

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Phosphino Hydrazones as Suitable Ligands in the Asymmetric Suzuki–Miyaura Cross-Coupling

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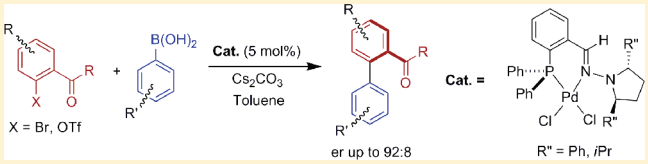
Supporting Information

ABSTRACT: Phosphino hydrazones derived from C_2-symmetric hydrazines exhibit excellent catalytic activity and provide good enantioselectivities in the asymmetric Suzuki–Miyaura cross-coupling to axially chiral biaryls, in particular for the most challenging reactions of monocyclic, functionalized aryl bromides and triflates. X-ray analysis of preformed [Pd(P/N)Cl_2] precatalysts [(P/N) = phosphino hydrazone] revealed a strong n–π conjugation in the hydrazone moiety, identified by a high planarity degree at the pyrrolidine N(sp^3) atom, that makes rotations around N–N bonds inconsequential. The complexes are also characterized by an envelope-like conformation with the Pd atom placed at the opposite side to the 2-phenyl group on the nearest stereogenic center of the pyrrolidine group. The isolation and structural analysis of oxidative addition intermediates indicate that the configurational stability of Pd–C(Ar) bonds is dependent on the substitution pattern in the aryl bromide.



INTRODUCTION

Asymmetric, heterobidentate ligands with different electronic properties constitute an important family of compounds for their applications in catalysis. In fact, transition-metal complexes carrying such type of ligands may reach very high levels of activity and selectivity in some reactions as a result of the *trans*-influence. Among them, P/N ligands are established as the most popular ligand class; after the pioneering work of the Helmchen,[1] Pfaltz,[2] and Williams[3] groups on the use of phosphino-oxazolines (PHOX) in Pd-catalyzed allylic substitutions,[4] these compounds have found applications in many other reactions and can therefore be considered as "privileged ligands"[5] in asymmetric catalysis. The asymmetric Suzuki–Miyaura cross-coupling to biaryls constitutes a particularly challenging reaction, as it requires catalysts that combine a high activity to achieve reactions with highly hindered coupling partners (unavoidable if the newly created Ar–Ar′ bond will be configurationally stable) and a geometry able to drive enantiocontrolled reactions. In this context, P/N ligands have played a predominant role, providing good results for several types of substrates.[6] Additional studies have also been carried out using different ligands such as mono-[7] or diphosphines,[8] dienes,[9] phenyl-bis(oxazoline),[10] or heterocyclic carbenes,[11] but the collected results are in general modest in terms of generality and enantioselectivity. We have recently reported on the use of phosphine-free C_2-symmetric glyoxal bis-hydrazone **1** as the ligand (Figure 1),[12] which provides very good enantioselectivities at low temperatures, particularly for the synthesis of unfunctionalized binaphthalenes. The long reaction times required for completion, and the lower reactivity and/or enantioselectivities collected for some types of substrate prompted us to modify the structure of the catalyst. Toward this goal, we reasoned that ligands **2** combining a hydrazone unit (that provides an excellent chiral environment in the bis–hydrazone case) and a phosphine donor to build the successful heterobidentate P/N architecture (expected to provide a better reactivity) would be interesting candidates for the asymmetric Suzuki–Miyaura reaction. A survey of the pertinent literature revealed that, in spite of their availability, only a couple of representatives of this class of ligands have been reported. Thus, Mino and co-workers[13] have reported the use of prolinol-derived phosphino hydrazones **3**–**5** in Pd-catalyzed asymmetric allylic alkylations, and, more recently, Widhalm's group[14] reported binaphthyl-based azepine derivatives **6** and their use as ligands in the same reaction (Figure 2). Their use in cross-coupling reactions (or any other applications) remains unexplored.

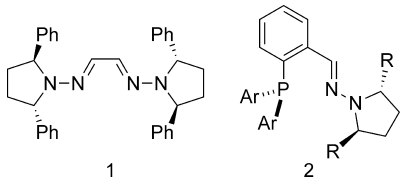


Figure 1. Hydrazone-based ligands **1** and **2**.

Received: March 14, 2012
Published: April 17, 2012

   dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740–4750

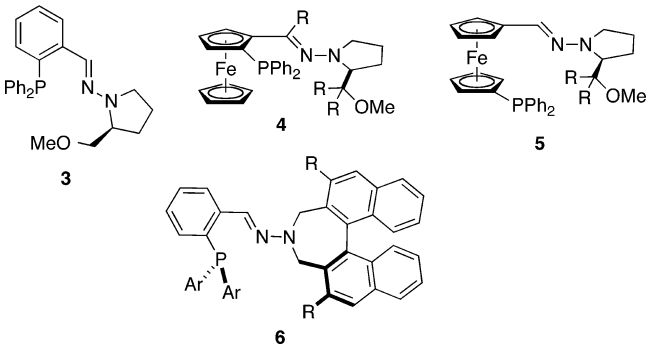


Figure 2. Phosphino hydrazones in asymmetric catalysis.

RESULTS AND DISCUSSION

As in previous studies with bis-hydrazones,[12,15] C_2-symmetric hydrazines were chosen as precursors of phosphino hydrazones, as the introduction of this substructure is the key design strategy to make N–N bond rotations inconsequential. Thus, and in contrast with monosubstituted hydrazine derivatives, the maintenance of an asymmetric environment around the metal center is granted in their corresponding complexes (Figure 3).

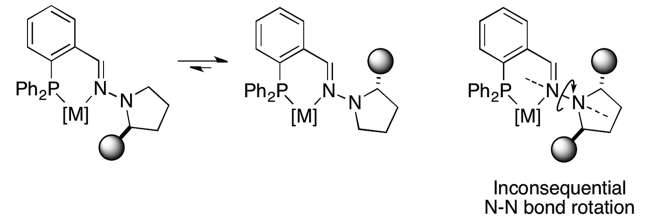
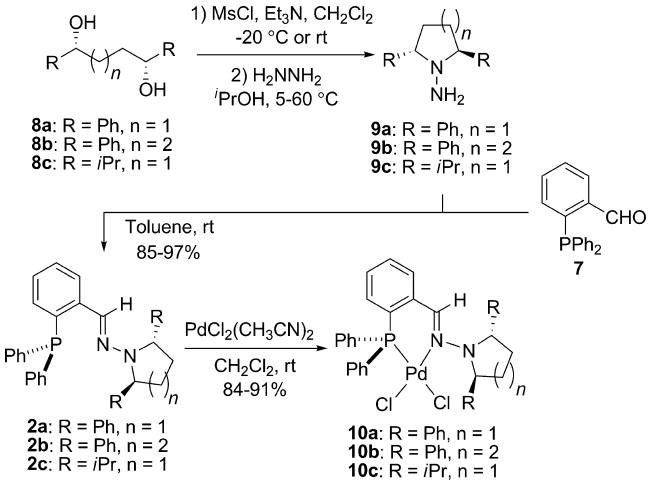


Figure 3. C_2-Symmetry as the key strategy to make N–N bond rotations inconsequential.

In order to check the suitability of the proposed phosphino hydrazone ligands, we started synthesizing representatives **2a–c** from commercially available 2-(diphenylphosphino)benzaldehyde **7** and C_2-symmetric hydrazines **9a–c**. Diphenyl-substituted pyrrolidine **9a** and piperidine **9b** derivatives were synthesized from the corresponding known diols **8a,b** after mesylation and reaction with hydrazine hydrate as described previously.[15,16] Then, a simple condensation with **7** afforded the desired heterobidentate ligands **2a** and **2b** in 97 and 82% yield, respectively (Scheme 1).

Scheme 1. Synthesis of Phosphino Hydrazones 2a–c and Pd Complexes 10a–c



1-Amino-2,5-diisopropylpyrrolidine **9c** was obtained from commercially available 1,4-diol **8c** following a similar procedure, though higher reaction temperatures were required in the cyclization step. In this case, the product **9c** did not survive the standard workup, and therefore, the crude reaction mixture was made to react with **7** to afford the desired ligand **2c** in 85% overall yield from **8c**. Reactions of phosphino hydrazones **2a–c** with $[PdCl_2(CH_3CN)_2]$ readily afforded neutral Pd(II) complexes **10a–c** in nearly quantitative yields. The ^{1}H NMR spectrum at 295 K of these complexes showed broad signals attributed to slow N–N bond rotations, making it difficult to obtain any valuable information about the geometry of the coordinated P,N ligands in solution. In the solid state, however, the structures of **10a** and **10c** could be analyzed by single-crystal X-ray diffractometry (Figures 4 and 5).

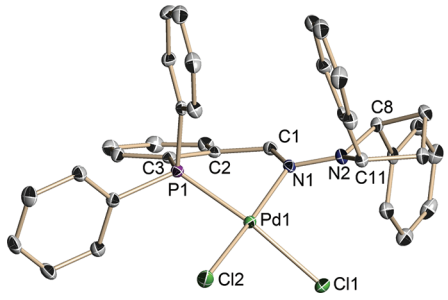


Figure 4. ORTEP drawing of complex **10a**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (deg): Pd(1)–P(1) 2.2172(9), Pd(1)–N(1) 2.086(2), Pd(1)–Cl(1) 2.401(1), Pd(1)–Cl(2) 2.2751(9), N(1)–N(2) 1.354(4), Cl(1)–Pd(1)–Cl(2) 89.23(3), P(1)–Pd(1)–N(1) 87.72(7).

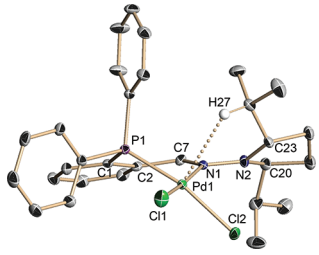


Figure 5. ORTEP drawing of complex **10c**. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (deg): Pd(1)–P(1) 2.2237(7), Pd(1)–N(1) 2.091(2), Pd(1)–Cl(1) 2.2820(7), Pd(1)–Cl(2) 2.3645(7), N(1)–N(2) 1.363(3), Cl(1)–Pd(1)–Cl(2) 88.99(3), P(1)–Pd(1)–N(1) 88.81(6).

In both cases, as expected, an efficient n→π conjugation in the hydrazone moiety was deduced from the low pyramidalization degree at the N(sp^3) atoms [virtual dihedral angles N(1)–N(2)–C(8)–C(11) = 159.6° for **10a** and N(1)–N(2)–C(20)–C(23) = 162.8° for **10c**][17,18] and the torsion angles C(1)–N(1)–N(2)–C(8) = 2.3(4)° and C(7)–N(1)–N(2)–C(20) = −18.8(4)° for **10a** and **10c**, respectively. Such a conjugation should consequently increase the electronic density in the hydrazone fragment. The longer Pd–Cl bond *trans* to the phosphine [Pd–Cl(1) = 2.401 Å for **10a** and Pd–Cl(2) = 2.365 Å for **10c**] compared to the Pd–Cl bond *trans* to the nitrogen atom [Pd–Cl(2) = 2.275 Å for **10a** and Pd–Cl(1) = 2.282 Å for **10c**] reflects the stronger *trans* influence of the phosphine terminus. Both complexes show the expected square-planar

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740–4750

geometry in the Pd center, with the ligand-containing palladacycle adopting a slightly distorted envelope-like conformation that places the Pd atom below the plane defined by P−C(1)−C(2)−C(3) (conformer E_{Pd} in Figure 6), the angle between this

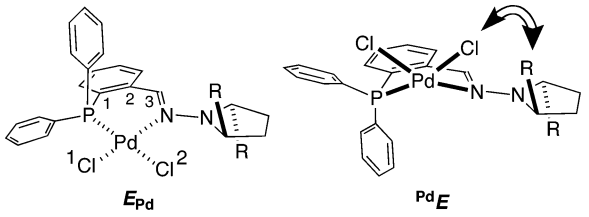
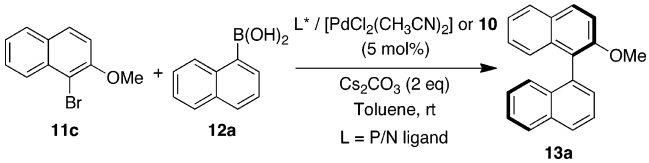


Figure 6. Envelope-like conformations in complexes **10**.

plane and the Pd coordination plane [defined by P−N−Pd−Cl(1)−Cl(2)] being 55.3° and 54.1°, respectively. As the most significant difference, the structure of **10c** exhibits an apical Pd−H interaction with the tertiary isopropyl CH bond [Pd−H(27) = 2.677 Å]. In solution, an alternative conformation with the Pd atom placed above the mentioned plane (^{Pd}E in Figure 6) could in principle be considered, but it can be disregarded for the severe steric interaction that would arise between one of the chlorine atoms and the R group in the nearest stereogenic center if the n−π conjugation is preserved.

Precatalysts prepared in situ from ligands **2a−c** were then tested in the asymmetric Suzuki−Miyaura reaction. To this aim, 1-bromo-2-methoxynaphthalene **11c** and 1-naphthyl boronic acid **12a** (Table 1) were chosen as model substrates, a relatively

Table 1. Screening of P/N Ligands in the Reaction of 11c with 12a[a]

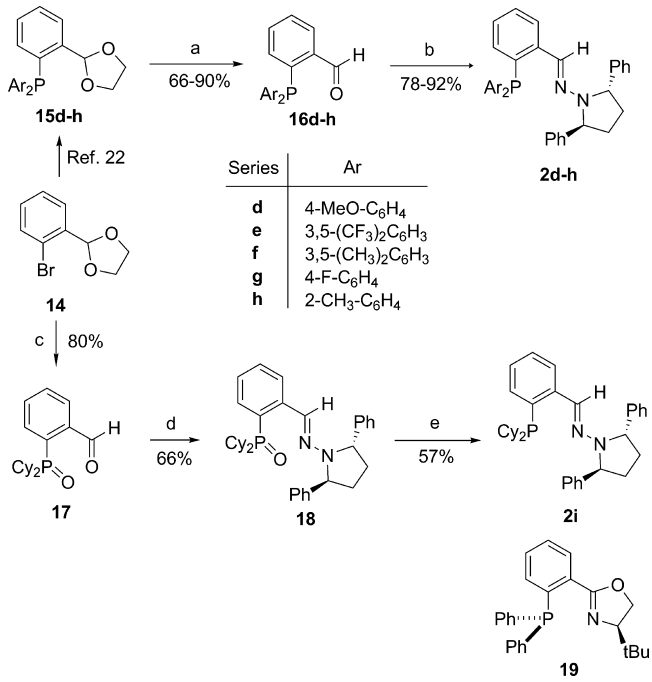


entry	precat[b]	R in PR_2	time (h)	yield[c] (%)	er[d]
1	**2a**/[Pd]	Ph	15	90	**83:17**
2	**2b**/[Pd]	Ph	15	91	59:41
3	**2c**/[Pd]	Ph	15	80	**88:12**
4	**2d**/[Pd]	*p*-$MeOC_6H_3$	24	72	79:21
5	**2e**/[Pd]	3,5-$(CF_3)_2C_6H_3$	24	53	53:47
6	**2f**/[Pd]	3,5-$Me_2C_6H_4$	24	86	75:25
7	**2g**/[Pd]	*p*-FC_6H_4	24	81	72:28
8	**2h**/[Pd]	*o*-tolyl	24	99	68:32
9	**2i**/[Pd]	Cy	24	20	50:50
10	**18**/[Pd]	Ph	15	97	50:50
11	**19**/[Pd]	Ph	15	94	50:50
12	**10a**	Ph	15	**97**[e]	**78:22**
13	**10c**	Ph	15	**90**	**90:10**

[a]Reactions were performed at room temperature on a 0.1 mmol scale. [b][Pd] = $PdCl_2(CH_3CN)_2$. [c]Isolated yields after column chromatography. [d]Determined by HPLC on chiral stationary phases. [e]A catalyst loading of 1 mol % afforded **13a** in 70% yield and er = 81:19 after 48 h.

demanding system for the poor reactivity of the electron-rich bromide and the possible interferences introduced by the neighbor methoxy group. The reactions carried out at room temperature in toluene as the solvent and using Cs_2CO_3 as the base afforded the desired coupling product **13a**[19] in excellent yields (89−97%), confirming a very good catalytic activity, with enantioselectivities ranging from er 59:41 to 88:12 (entries 1−3). The analysis of these results indicates that, as previously observed in related catalysts[12,15] or auxiliaries,[20] the pyrrolidine-based phosphino hydrazones **2a,c** provide better chiral environments than the piperidine-based analogue **2b**, a fact that can be attributed to the higher conformational rigidity associated with the stronger n−π conjugation. Though better enantioselectivity (er = 95:5) was observed using the previously reported bis-hydrazone **1** as the ligand under the same reaction conditions, ligands **2a** and **2c** can be considered as promising alternatives in terms of catalytic activity. Thus, the reaction carried out with **1** required 7 days (versus 15 h for **2a** or **2c**) to afford a lower 61% yield.[21] Additional structural variability was introduced by modification of the phosphino moiety. Thus, ligands **2d−h** with different PAr_2 groups were synthesized by reaction of the corresponding diarylphosphinobenzaldehydes **16d−h**, available from a common intermediate **14** via acetals **15d−h**,[22] with (2*S*,5*S*)-1-amino-2,5-diphenylpyrrolidine **9a** (Scheme 2). Following a modified procedure, the synthesis of

Scheme 2. Synthesis of Phosphino Hydrazone Ligands 2d−i[a]



[a]Reagents and conditions: (a) acetone/H_2O, *p*-TsOH (cat.), reflux; (b) toluene, rt; (c) (1) *t*BuLi, Et_2O, −78 °C; (2) $ClPCy_2$, −78 °C→ rt; (3) acetone/H_2O, *p*-TsOH (cat.), reflux; (d) **9a**, toluene, rt; (e) $HSiCl_3$, Et_3N, toluene, reflux.

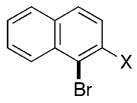
the dicyclohexyl derivative **2i** was accomplished from phosphine oxide intermediate **17** by condensation with **9a** followed by reductive deoxygenation of the resulting product **18**. Finally, a "privileged" ligand such as (*S*)-4-*tert*-butyl-2-[2-(diphenylphosphino)phenyl]-2-oxazoline **19**[23] was included in the study for comparative purposes.

The behavior of these modified ligands was analyzed using the same model reaction for comparison. Unfortunately, a higher steric demand by the PAr_2 group had a detrimental effect in the enantioselectivity (entries 5, 6, and 8). Taking ligand **2a** as a reference, the modulation of the donor ability of the P atom by introduction of electron-donating (entries 4 and 8) or -withdrawing (entries 5 and 7) functionalities in the Ar rings

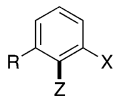
dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740−4750

was also unsuccessfully investigated. Unexpectedly, dicyclohexyl derivative **2i** showed a poor catalytic activity and afforded the product **13a** in racemic form (entry 9). This result suggests that a much better P donor facilitated decoordination of the hydrazone N(sp^2) atom, making the ligand behave as a monodentate achiral phosphane.[24] Finally, the catalysts prepared in situ from phosphino oxazoline **19** were shown to be active but not selective, affording **13a** in a nearly quantitative yield but in racemic form (entry 11). Reactions carried out with preformed complexes **10a** or **10c** afforded slightly improved results (entries 12 and 13), and therefore, these precatalysts were used in successive studies aimed to explore the scope of the new ligands in the asymmetric Suzuki–Miyaura cross-coupling. Thus, a variety of aryl bromides or triflates **11**, **20**, and **21** were made to react with boronic acids **12** or **22** (Chart 1),

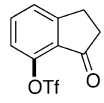
Chart 1. Coupling Partners 11, 12, and 20–22



11a: X = H
11b: X = Me
11c: X = OMe
11d: X = CHO
11e: X = CO_2Me



20a: R = H, X = CHO, Z = Br
20b: R = H, X = CHO, Z = OTf
20c: R = Me, X = CHO, Z = Br



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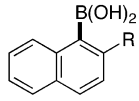
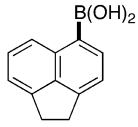
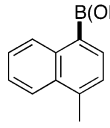


12a: R = H
12b: R = Me
12c: R = OMe
12d: R = Cy



12e



12f

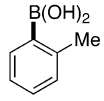


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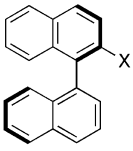
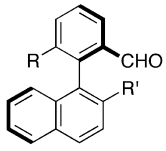
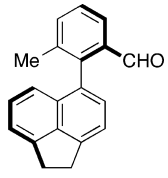
Chart 2. Coupling Products 13 and 23–25



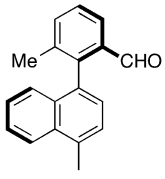
13a: X = OMe
13b: X = Me
13c: X = CHO
13d: X = CO_2Me



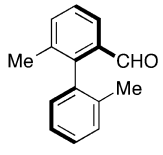
23a: R = H, R' = Me
23b: R = Me, R' = H



23c



23d



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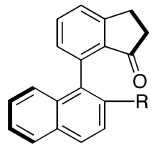


25a: R = Me
25b: R = Cy

affording the expected coupling products **13** and **23–25** (Chart 2, Table 2). In addition to the already mentioned results for the model reaction (entries 1 and 2), the synthesis of **13a** was alternatively performed from aryl bromide **11a** and boronic acid **12c**, substrates with exchanged substitution patterns. This reaction, however, does not take place at room temperature, indicating that the catalyst is more sensitive to steric bulk on the boronic acid **12** than on the aryl bromide **11**. Heating to 80 °C for 28 h was required for the reaction to complete, affording the product **13a** in good yield, though with a much lower enantioselectivity (er 69:31, entry 3). In general, a moderate level of enantioselectivity was observed for other 1,1′-binaphthyl derivatives **13b–d** (entries 4–7). More interesting results were observed for the coupling of phenyl bromides **20a**,**c** or triflate **20b** with boronic acids **12a**,**b**,**e**,**f** to afford the phenyl–naphthyl coupling products **23a–d** (entries 8–14) in good enantiomeric ratios (er 89:11 to 92:8). Even the more challenging coupling of **20c** with **22** afforded the biphenyl derivative **24** in good enantiomeric ratios (er up to 91:9, entries 15–17). Finally, the coupling of cyclic indanone **21** with boronic acids **12a** and **12b** afforded coupling products **25a** and **25b** in good yields and enantiomeric ratios of 89:11 and 86:14, respectively (entries 18 and 19). In general, diisopropyl-substituted derivative **10c** afforded slightly better results, but diphenyl derivative **10a** afforded competitive results in some cases (entries 6, 9, and 15), providing the coupling products in much better yields and similar enantioselectivities. Interestingly, these results are complementary with those observed for catalysts based in bis-hydrazone ligand **1**. Thus, while **1** proved to be a superior catalyst for the coupling of electron-rich and unfunctionalized naphthyl bromides,[12] this system was unsuccessfully applied to the activation of electron-poor substrates such as **20** or **21** (8–19), even at higher temperatures. In contrast with the couplings performed with C_2-symmetric bis-hydrazones as ligands,[12] two possible regioisomers of the oxidative addition intermediates must be considered for precatalysts **10**. Because of the higher *trans* influence of the phosphine ligand, the naphthyl fragment should expectedly be placed at a position *trans* to the hydrazone sp^2 N atom, far away from the chiral environment generated by the pyrrolidine ring.

As the origin of the enantioselectivity is therefore not clear, we decided to acquire additional information by performing a structural study of the isolated oxidative addition intermediates. To this aim, reaction of 1 equiv of ligand **2a** with 1 equiv of 1-bromonaphthalene **11a** in the presence of [Pd(COD)-(CH_2SiMe_3)$_2$][26] **26** (Scheme 3) afforded the expected oxidative addition intermediate **27a** in 70% yield as a 1:1 mixture of atropoisomers (^{31}P NMR: δ 21.7 and 22.2 ppm). Crystallization from CH_2Cl_2/acetone gave good quality yellow crystals that were analyzed by X-ray diffractometry (Figure 7). Surprisingly, the structure of **27a** exhibits characteristics very similar to those previously discussed for precatalyst **10a** or its analogue **10c**. As in these cases, a high degree of conjugation in the hydrazone moiety was again deduced from the N(sp^3) pyramidalization degree [expressed by the virtual angle N(1)–N(2)–C(20)–C(23) = 163.4° and the torsion angle C(7)–N(1)–N(2)–C(20) = 7.7(5)°]. Additionally, the complex shows again the envelope-like E_{Pd} conformation, with the Pd coordination plane [calculated as the plane fitting through P(1)–N(1)–Pd(1)–C(36)–Br(1)] strongly deviated from the plane containing the benzaldimine ring and the P and N atoms [plane fitting through P(1)–C(1)–C(2)–C(7)–N(1); dihedral angle between planes = 64.0°], with the Pd atom again placed on the opposite side of the Ph group at the nearest stereogenic center. Although X-ray structural analysis shows only one of the two possible atropoisomers in the solid state [(*Sa*) configuration in the C–Pd bond], this chiral axis proved to be configurationally labile in solution, and a free rotation around the C–Pd bond was observed at ~80 °C; variable-temperature ^{31}P NMR studies showed coalescence of ^{31}P signals to a single peak at 21.7 ppm. Isolated intermediate **27a** was treated with 2-methoxy-1-naphthylboronic acid **12c** to afford **13a** in a 65% yield and 68:32 er (70:30 er was obtained in the catalytic reaction).

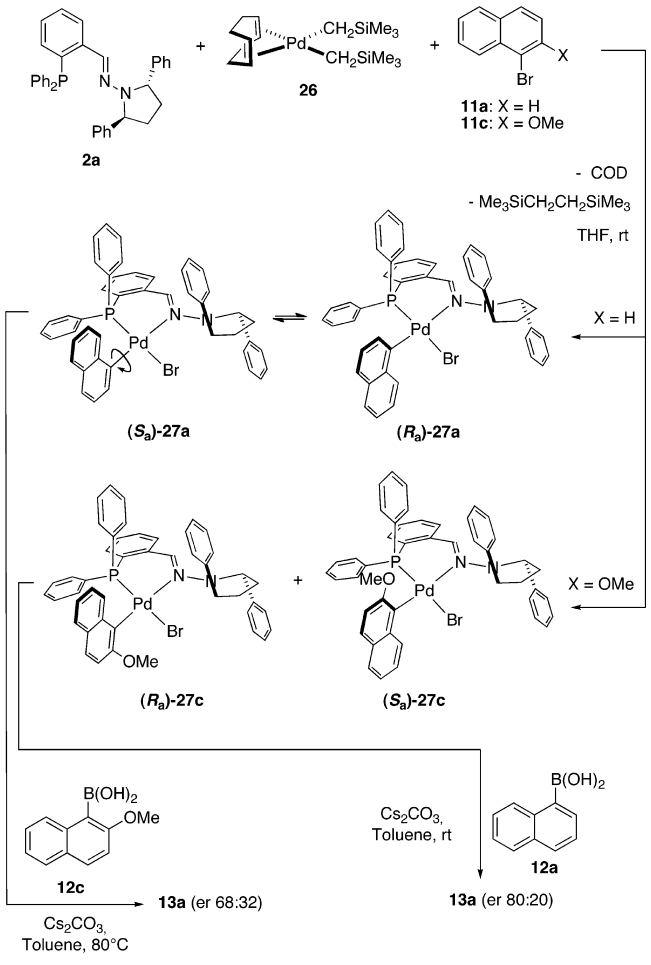
dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740–4750

Table 2. Asymmetric Suzuki–Miyaura Cross–couplings to Enantiomerically Enriched Biaryls

entry	ArX[a]	Ar′B(OH)$_2$	cat.	T (°C)	t (h)	product	conf	yield[b] (%)	er[c]
1	**11c**	**12a**	**10a**	rt	15	**13a**	*S*[d]	97	78:22
2	**11c**	**12a**	**10c**	rt	15	**13a**	*S*[d]	90	**90:10**
3	**11a**	**12c**	**10a**	80	28	**13a**	*S*[d]	93	69:31
4	**11b**	**12a**	**10c**	rt	14	**13b**	*R*[e]	87	74:26
5	**11d**	**12a**	**10c**	rt	24	**13c**	*S*[g]	66	77:23
6	**11e**	**12a**	**10a**	45	48	**13d**	*S*[g]	91	79:21
7	**11e**	**12a**	**10c**	45	48	**13d**	*S*[g]	30	82:18
8	**20a**	**12b**	**10c**	45	48	**23a**	*S*[f]	67	**91:9**
9	**20b**	**12b**	**10a**	45	24	**23a**	*S*[f]	95	**90:10**
10	**20b**	**12b**	**10c**	rt	72	**23a**	*S*[f]	55	**92:8**
11	**20c**	**12a**	**10c**	rt	6	**23b**	*S*[g]	73	87:13
12	**20c**	**12a**	**10c**	0	48	**23b**	*S*[g]	55	**89:11**
13	**20c**	**12e**	**10c**	rt	16	**23c**	*S*[g]	83	**91:9**
14	**20c**	**12f**	**10c**	rt	30	**23d**	*S*[g)]	65	**90:10**
15	**20c**	**22**	**10a**	rt	15	**24**	*R*[g]	88	86:14
16	**20c**	**22**	**10c**	rt	15	**24**	*R*[g]	74	86:14
17	**20c**	**22**	**10c**	0	72	**24**	*R*[g]	72	**91:9**
18	**21**	**12b**	**10c**	45	18	**25a**	*S*[g]	91	**89:11**
19	**21**	**12d**	**10c**	45	24	**25b**	*S*[g]	64	**86:14**

[a]Reactions were performed at 0.1 mmol scale using 5 mol % of catalyst. [b]Isolated yield after column chromatography. [c]Determined by HPLC on chiral stationary phases. [d]The absolute configuration was assigned by comparison with literature data. See ref 19 and the Supporting Information. [e]The absolute configuration was assigned by comparison with literature data. See ref 25 and the Supporting Information. [f]The absolute configuration was assigned by chemical correlation after oxidation and condensation with dimethylbenzylamine. See ref 6g and the Supporting Information. [g]The absolute configuration was assigned by analogy.

Scheme 3. Synthesis of Oxidative Addition Intermediates



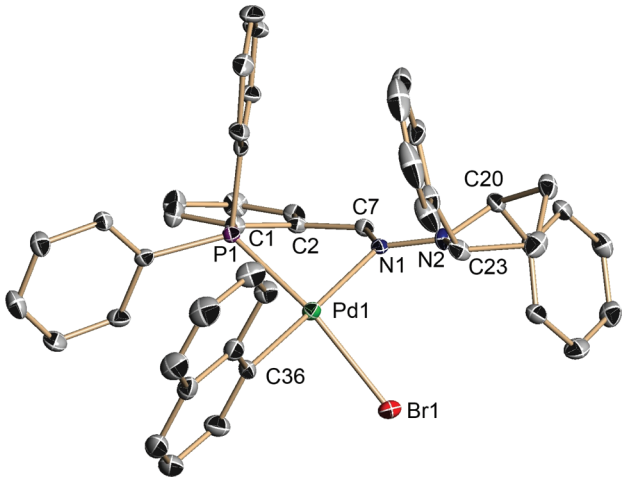


Figure 7. ORTEP drawing of intermediate **27a**.

Following the same procedure as before, but using 1-bromo-2-methoxynaphthalene **11c** as the starting material, intermediate **27c** was obtained as a 7:1 mixture of atropoisomers (^{31}P NMR: δ 25.4 and 26.1 ppm), but in this case the chiral axis proved to be stable at temperatures up to 80 °C. Treatment of this mixture with 1-naphthylboronic acid **12a** at rt resulted in the formation of the corresponding coupling product **13a** in 92% yield and 80:20 er (83:17 er was obtained in the catalytic reaction). These data suggest that both the oxidative addition and the transmetalation steps influence the stereochemical course of the reaction. In the case of less hindered aryl bromides (as demonstrated for **11a**, proposed by analogy for **20a**, **20b**, and **21**), a rapid interconversion of atropoisomeric C–Pd bonds takes place in the oxidative addition step that, therefore, appears to be irrelevant in terms of enantioselectivity. On the other

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740–4750

hand, the oxidative addition to more hindered aryl bromides affords configurationally stable intermediates and the stereochemical outcome in these cases could be mainly controlled by the oxidative addition step.

CONCLUSIONS

In conclusion, readily available heterobidentate C_2-symmetric phosphino hydrazones from 2,5-disubstituted 1-aminopyrrolidines constitute a useful ligand class with interesting structural features. As a first application, their corresponding L/$PdCl_2$ complexes have been used in the asymmetric Suzuki−Miyaura cross-coupling to afford functionalized biaryls in good yields and enantioselectivities, the scope being complementary to that of C_2-symmetric bis-hydrazones.

EXPERIMENTAL SECTION

General Experimental Methods. Solvents were purified and dried by standard procedures. Flash chromatography was carried out on silica gel (40−63 μm or 15−40 μm). Melting points were recorded in a metal block and are uncorrected. ^{1}H NMR spectra were recorded at 300, 400, or 500 MHz; ^{13}C NMR spectra were recorded at 75, 100 or 125 MHz, with the solvent peak used as the internal reference. CI and FAB mass spectra and high resolution mass spectra were recorded in an AUTOSPEC-Q mass spectrometer (three sectors high-resolution mass spectrometer with added quadrupole). EI mass spectra and high-resolution mass spectra were recorded in a QTRAP mass spectrometer (hybrid triple quadrupole/linear ion trap mass spectrometer). Comercially available boronic acids were used as received. 2-(Diphenylphosphino)benzaldehyde, 1-bromo-2-methylnaphtalene (90%), and (3*R*,6*R*)-2,7-dimethyl-3,6-octanediol were purchased from commercial suppliers. (2*S*,5*S*)-1-Amino-2,5-diphenylpyrrolidine and (2*S*,6*S*)-1-amino-2,6-diphenylpiperidine were prepared as described previously.[15] Palladium complex $[Pd(CH_3CN)_2Cl_2]$,[26] 1-bromo-2-methoxynaphthalene,[27] 1-naphthyl-2-methoxyboronic acid,[28] 1-naphthyl-2-methylboronic acid,[29] methyl 1-bromo-2-naphthoate,[30] 2-bromo-3-methylbenzaldehyde,[31] 7-trifluoromethanesulfonyl-1-indanone,[32] 2-acetylphenyl trifluoromethanesulfonate,[33] methyl 2-trifluoromethanesulfonyloxybenzoate,[34] and *o*-trifluoromethanesulfonyl salicylaldehyde[35] were prepared according to the literature procedures. Enantiomeric excesses (ee) were measured by HPLC on chiral stationary phases with ^{i}PrOH/*n*-hexane mixtures as the eluents.

General Procedure for the Synthesis of Phosphino Ethylene Acetals 15. A solution of 2-bromobenzaldehyde ethylene acetal **14** in Et_2O was cooled to −78 °C, and *t*-BuLi was added. The reaction mixture was stirred at −78 °C for 1 h, and then the corresponding chlorodiarylphosphine was added dropwise and the reaction was allowed to warm slowly to room temperature and was stirred overnight. H_2O was added, and the layers were separated. The aqueous portion was extracted with Et_2O, the combined organics were dried and concentrated, and the resulting residue was purified by flash chromatography. Yields and characterization data for compounds **15** are as follows:

2-(Di-4-methoxyphenylphosphino)benzaldehyde Ethylene Acetal (15d). Following the general procedure using 2-bromobenzaldehyde ethylene acetal **14** (2.97 mmol, 443 μL), *t*-BuLi (5.94 mmol), and chlorobis(4-methoxyphenyl)phosphine (3.56 mmol, 1 g), flash chromatography (EtOAc/hexane 1:7) gave **15d** (1.04 g, 88%) as a white foam. Spectroscopic and physical data matched those reported in the literature:[37] *m*/*z* (CI) 395 (M^+ + 1, 45), 366 (20), 365 (100), 321 (35), 287 (20); HRMS (CI) *m*/*z* calcd for $C_{23}H_{24}O_4P$ 395.1412, found 395.1419.

2-(Di-3,5-bistrifluoromethylphenylphosphino)benzaldehyde Ethylene Acetal (15e). Following the general procedure using 2-bromobenzaldehyde ethylene acetal **14** (1.69 mmol, 252 μL), *t*-BuLi (3.38 mmol), and chlorobis(3,5-bistrifluoromethylphenyl)phosphine (2.03 mmol, 1 g), flash chromatography (EtOAc/hexane 1:10) gave **15e** (734 mg, 72%) as a yellow foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 2H), 7.76−7.73 (m, 1H), 7.67 (d, 3H, *J* = 6.4 Hz), 7.52 (t, 1H, *J* = 7.6 Hz), 7.38 (t, 1H, *J* = 7.6 Hz), 6.94 (t, 1H, *J* = 6.4 Hz), 6.34 (d, 1H, *J* = 4 Hz), 4.06−3.95 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2 (d, *J* = 24 Hz), 140.0 (d, *J* = 17 Hz), 134.0, 133.0 (d, *J* = 19 Hz), 132.0 (d *J* = 6 Hz), 131.6 (m), 130.0, 129.6, 127.3 (d, *J* = 7 Hz), 122.9 (q, *J* = 271 Hz), 122.8 (m), 102.2 (d, *J* = 18 Hz), 65.1; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −14.2. *m*/*z* (CI) 607 (M^+ + 1, 75), 635 (20), 608 (20), 588 (30), 587 (100), 577 (85), 73 (45); HRMS (CI) *m*/*z* calcd for $C_{25}H_{16}O_2F_{12}P$ 607.0696, found 607.0689.

2-(Di-3,5-dimethylphenylphosphino)benzaldehyde Ethylene Acetal (15f). Following the general procedure using 2-bromobenzaldehyde ethylene acetal **14** (3 mmol, 447 μL), *t*-BuLi (6 mmol), and chlorobis(3,5-dimethylphenyl)phosphine (3.61 mmol, 1.0 g), flash chromatography (EtOAc/hexane 1:10) gave **15f** (720 mg, 61%) as a white foam: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, 1H, *J* = 7.2 and 3.6 Hz), 7.39 (t, 1H, *J* = 7.4 Hz), 7.29−7.25 (m, 1H), 7.01−6.98 (m, 1H), 6.95 (s, 2H), 6.88 (d, 4 H, *J* = 8 Hz), 6.44 (d, 1H, *J* = 4.8 Hz), 4.13−4.01 (m, 2H), 4.00−3.97 (m, 2H), 2.25 (s, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.0 (d, *J* = 21 Hz), 137.7 (d, *J* = 7 Hz), 136.6 (d, *J* = 9 Hz), 134.2, 131.4 (d, *J* = 20 Hz), 130.4, 129.7, 129.1 (d, *J* = 21 Hz), 126.2 (d, *J* = 6 Hz), 101.7 (d, *J* = 24 Hz), 65.4, 21.3; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −17.2. *m*/*z* (CI) 391 (M^+ + 1, 100), 390 (25); HRMS (CI) *m*/*z* calcd for $C_{25}H_{28}O_2P$ 391.1827, found 391.1823.

2-(Di-4-fluorophenylphosphino)benzaldehyde Ethylene Acetal (15g). Following the general procedure using 2-bromobenzaldehyde ethylene acetal **14** (3.25 mmol, 485 μL), *t*-BuLi (6.5 mmol), and chlorobis(4-fluorophenyl)phosphine (3.9 mmol, 1 g), flash chromatography (EtOAc/hexane 1:10) gave **15g** (650 mg, 54%) as a white foam. Spectroscopic and physical data matched those reported in the literature:[37] *m*/*z* (CI) 371 (M^+ + 1, 50), 351 (25), 341 (100), 297 (30); HRMS (CI) *m*/*z* calcd for $C_{21}H_{18}F_2O_2P$ 371.1012, found 371.0999.

2-(Di-*o*-tolylphosphino)benzaldehyde Ethylene Acetal (15h). Following the general procedure using 2-bromobenzaldehyde ethylene acetal **14** (4.8 mmol, 715 μL), *t*-BuLi (9.6 mmol), and chlorobis(*o*-tolyl)phosphine (4.02 mmol, 1.0 g), flash chromatography (EtOAc/hexane 1:10) gave **15h** (950 mg, 55%) as a white foam. Spectroscopic and physical data matched those reported in the literature.[38]

General Procedure for the Synthesis of Phosphine Aldehydes 16d−h. Ethylene acetal **15d−h** (1 mmol) was dissolved in acetone (14 mL) and H_2O (0.5 mL), and a catalytic amount of *p*-toluenesulfonic acid was added. The reaction mixture was heated to reflux overnight, cooled to rt, diluted with Et_2O, and washed with H_2O. The organic layer was dried, concentrated, and purified by flash chromatography. Yields and characterization data for compounds **16** are as follows:

2-(Di-4-fluorophenylphosphino)benzaldehyde (16d). Following the general procedure using 2-(di-4-methoxyphenylphosphino)-benzaldehyde ethylene acetal **15d** (2.01 mmol, 1.02 g), flash chromatography (EtOAc/hexane 1:7) gave **16d** (614 mg, 66%) as a yellow foam. Spectroscopic and physical data matched those reported in the literature:[37] *m*/*z* (CI) 350 (M^+, 85), 352 (25), 351 (100), 321 (25), 243 (20); HRMS (CI) *m*/*z* calcd for $C_{21}H_{19}O_3P$ 350.1072, found 350.1081.

2-(Di-3,5-bistrifluoromethylphenylphosphino)benzaldehyde (16e). Following the general procedure using 2-(di-3,5-bistrifluoromethylphenylphosphino)benzaldehyde ethylene acetal **15e** (1.21 mmol, 734 mg), flash chromatography (EtOAc/hexane 1:10) gave **16e** (560 mg, 82%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.12 (d, 1H, *J* = 3.5 Hz), 8.09−8.05 (m, 1H), 7.91 (s, 2H), 7.71 (t, 1H, *J* = 7.5 Hz), 7.68 (d, 3H, *J* = 6.5 Hz), 7.61 (t, 1H, *J* = 7.5 Hz), 6.87 (dd, 1H, *J* = 7.5 and 4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.0−191.9 (m), 139.7 (d, *J* = 18 Hz), 138.6 (dd, *J* = 15 and 6 Hz), 136.3 (dd, *J* = 29 and 3 Hz), 135.6 (dd, *J* = 10 and 4 Hz), 134.5 (d, *J* = 4 Hz), 133.8 (m), 132.9−132.0 (m), 130.4, 129.9, 123.7−123.6 (m), 123.2 (q, *J* = 271 Hz); ^{31}P NMR (202.4 MHz, $CDCl_3$) δ −11.6. *m*/*z* (CI) 563 (M^+ + 1, 100), 591 (25), 564 (25), 562 (75), 544 (25),

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740−4750

543 (90), 533 (20); HRMS (CI) m/z calcd for $C_{23}H_{12}OF_{12}P$ 563.0434, found 563.0451.

2-(Di-3,5-dimethylphenylphosphino)benzaldehyde (16f). Following the general procedure using 2-(di-3,5-dimethylphenylphosphino)benzaldehyde ethylene acetal **15f** (700 mg, 1.79 mmol), flash chromatography (EtOAc/hexane 1:10) gave **16f** (520 mg, 84%) as a white foam. Spectroscopic and physical data matched those reported in the literature.[39]

2-(Di-4-fluorophenylphosphino)benzaldehyde (16g). Following the general procedure using 2-(di-4-fluorophenylphosphino)-benzaldehyde ethylene acetal **15g** (1.31 mmol, 638 mg), flash chromatography (EtOAc/hexane 1:10) gave **16g** (402 mg, 69%) as a white foam: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.52 (d, 1H, J = 1.2 Hz), 7.99−7.95 (m, 1H), 7.88−7.84 (m, 1H), 7.60 (dd, 1H, J = 8.3 and 1.8 Hz), 7.50−7.48 (m, 3H), 7.37−7.33 (m, 3H), 7.30−7.27 (m, 2H), 6.99−6.97 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.7 (d, J = 19 Hz), 138.5 (d, J = 15 Hz), 136.1 (d, J = 9.8 Hz), 134.1 (d, J = 20 Hz), 133.7 (d, J = 28.2 Hz), 130.6 (d, J = 3.9 Hz), 128.9 (d, J = 31.1 Hz), 128.7 (d, J = 7 Hz); ^{31}P NMR (202.4 MHz, $CDCl_3$) δ −11.6 m/z (CI) 326 (M^+, 75), 327 (100), 307 (20), 297 (40); HRMS (CI) m/z calcd for $C_{19}H_{13}F_2OP$ 326.0672, found 326.0671.

2-(Di-*o*-tolylphosphino)benzaldehyde (16h). Following the general procedure using 2-(di-*o*-tolylphosphino)benzaldehyde ethylene acetal **15h** (920 mg, 2.54 mmol), flash chromatography (EtOAc/hexane 1:10) gave **16h** (729 mg, 90%) as a white foam. Spectroscopic and physical data matched those reported in the literature.[38]

2-(Dicyclohexylphosphoryl)benzaldehyde (17). Following the general procedure for the lithiation/phosphonylation step and using 2-bromobenzaldehyde ethylene acetal **14** (1.15 g, 5 mmol), the corresponding, oxidized phoshoryl acetal was obtained and used in the acetal deprotection step without purification. Following the general procedure for the acetal deprotection step, flash chromatography (EtOAc/*n*-hexane 1:2) gave **17** (1.2 g, 80%) as a colorless viscous oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.78 (br s, 1H), 8.01 (br s, 1H), 7.72−7.65 (m, 3H), 2.21−2.05 (m, 4H), 1.82−1.62 (m, 6H), 1.40−1.02 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.7, 132.7, 132.6, 131.5, 131.3, 36.3, 35.7, 26.3, 26.2, 26.1, 25.7, 25.6, 25.2; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ +50.8; HRMS (CI) m/z calcd for $C_{19}H_{27}O_2P$ 318.1749, found 318.1750.

General Procedure for the Synthesis of Hydrazones 2a−h and 18. Aldehyde **7**, **16d−h**, or **17** (1 mmol) was added to a stirred solution of the corresponding hydrazine (1.4 mmol) in toluene (2 mL). The reaction mixture was stirred at rt for 3 h, and then the reaction crude was concentrated to dryness and purified by flash chromatography. Yields and characterization data for compounds **2a−i** are as follows:

(2*S*,5*S*)-1-[2-(Diphenylphosphino)benzylideneamino]-2,5-diphenylpyrrolidine (2a). Following the general procedure, flash chromatography (toluene/*n*-hexane 1:2, 1% Et_3N) gave **2a** (683 mg, 97%) as a white foam: $[\alpha]^{20}_D$ −192.6 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.9−7.6 (m, 1H), 7.46 (d, 1H, J = 4.1 Hz), 7.32−7.09 (m, 20H), 6.94 (t, 2H, J = 7.5 Hz), 6.67 (d, 1H, J = 5.1 Hz), 5.00 (d, 2H, J = 5.9 Hz), 2.49−2.43 (m, 2H), 1.74−1.71 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.2, 140.7 (d, $J_{C,P}$ = 19 Hz), 137.1 (d, $J_{C,P}$ = 11 Hz), 136.1 (d, $J_{C,P}$ = 11 Hz), 133.9 (d, $J_{C,P}$ = 19 Hz), 133.6 (d, $J_{C,P}$ = 19 Hz), 132.9, 130.5 (d, $J_{C,P}$ = 26 Hz), 128.5, 128.3, 128.2, 126.6, 126.5, 126.4, 126.0, 124.3 (d, $J_{C,P}$ = 4 Hz), 65.2, 31.3; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −14.5; m/z (CI) 511 (M^+ + 1, 65), 288 (100), 222 (70); HRMS (CI) m/z calcd for $C_{35}H_{31}N_2P$ 511.2303, found 511.2307. Anal. Calcd for $C_{35}H_{31}N_2P$: C, 82.35; H, 6.07; N, 5.48. Found: C, 81.90; H, 6.17; N, 5.23.

(2*S*,5*S*)-1-[2-(Diphenylphosphino)benzylideneamino]-2,5-diphenylpiperidine (2b). Following the general procedure, flash chromatography (toluene/*n*-hexane 1:2, 1% Et_3N) gave **2b** (630 mg, 82%) as a white foam: $[\alpha]^{20}_D$ −148.3 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, 1H, J = 5.5 Hz), 7.49 (m, 1H), 7.39−7.29 (m, 12H), 7.25−7.20 (m, 6H), 7.14 (t, 1H, J = 7.5 Hz), 7.05 (t, 1H, J = 7.5 Hz), 7.01 (t, 1H, J = 7.5 Hz), 6.73 (dd, 1H, J = 7.5, 5.0 Hz), 4.98 (t, 2H, J = 5.5 Hz), 2.09−2.00 (m, 4H), 1.60−1.58 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.0, 141.0 (d, $J_{C,P}$ = 21 Hz), 137.1 (d, $J_{C,P}$ = 14 Hz), 136.1 (d, $J_{C,P}$ = 12 Hz), 133.8 (d, $J_{C,P}$ = 9 Hz), 133.7 (d, $J_{C,P}$ = 10 Hz), 133.1, 130.8 (d, $J_{C,P}$ = 28 Hz), 128.7, 128.5, 128.4, 128.3, 128.3, 128.1, 127.6, 126.9, 126.5, 125.9 (d, $J_{C,P}$ = 14 Hz), 124.2 (d, $J_{C,P}$ = 5 Hz), 61.1, 30.6, 18.5; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −16.0; m/z (CI) 525 (M^+ + 1, 10), 290 (60), 288 (20), 238 (100), 236 (70); HRMS (CI) m/z calcd for $C_{36}H_{34}N_2P$ 525.2460, found 525.2463.

(2*S*,5*S*)-1-[2-(Diphenylphosphino)benzylideneamino]-2,5-diisopropylpyrrolidine (2c). A solution of (3*R*,6*R*)-2,7-dimethyloctane-3,6-diol (244 mg, 1.40 mmol) and Et_3N (490 μL, 3.5 mmol, 2.5 equiv) in dry CH_2Cl_2 (3 mL) was cooled to −30 °C, and MsCl (275 μL, 3.5 mmol) was dropwise added. The reaction mixture was warmed to room temperature and was stirred overnight at this temperature. NH_4Cl (saturated aqueous solution, 5 mL) was added, and the organic phase washed with water, brine, and satd $NaHCO_3$. The organic layer was dried ($MgSO_4$), concentrated to dryness, and redissolved in 2-propanol (1.5 mL). $NH_2NH_2{\cdot}H_2O$ (2.0 mL, 42 mmol, 30 equiv) was then added, and reaction mixture was vigorously stirred at 60 °C for 14 h. The reaction crude was cooled to rt, diluted with Et_2O (10 mL), washed with satd $NaHCO_3$ (2 × 5 mL) and brine (1 × 5 mL), and dried ($MgSO_4$). The resulting crude hydrazine (1.38 mmol, 235 mg) was used according to the general procedure for the synthesis of hydrazones. Flash chromatography (toluene/hexane 1:2, 1% Et_3N) gave **2c** (519 mg, 85%) as a white foam: $[\alpha]^{20}_D$ −153.4 (c 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (ddd, 1H, J = 7.8, 4.2, 0.6 Hz), 7.45 (d, 1H, J = 5.1 Hz), 7.36−7.25 (m, 12H), 7.00 (t, 1H, J = 7.5 Hz), 6.68 (ddd, 1H, J = 7.7, 5.5, 0.9 Hz), 3.58 (m, 2H), 2.11−2.02 (m, 2H), 1.77−1.68 (m, 2H), 1.66−1.56 (m, 2H), 0.78 (d, 6H, J = 6.9 Hz), 0.58 (d, 1H, J = 6.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.6, 134.6, 134.3 (d, $J_{C,P}$ = 20 Hz), 133.9 (d, $J_{C,P}$ = 20 Hz), 132.8, 129.7, 128.7 (d, $J_{C,P}$ = 7 Hz), 128.5 (d, $J_{C,P}$ = 7 Hz), 128.4, 125.8, 123.3, 65.8, 28.2, 23.4, 19.4, 16.0; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −12.3; HRMS (CI) m/z calcd for $C_{29}H_{35}N_2P$ 442.2538, found 442.2540.

(2*S*,5*S*)-1-[2-(Di-4-methoxyphenylphosphino)benzylideneamino]-2,5-diphenylpyrrolidine (2d). Following the general procedure, flash chromatography (EtOAc/*n*-hexane 1:7) gave **2d** (656 mg, 83%) as a light yellow foam: $[\alpha]^{20}_D$ −92.0 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, 1H, J = 7.8, 4.2 Hz), 7.40 (d, 1H, J = 5.5 Hz), 7.30−7.24 (m, 5H), 7.20 (d, 2H, J = 7.2 Hz), 7.11 (dd, 6H, J = 6.8, 1.6 Hz), 6.96 (t, 1H, J = 7.6 Hz), 6.92−6.87 (m, 4H), 6.71 (d, 2H, J = 8.8 Hz), 6.67−6.63 (m, 1H), 5.01 (d, 2H, J = 6.8 Hz), 3.83 (s, 3H), 3.79 (s, 3H), 2.48−2.44 (m, 2H), 1.79−1.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9 (d, $J_{C,P}$ = 22 Hz), 143.2, 135.5 (d, $J_{C,P}$ = 21 Hz), 135.1 (d, $J_{C,P}$ = 21 Hz), 132.5, 128.4 (d, $J_{C,P}$ = 2 Hz), 128.3, 126.6, 126.4 (d, $J_{C,P}$ = 2 Hz), 126.1, 114.1 (d, $J_{C,P}$ = 4 Hz), 114.0 (d, $J_{C,P}$ = 4 Hz), 65.2, 55.2, 55.1, 31.3; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −17.0; m/z (CI) 569 (M^+ −1); HRMS (CI) m/z calcd for $C_{37}H_{34}N_2O_2P$ 569.2358, found 569.2349.

(2*S*,5*S*)-1-[2-(Di-3,5-bistrifluoromethyphenylphosphino)-benzylideneamino]-2,5-diphenylpyrrolidine (2e). Following the general procedure, flash chromatography (EtOAc/*n*-hexane 1:10) gave **2e** (973 mg, 90%) as a light yellow viscous oil: $[\alpha]^{20}_D$ −59.1 (c 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.61 (s, 1H), 7.43−7.40 (m, 3H), 7.33 (d, 2H, J = 6.4 Hz), 7.29 (d, 1H, J = 8.4 Hz), 7.23 (d, 4H, J = 7.6 Hz), 7.19−7.14 (m, 3H), 7.06−7.00 (m, 5H), 6.50 (dd, 1H, J = 6.6, 4.4 Hz), 4.95 (d, 2H, J = 6.8 Hz), 2.47−2.42 (m-2H), 1.78−1.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 142.0, 140.9, 133.7, 133.6 (m), 133.4 (m), 132.8 (m), 132.6 (m), 129.9 (q, $J_{C,F}$ = 272 Hz), 129.8, 128.5, 128.4, 127.4 (d, $J_{C,P}$ = 11 Hz), 126.9, 125.9, 122.5−122.4 (m), 65.1, 31.1; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −9.7. m/z (CI) 782 (M^+); HRMS (CI) m/z calcd for $C_{39}H_{27}F_{12}N_2P$ 782.1720, found 782.1717.

(2*S*,5*S*)-1-[2-(Di-3,5-dimethylphenylphosphino)-benzylideneamino]-2,5-diphenylpyrrolidine (2f). Following the general procedure, flash chromatography (EtOAc/*n*-hexane 1:15) gave **2f** (724 mg, 92%) as a light yellow viscous oil: $[\alpha]^{20}_D$ −125.0 (c 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (ddd, 1H, J = 8.0, 4.3, 1.3 Hz), 7.48 (d, 1H, J = 4.8 Hz), 7.27−7.23 (m, 4H), 7.19−7.15 (m, 2H), 7.14−7.12 (m, 4H), 6.99−6.95 (m, 2H), 6.86−6.85 (m, 1H),

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740−4750

6.81−6.79 (m, 2H), 6.71−6.68 (m, 1H), 6.62−6.59 (m, 2H), 5.03 (d, 2H, J = 6.8 Hz), 2.54−2.37 (m-2H), 2.27 (s, 6H), 2.20 (s, 6H), 1.82−1.74 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.2, 137.5 (d, $J_{C,P}$ = 7 Hz), 137.3 (d, $J_{C,P}$ = 7 Hz), 133.1, 131.8 (d, $J_{C,P}$ = 20 Hz), 131.3 (d, $J_{C,P}$ = 19 Hz), 130.2, 128.3 (d, $J_{C,P}$ = 4 Hz), 128.2, 126.6, 126.5, 126.1, 124.2 (d, $J_{C,P}$ = 4 Hz), 65.3, 31.4, 21.3, 21.2; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −14.7; m/z (CI) 782 (M^+); HRMS (CI) m/z calcd for $C_{39}H_{39}N_2P$ 566.2851, found 566.2847.

(2*S*,5*S*)-1-[2-(Di-4-fluorophenylphosphino)benzylideneamino]-2,5-diphenylpyrrolidine (2g). Following the general procedure, flash chromatography (EtOAc/*n*-hexane 1:20) gave **2g** (587 mg, 78%) as a white foam: $[\alpha]^{20}_D$ −108.3 (c 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.61 (m, 1H), 7.37−7.30 (m, 2H), 7.26−7.14 (m, 6H), 7.14−7.07 (m, 6H), 7.04−6.97 (m, 4H), 6.91−6.81 (m, 3H), 6.61−6.58 (m, 1H), 5.02 (d, 2H, J = 6.8 Hz), 2.53−2.42 (m, 2H), 1.81−1.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 135.9 (dd, J = 21, 8 Hz), 135.3 (dd, J = 21, 8 Hz), 134.0 (d, J = 20 Hz), 133.7 (d, J = 20 Hz), 133.0, 132.6, 129.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 126.7, 126.6, 126.4, 126.1, 126.0, 124.8 (d, $J_{C,P}$ = 4 Hz), 65.2, 31.4; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ −16.2; m/z (CI) 546 (M^+); HRMS (CI) m/z calcd for $C_{35}H_{29}F_2N_2P$ 546.2036, found 546.2035.

(2*S*,5*S*)-1-[2-(Di-*o*-tolylphosphino)benzylideneamino)-2,5-diphenylpyrrolidine (2h). Following the general procedure, flash chromatography (toluene/*n*-hexane 1:2) gave **2h** (635 mg, 85%) as a light yellow foam: $[\alpha]^{20}_D$ −138.2 (c 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, 1H, J = 7.3 and 4.3 Hz), 7.50 (d, 1H, J = 5.5 Hz), 7.24−7.23 (m, 5H), 7.20−7.17 (m, 4H), 7.12−7.10 (m, 3H), 7.07−7.05 (m, 1H), 6.95 (t, 2H, J = 7.3 Hz), 6.68 (dd, 1H, J = 6.8, 4.3 Hz), 6.60 (dd, 1H, J = 7.0, 4.5 Hz), 6.54 (dd, 1H, J = 6.8, 4.3 Hz), 5.02 (d, 2H, J = 6.5 Hz), 2.49−2.45 (m-2H), 2.27 (s, 3H), 2.06 (s, 3H), 1.78−1.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.1, 142.4 (d, $J_{C,P}$ = 26 Hz), 141.3 (d, $J_{C,P}$ = 17 Hz), 134.8 (d, $J_{C,P}$ = 46 Hz), 133.4 (d, $J_{C,P}$ = 33 Hz), 132.9, 129.9 (d, $J_{C,P}$ = 5 Hz), 128.6, 128.4, 128.3, 126.8, 126.6, 126.1, 126.0, 125.9, 125.8, 124.2, 65.3, 31.4, 26.9; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ −31.2. m/z (EI) 538 (M^+); HRMS (EI) m/z calcdfor $C_{37}H_{35}N_2P$ 538.2538, found 538.2540.

(2*S*,5*S*)-1-[2-(Dicyclohexylphosphoryl)benzylideneamino]-2,5-diphenylpyrrolidine (18). Following the general procedure, flash chromatography (EtOAc/*n*-hexane 1:2) gave **18** (491 mg, 66%) as a light yellow foam: $[\alpha]^{20}_D$ −100.0 (c 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.36 (m, 4H), 7.32−7.27 (m, 9H), 7.14 (br s, 1H), 5.26 (br s, 2H), 2.62−2.56 (m, 2H), 1.90−1.81 (m, 4H), 1.77−1.45 (m, 8H), 1.42−0.85 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 130.6, 128.5, 126.8, 126.4, 126.2, 125.2 (d, $J_{C,P}$ = 9 Hz), 65.3 (br s), 37.3 (d, $J_{C,P}$ = 67 Hz), 31.3, 26.5 (d, $J_{C,P}$ = 12 Hz), 26.4, 26.3, 26.2, 26.2, 26.1, 24.8; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ + 50.5; HRMS (EI) m/z calcd for $C_{35}H_{43}N_2OP$ 538.3113, found 538.3112.

(2*S*,5*S*)-1-[2-(Dicyclohexylphosphino)benzylideneamino]-2,5-diphenylpyrrolidine (2i). To a stirred solution under argon of **18** (0.5 mmol, 269 mg) in dry toluene (8 mL) were added dry Et_3N (15 mmol, 2.1 mL) and $HSiCl_3$ (7.5 mmol, 750 μL). The reaction mixture was stirred at 110 °C for 24 h, satd $NaHCO_3$ (1 mL) was added, and the reaction crude was filtered through Celite and concentrated to dryness. Flash chromatography (EtOAc/*n*-hexane 1:20) gave **2i** (150 mg, 57%) as a yellow foam: $[\alpha]^{20}_D$ −82.2 (c 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, 1H, J = 5.0 Hz), 7.75 (dd, 1H, J = 7.6, 3.0 Hz), 7.35−7.32 (m, 4H), 7.29−7.26 (m, 4H), 7.22−7.20 (m, 3H), 7.12 (t, 1H, J = 7.6 Hz), 7.05 (d, 1H, J = 7.6 Hz), 5.22 (d, 2H, J = 6.5 Hz), 2.61−2.52 (m, 2H), 1.88−1.72 (m, 4H), 1.70−1.55 (m, 4H), 1.53−1.39 (m, 4H), 1.36−1.15 (m, 8H), 1.05−0.85 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 131.9 (d, $J_{C,P}$ = 35 Hz), 128.4, 128.2, 126.6, 126.3, 125.5, 124.0 (d, $J_{C,P}$ = 4 Hz), 65.0, 34.0 (d, $J_{C,P}$ = 15 Hz), 32.1 (d, $J_{C,P}$ = 12 Hz), 31.4, 30.0 (br s), 29.7, 29.3, 34.0 (d, $J_{C,P}$ = 8 Hz), 27.9, 27.4 (d, $J_{C,P}$ = 14 Hz), 27.1 (d, $J_{C,P}$ = 8 Hz), 27.0 (d, $J_{C,P}$ = 13 Hz), 26.8 (d, $J_{C,P}$ = 9 Hz), 26.4, 26.1; ^{31}P NMR (202.4 MHz, $CDCl_3$) δ −18.7; HRMS (EI) m/z calcd for $C_{35}H_{43}N_2P$ 522.3164, found 522.3162.

General Procedure for the Synthesis of Palladium Complexes 10a−c. A solution of **2a−c** (0.3 mmol) in dry CH_2Cl_2 (5 mL) under argon was transferred via cannula to a deoxygenated round-bottom flask containing $[PdCl_2(CH_3CN)_2]$ (0.3 mmol, 75 mg). The reaction mixture was stirred at room temperature overnight, concentrated to dryness, washed with *n*-pentane, and dried in vacuo to give the palladium dichloride complex. Yields and characterization data for compounds **10a−c** are as follows:

(2*S*,5*S*)-1-[2-(Diphenylphosphino)benzylideneamino]-2,5-diphenylpyrrolidine $PdCl_2$ complex (10a). Prepared according to the general procedure, **10a** was obtained as an orange solid (167 mg, 84%). X-ray quality crystals were grown by slow diffusion of *n*-hexane into a solution of **10a** in CH_2Cl_2: mp = 206−208 °C dec; $[\alpha]^{20}_D$ = −806.7 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, CD_2Cl_2, 25 °C) δ 7.46−7.03 (m, 22H), 6.92 (dd, 1H, J = 7.5, 4.5 Hz), 6.76 (dd, 1H, J = 10.2, 8.1 Hz), 6.09 (br s, 2H), 2.61 (br s, 2H), 1.82 (br s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2, 25 °C) δ 140.3 (d, J_{C-P} = 8 Hz), 138.5 (d, J_{C-P} = 14 Hz), 134.7, 134.6, 134.0 (d, J_{C-P} = 11 Hz), 133.7 (d, J_{C-P} = 9 Hz), 133.1, 132.8 (d, J_{C-P} = 11 Hz), 132.4, 131.7, 130.5 (d, J_{C-P} = 8 Hz), 129.5 (d, J_{C-P} = 12 Hz), 129.3, 129.1, 128.8 (d, J_{C-P} = 12 Hz), 128.2 (d, J_{C-P} = 11 Hz), 128.0, 127.8, 126.4, 124.6 (d, J_{C-P} = 51 Hz), 117.8 (d, J_{C-P} = 51 Hz), 67.4 (br s), 32.2; ^{31}P NMR (202.4 MHz, CD_2Cl_2) δ +28.1. m/z (CI) 616 (M^+ − 2 Cl, 4), 511 (13), 288 (100); HRMS (CI) m/z calcd for $C_{35}H_{31}N_2PPd$ 616.1260, found 616.1274.

(2*S*,5*S*)-1-[2-(Diphenylphosphinobenzylideneamino]-2,5-diphenylpiperidine $PdCl_2$ Complex (10b). Prepared according to the general procedure, starting from **2b** (0.23 mmol, 118 mg) and $[PdCl_2(CH_3CN)_2]$ (0.23 mmol, 59 mg), **10b** was obtained as an orange solid (147 mg, 91%): mp = 178−180 °C; $[\alpha]^{20}_D$ = −261.8 (c 0.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 7.67−6.95 (m, 24H), 6.72 (dd, 1H, J = 9.9, 7.8 Hz), 6.50 (br s, 1H), 2.10−1.92 (m, 2H), 1.70−1.55 (m, 2H), 1.50−1.36 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 148.0 (d, J_{C-P} = 9 Hz), 141.5, 136.8 (d, J_{C-P} = 11 Hz), 134.2 (d, J_{C-P} = 10 Hz), 134.0, 133.2 (d, J_{C-P} = 10 Hz), 132.8 (d, J_{C-P} = 12 Hz), 132.3 (d, J_{C-P} = 20 Hz), 131.5, 131.0 (d, J_{C-P} = 8 Hz), 129.0, 128.8, 128.1, 127.9 (d, J_{C-P} = 13 Hz), 126.9 (br s), 126.0 (d, J_{C-P} = 25 Hz), 125.2, 124.5 (d, J_{C-P} = 51 Hz), 118.7 (d, J_{C-P} = 51 Hz), 64.3, 29.6, 18.1; ^{31}P NMR (161.7 MHz, $CDCl_3$, 25 °C) δ + 28.5. m/z (FAB) 665 (M^+ − Cl, 24), 629, 154; HRMS (FAB) m/z calcd for $C_{36}H_{33}N_2PClPd$ 665.1105, found 665.1112.

(2*S*,5*S*)-1-[2-(Diphenylphosphino)benzylideneamino]-2,5-isopropylpyrrolidine $PdCl_2$ Complex (10c). Prepared according to the general procedure, **10c** was obtained as an orange solid (160 mg, 89%). X-ray quality crystals were grown by slow diffusion of diethyl ether into a solution of **10c** in CH_2Cl_2: mp = 153−155 °C; $[\alpha]^{20}_D$ = −1036.0 (c 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C) δ 7.60 (br s, 2H), 7.50−7.37 (m, 10H), 7.23 (t, 1H, J = 7.0 Hz), 7.09 (m, 1H), 6.68 (dd, 1H, J = 9.5, 8.1 Hz), 2.33 (br s, 2H), 1.89 (br s, 2H), 1.75 (br s, 2H), 1.65 (br s, 2H), 0.84 (br d, J = 5.4 Hz, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) broad signals were observed at 295 K; some peaks were not observed, δ 134.8 (d, J_{C-P} = 10 Hz), 134.1, 133.1, 132.9, 132.6 (d, J_{C-P} = 10 Hz), 132.0, 131.8, 129.9 (d, J_{C-P} = 8 Hz), 129.3 (d, J_{C-P} = 11 Hz), 128.1 (d, J_{C-P} = 12 Hz), 22.7, 19.6, 16.0; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ +28.1; m/z (CI) 548 (M^+ − 2Cl, 20), 442 (100); HRMS (CI) m/z calcd for $C_{29}H_{35}N_2PPd$ (M^+ − 2Cl) 547.9210, found 547.9203.

Isolation of Intermediate 27a. Following a described procedure,[6g] a Schlenk tube was charged inside a drybox with ligand **2a** (0.1 mmol, 39 mg) and $[Pd(cod)(CH_2TMS)_2]$ (0.1 mmol, 39 mg). The Schlenk tube was placed outside the drybox, and after cycles of vacuum−argon, a solution of 1-bromonaphthalene (0.1 mmol, 28 μL) in dry and deoxygenated THF (3 mL) was transferred via cannula. The reaction mixture was stirred overnight at rt, and the precipitation of a yellow solid was observed. The mixture was concentrated to dryness, and the yellow solid was washed with dry, deoxygenated *n*-hexane and dried in vacuum to obtain 58 mg (70%) of product. X-ray quality crystals were obtained by slow evaporation of a solution of **27a** in CH_2Cl_2/acetone mixture: mp = 160−162 °C dec; $[\alpha]^{20}_D$ = −267.0 (c 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) a 1:1 mixture of diastereoisomers in the C−Pd bond was observed at this temperature, δ 8.56 (t, 1H, J = 7.6 Hz), 7.52−6.93 (m, 27H), 6.88 (br s, 1H), 6.73 (br s, 2H), 6.45−6.36 (br s, 2H), 6.21 (t, 1H, J = 8.8 Hz), 2.70 (br s, 2H), 1.80 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C) broad signals were observed at 25 °C and

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740−4750

some peaks were not observed, δ 139.8, 139.1, 138.6, 138.0, 135.4, 134.6, 134.0, 133.8, 133.6, 133.4, 133.2, 132.6, 132.5, 132.4, 131.9, 131.8, 131.4, 131.3, 130.7, 130.5, 129.3, 129.1, 128.8, 128.7, 128.6, 128.5, 128.2, 127.4, 127.3, 127.2, 127.0, 126.8, 126.2, 125.5, 124.3, 123.7, 123.4, 122.9, 122.7, 122.5, 65.7 (br s), 31.5, 31.2; ^{31}P NMR (161.7 MHz, $CDCl_3$) δ +22.2, 21.7 (^{31}P signals coalesce to only one peak at 21.7 ppm at 80 °C); HRMS (CI) *m*/*z* calcd for $C_{45}H_{38}BrN_2PPd$ 822.0991, found 822.0989.

General Procedure for the Suzuki Coupling Reactions. In a typical run, a dried Schlenk tube containing a magnetic stir bar was charged with Cs_2CO_3 (2 equiv, 65.2 mg), 5 mol % of catalyst, and boronic acid (0.15 mmol). After cycles of vacuum−argon (three times), dry solvent (0.5 mL) and aryl bromide or triflate (0.1 mmol) were added (solid aryl bromides or triflates were added during the initial charge). The Schlenk tube was sealed, and the reaction mixture was stirred at rt−80 °C until consumption of the aryl bromide (by TLC). The reaction mixture was filtered through Celite and concentrated under reduced pressure, and the crude was purified by flash chromatography using *n*-hexane or *n*-hexane/EtOAc mixture as solvents. Yields and characterization data for compounds **13**, and **23**−**25** are as follows:

(*S*)-2-Methoxy-1,1′-binaphthyl (13a) (Table 2, Entry 2). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 15 h at room temperature, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 200:1) gave 25.6 mg (90%) of the title compound as a white solid: $[\alpha]^{20}_D$ +8.0 (*c* 1.0, $CHCl_3$) for 80% ee [lit.[40] $[\alpha]^{25}_D$= −31.4 (*c* 2.1, THF) for (*R*)-enantiomer with 99% ee]. Spectroscopic and physical data matched those reported in the literature.[12] HPLC (Chiracel OJ, 2-propanol/*n*-hexane 5:95, flow 1.0 mL/min, *T* = 30 °C) t_R 10.76 min (major) and 21.08 min (minor).

(*R*)-2-Methyl-1,1′-binaphthyl (13b) (Table 2, Entry 5). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 14 h at room temperature, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 200:1) gave 23.4 mg (87%) of the title compound as a white solid: $[\alpha]^{20}_D$ −15.0 (*c* 0.9, $CHCl_3$) for 49% ee [lit.[25] $[\alpha]^{20}_D$= −43.9 (*c* 1.0, $CHCl_3$) for (*R*)-enantiomer with 99% ee]. Spectroscopic and physical data matched those reported in the literature.[25] HPLC (Chiracel OJ, 2-propanol/*n*-hexane 5:95, flow 1.0 mL/min, *T* = 30 °C) t_R 6.78 min (major) and 11.19 min (minor).

Methyl (1,1′-Binaphthyl)-2-carboxaldehyde (13c) (Table 2, Entry 6). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 24 h at room temperature, flash chromatography (*n*-hexane/toluene 2:1) gave 18.6 mg (66%) of the title compound as a colorless oil: $[\alpha]^{20}_D$ +54.0 (*c* 1.1, $CHCl_3$) for 54% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.69 (d, 1H, *J* = 1.0 Hz), 8.16 (d, 1H, *J* = 8.5 Hz), 8.05 (d, 1H, *J* = 3.5 Hz), 8.03 (d, 1H, *J* = 3.5 Hz), 7.98 (t, 2H, *J* = 7.5 Hz), 7.66−7.59 (m, 2H), 7.52−7.49 (m, 2H), 7.39−7.37 (m, 1H), 7.35−7.30 (m, 2H), 7.22 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 144.9, 136.1, 133.5, 133.3, 133.0, 132.9,132.1, 129.2, 128.9, 128.8, 128.7, 128.3, 128.2, 127.7, 127.0, 126.8, 126.3, 126.2,125.0, 122.1; HRMS (CI) *m*/*z* calcd for $C_{21}H_{14}O$ 282.1045, found 282.1046; HPLC (Daicel Chiralpak IC, 2-propanol/*n*-hexane 1:99, flow 1.0 mL/min, *T* = 30 °C) t_R 9.86 min (minor) and 10.55 min (major).

Methyl (1,1′-Binaphthyl)-2-carboxylate (13d) (Table 2, Entry 7). Following the general procedure, using the catalyst **10a** (5 mol %, 3.4 mg) and toluene (0.5 mL) as solvent, after 48 h at 45 °C, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 200:1) gave 28.4 mg (91%) of the title compound as a white solid: $[\alpha]^{20}_D$ −18.0 (*c* 0.9, $CHCl_3$) for 59% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88−7.73 (m, 5H), 7.40−7.22 (m, 3H), 7.16−6.98 (m, 5H), 3.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 140.2, 136.9, 134.8, 133.2, 133.1, 132.9, 128.6, 128.2, 128.1, 128.0, 127.8, 127.8, 127.6, 126.9, 126.7, 126.0, 126.0, 125.7, 125.7, 125.1, 51.8; *m*/*z* (CI) 313 (M^+ + 1, 100); HRMS (CI) *m*/*z* calcd for $C_{22}H_{17}O_2$ 313.1228, found 313.1226; HPLC (Chiracel OJ, 2-propanol/*n*-hexane 5:95, flow 1.0 mL/min, *T* = 30 °C) t_R 11.17 min (major) and 14.08 min (minor).

2-(2′-Methylnaphthyl)benzaldehyde (23a) (Table 2, Entry 9). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 48 h at 45 °C, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 100:1) gave 16.5 mg (67%) of the title compound as a white solid: $[\alpha]^{20}_D$ −21.0 (*c* 1.1, $CHCl_3$) for 82% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.13 (d, 1H, *J* = 8.0 Hz), 7.85 (t, 2H, *J* = 8.0 Hz), 7.72 (t, 1H, *J* = 7.5 Hz), 7.58 (t, 1H, *J* = 7.0 Hz), 7.46−7.43 (m, 2H), 7.37−7.32 (m, 2H), 7.19 (d, 1H, *J* = 9.5 Hz) 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.1, 143.8, 134.7, 134.2, 133.3, 133.2, 131.8, 131.5, 128.3, 128.2, 128.1, 127.9, 127.2, 126.5, 125.7, 125.2, 20.8; *m*/*z* (EI) 246 (M^+, 100); HRMS (EI) *m*/*z* calcd for $C_{18}H_{14}O$ 246.1045, found 246.1049; HPLC (Daicel Chiralpak IC, 2-propanol/*n*-hexane 1:99, flow 1.0 mL/min, *T* = 30 °C) t_R 7.9 min (major) and 9.3 min (minor).

3-Methyl-2-naphthylbenzaldehyde (23b) (Table 2, Entry 13). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 48 h at 0 °C, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 100:1) gave 14.0 mg (55%) of the title compound as a colorless oil: $[\alpha]^{20}_D$ + 242.0 (*c* 0.55, $CHCl_3$) for 79% ee; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.46 (d, 1H, *J* = 0.9 Hz), 7.93−7.96 (m, 3H), 7.60−7.48 (m, 4H), 7.40−7.27 (m, 3H), 1.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.5, 143.6, 138.3, 135.4, 135.2,134.4, 133.5, 132.5, 128.5, 128.4, 128.0, 127.9, 126.8, 126.2, 125.6, 125.2, 124.6, 19.5; *m*/*z* (EI) 246 (M^+, 100); HRMS (EI) *m*/*z* calcd for $C_{18}H_{14}O$ 246.1045, found 246.1048. HPLC (Daicel Chiralpak IC, 2-propanol/*n*-hexane 1:99, flow 1.0 mL/min, *T* = 30 °C) t_R 11.1 min (major) and 11.8 min (minor).

3-Methyl-2-acenaphthalenebenzaldehyde (23c) (Table 2, Entry 14). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 16 h at room temperature flash chromatography (toluene/*n*-hexane 1:2) gave 22.5 mg (83%) of the title compound as a colorless oil: $[\alpha]^{20}_D$ +44.0 (*c* 1.65, $CHCl_3$) for 82% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.52 (d, 1H, *J* = 0.8 Hz), 7.93 (dd, 1H, *J* = 7.8, 0.7 Hz), 7.58 (dd, 1H, *J* = 7.5, 0.6 Hz), 7.39−7.36 (m, 2H), 7.32 (d, 1H, *J* = 6.8 Hz), 7.28 (d, 1H, *J* = 7.0 Hz), 3.48 (s, 4H), 2.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.9, 146.5, 146.4, 143.5, 139.2, 138.5, 135.4, 135.3, 130.9, 129.7, 129.6, 128.6, 127.8, 124.6, 120.7, 119.8, 118.8, 30.6, 30.2, 19.7; HRMS (EI) *m*/*z* calcd for $C_{20}H_{16}O$ 272.1201, found 272.1203; HPLC (Daicel Chiralpak IC, 2-propanol/*n*-hexane 1:99, flow 1.0 mL/min, *T* = 30 °C) t_R 9.68 min (major) and 10.20 min (minor).

3-Methyl-2-acenaphthalenebenzaldehyde (23d) (Table 2, Entry 15). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 30 h at room temperature, flash chromatography (toluene → *n*-hexane 1:2) gave 16.8 mg (65%) of the title compound as a colorless oil: $[\alpha]^{20}_D$ +51.0 (*c* 0.55, $CHCl_3$) for 80% ee; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 (d, 1H, *J* = 1 Hz), 8.10 (d, 1H, *J* = 8.5 Hz), 7.94 (dd, 1H, *J* = 7.8, 0.8 Hz), 7.59−7.53 (m, 2H), 7.49 (t, 1H, *J* = 6.8 Hz), 7.42−7.38 (m, 2H), 7.30 (dd, 1H, *J* = 8.0, 0.5 Hz), 7.23 (d, 1H, *J* = 7.0 Hz), 2.79 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.7, 144.0, 138.5, 135.4, 135.3,134.8, 132.6, 132.5, 132.4, 127.9, 127.6, 126.3, 126.2, 126.0, 124.6, 124.5; HRMS (EI) *m*/*z* calcd for $C_{19}H_{16}O$ 260.1201, found 260.1203; HPLC (Daicel Chiracel OJ, 2-propanol/*n*-hexane 1:99, flow 1.0 mL/min, *T* = 30 °C) t_R 6.83 min (major) and 8.96 min (minor).

3-Methyl-2-(*o*-tolyl)benzaldehyde (24) (Table 2, Entry 18). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 72 h at room temperature, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 100:1) gave 15 mg (72%) of the title compound as a colorless oil: $[\alpha]^{20}_D$ +37.0 (*c* 0.59, $CHCl_3$) for 82% ee; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.61 (d, 1H, *J* = 0.6 Hz), 7.86 (d, 1H, *J* = 7.2 Hz), 7.54 (dd, 1H, *J* = 7.5, 0.6 Hz), 7.43−7.27 (m, 4H), 7.10 (d, 1H, *J* = 7.2 Hz), 2.04 (s, 3H), 1.99 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.7, 145.1, 137.3, 136.3, 136.2, 135.5, 134.1, 130.1, 129.6, 128.1, 127.6, 125.9, 124.6, 19.9, 19.4; *m*/*z* (EI) 210 (M^+, 100); HRMS (EI) *m*/*z* calcd for $C_{15}H_{14}O$ 210.1045, found 210.1042; HPLC (Daicel Chiralpak IB, 2-propanol/*n*-hexane 0.1:99.9, flow 1.0 mL/min, *T* = 30 °C) t_R 8.9 (minor) and 9.5 min (major).

7-(2′-Methylnaphthyl)-1-indanone (25a) (Table 2, Entry 19). Following the general procedure, using the catalyst **10c** (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 12 h at 45 °C, flash

dx.doi.org/10.1021/jo300548z | J. Org. Chem. 2012, 77, 4740−4750

chromatography (*n*-hexane → *n*-hexane/EtOAc 100:1) gave 24.8 mg (91%) of the title compound as a white solid: $[\alpha]^{20}_{D}$ +296.0 (*c* 1.06, $CHCl_3$) for 78% ee; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (t, 2H, *J* = 8.1 Hz), 7.69 (t, 1H, *J* = 7.5 Hz), 7.57 (dd, 1H, *J* = 7.8, 0.9 Hz), 7.42 (d, 1H, *J* = 8.4 Hz), 7.37 (ddd, 1H, *J* = 8.0, 6.8, 1.2 Hz), 7.25 (ddd, 1H, *J* = 8.4, 6.8, 1.5 Hz), 7.18 (dd, 1H, *J* = 7.5, 0.8 Hz), 7.13 (d, 1H, *J* = 8.4 Hz), 3.22 (t, 2H, *J* = 6.0 Hz), 2.64−2.60 (m, 2H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0, 155.9, 138.5, 135.2, 134.6, 134.0, 132.9, 132.6, 131.9, 130.0, 128.4, 127.9, 127.4, 125.9, 125.6, 125.2, 124.5, 36.5, 25.5, 20.4; *m*/*z* (EI) 272 (M^+, 100); HRMS (EI) *m*/*z* calcd for $C_{20}H_{16}O$ 272.1201, found 272.1201; HPLC (Daicel Chiralpak IC, 2-propanol/*n*-hexane 10:90, flow 1.0 mL/min, *T* = 30 °C) t_R 14.2 min (minor) and 25.5 min (major).

7-(2′-Cyclohexylnaphthyl)-1-indanone (25b) (Table 2, Entry 20). Following the general procedure, using the catalyst 10c (5 mol %, 3.1 mg) and toluene (0.5 mL) as solvent, after 12 h at 45 °C, flash chromatography (*n*-hexane → *n*-hexane/EtOAc 100:1) gave 22 mg (64%) of the title compound as a white solid: $[\alpha]^{20}_{D}$ +135.0 (*c* 0.96, $CHCl_3$) for 72% ee; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, 1H, *J* = 6.8 Hz), 7.83 (d, 1H, *J* = 6.8 Hz), 7.67 (td, 1H, *J* = 6.0, 1.6 Hz), 7.58 (d, 1H, *J* = 6.0 Hz), 7.55 (dd, 1H, *J* = 6.8, 1.2 Hz), 7.34 (t, 1H, *J* = 5.6 Hz), 7.23 (t, 1H, *J* = 6.2 Hz), 7.16 (d, 1H, *J* = 6.0 Hz), 7.02 (d, 1H, *J* = 6.8 Hz), 3.24 (t, 2H, *J* = 4.2 Hz), 2.63−2.60 (m, 2H), 2.27 (t, 1H, *J* = 9.0 Hz), 1.73−1.71 (m, 4H), 1.63 (d, 1H, *J* = 10.4 Hz), 1.55−1.49 (m, 2H), 1.25−1.20 (m, 1H), 1.11−1.03 (m, 2H), 0.9−0.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 155.6, 142.1, 138.4, 135.5, 133.8, 133.6, 132.6, 131.7, 130.1, 127.8, 125.8, 125.6, 125.5, 124.6, 124.3, 41.8, 36.5, 34.4, 32.0, 29.6, 26.7, 26.1, 25.5; *m*/*z* (EI) 341 (M^++1, 100); HRMS (EI) *m*/*z* calcd for $C_{25}H_{25}O$ 341.1912, found 341.1908; HPLC (Daicel Chiralpak AD-H, 2-propanol/*n*-hexane 5:95, flow 1.0 mL/min, *T* = 30 °C) t_R 8.6 min (major) and 10.4 min (minor).

(*S*)-2-(2-Methyl-1-naphthyl)-*N*-(2-phenyl-2-propyl)benzamide. A solution of $NaClO_2$ (0.145 mmol) in H_2O (0.5 mL) was dropwise added (for 1 h at room temperature) to a stirred solution containing **23a** (25.5 mg, 0.104 mmol) in acetonitrile (0.4 mL), NaH_2PO_4 (0.03 mmol), and H_2O_2 35% (10 μL) in H_2O (0.1 mL). The reaction mixture was stirred at 10 °C for 2 h, and then a small amount of Na_2SO_3 was added to destroy the unreacted HOCl and H_2O_2. The organic phase was washed with 10% aqueous HCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (*n*-hexane/EtOAc 2:1) gave 2-(2-methylnaphthalen-1-yl)benzoic acid (19 mg, 70%). A mixture of this material (17.3 mg, 0.066 mmol) and $SOCl_2$ (105 μL, 1.45 mmol) was heated 6 h at 60 °C, cooled, and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (0.1 mL) and added to a solution containing cumylamine (11.4 μL, 0.079 mmol), Et_3N (14 μL, 0.099 mmol), and DMAP (1.2 mg, 15 mol %) in CH_2Cl_2 (0.2 mL). The mixture was stirred at room temperature for 12 h, and then it was diluted with ether, washed with 1 N HCl, $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated to dryness. Purification by flash chromatography (*n*-hexane/EtOAc 10:1) gave (*S*)-2-(2-methyl-1-naphthyl)-*N*-(2-phenyl-2-propyl)benzamide (20 mg, 82%). Spectroscopic and physical data matched those reported in the literature:[6g] $[\alpha]^{20}_{D}$ = +10.7 (*c* 0.4, $CHCl_3$) for a sample with er 87:13[41] [lit.[6g] $[\alpha]_D$ = −30.5 (*c* 0.33, $CHCl_3$) for (*R*)-enantiomer with er 96.5:3.5].

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra for compounds **15e−g**, **16e,g**, **2a−i**, **18**, **10a−c**, **27a**, **13c,d**, **23a−d**, **24**, and **25a,b**; HPLC chromatograms for compounds **13c,d**, **23a−d**, **24**, and **25a,b**; crystallographic data for compounds **10a**, **10c**, and **27a**. This information 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.

■ ACKNOWLEDGMENTS

We thank the Spanish "Ministerio de Ciencia e Innovación" (Grant Nos. CTQ2010-15297 and CTQ2010-14974 and a fellowship to B.E.), the European FEDER funds, and the Junta de Andalucía (Grant Nos. 2008/FQM-3833 and 2009/FQM-4537) for financial support. A.R. thanks the European Union for a Marie Curie Reintegration Grant (FP7-PEOPLE-2009-RG-256461).

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■ NOTE ADDED IN PROOF

After submission of this paper, two reports on the asymmetric Suzuki-Miyautra reaction have appeared: (a) Wang, S.; Li, J.; Miao, T.; Wu, W.; Li, Q.; Zhuang, Y.; Zhou, Z.; Qiu, L. *Org. Lett.* **2012**, *14*, 1966. (b) Tang, W.; Patel, N. D.; Xu, G.; Xu, X.; Savoie, J.; Ma, S.; Hao, M.-H.; Keshipeddy, S.; Capacci, A. G.; Wei, X.; Zhang, Y.; Gao, J. J.; Li, W.; Rodriguez, S.; Lu, B. Z.; Yee, N. K.; Senanayake, C. H. *Org. Lett.* **2012**, *14*, DOI: 10.1021/ol300659d.