JOC The Journal of Organic Chemistry

Article

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An Active, General, and Long-Lived Palladium Catalyst for Cross-Couplings of Deactivated (Hetero)aryl Chlorides and Bromides with Arylboronic Acids

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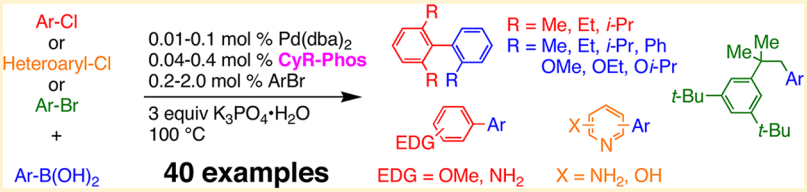
Supporting Information



ABSTRACT: An active, general, and long-lived palladium catalyst for Suzuki–Miyaura reactions of aryl and heteroaryl chlorides deactivated by steric hindrance, electron richness, and coordinating functional groups is reported. In reactions of arylbromide bearing two *o*-*tert*-butyl substituents, C(sp^3)–H arylation of the *tert*-butyl group, rather than the Suzuki–Miyaura reaction, proceeded in excellent yield. The key to the success of the reactions was the development of biphenylene-substituted dicyclohexylruthenocenylphosphine (CyR-Phos) as a supporting ligand.

INTRODUCTION

Since the discovery of the beneficial effects of the using P(*t*-Bu)$_3$ as a supporting ligand for palladium-catalyzed Buchwald–Hartwig amination of cheap but unreactive aryl chlorides,[1] the development of a number of ligands that greatly improve catalytic performance has expanded the substrate scope of palladium-catalyzed cross-coupling reactions.[2−4] Recently, we reported biphenylene-substituted di-*tert*-butylruthenocenylphosphine, R-Phos (Figure 1, left), as an effective ligand for sterically difficult Suzuki–Miyaura reactions.[5] That work was highlighted by the facile construction of highly crowded tetra-*ortho*-substituted biaryls from aryl chlorides. Here we report an active, general, and long-lived palladium catalyst for Suzuki–Miyaura reactions of aryl and heteroaryl chlorides using the dicyclohexylphosphino analogue, CyR-Phos (Figure 1, right). The catalyst generated from CyR-Phos enabled a broad substrate scope, low catalyst loading, and short reaction times in constructing tri-*ortho*-substituted biphenyls from aryl chlorides bearing two *ortho*-substituents (methyl, ethyl, and isopropyl) and a structurally diverse set of *ortho*-substituted arylboronic acids. The catalyst was also highly active in the reaction of further sterically hindered arylbromide bearing two *o*-*tert*-butyl substituents: C(sp^3)–H arylation of the *tert*-butyl group, rather than the Suzuki–Miyaura reaction, proceeded in excellent yield. The high catalytic performance was maintained in the reactions of aryl chlorides deactivated by electron-donating methoxy and amino groups. Tolerance toward the amino group was also observed in pyridyl and pyrimidyl chlorides bearing an unprotected amino group, which typically must be protected to prevent catalytic activity loss due to strong coordination to the catalyst.[6]

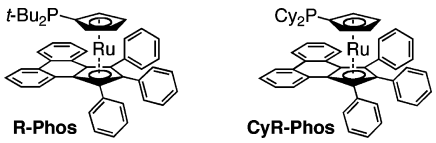


Figure 1. Biphenylene-substituted ruthenocenylphosphine ligands: R-Phos and CyR-Phos.

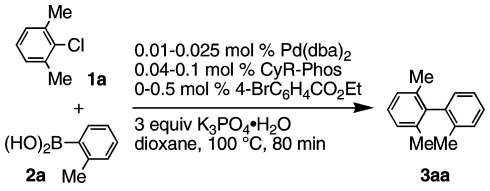
RESULTS AND DISCUSSION

Initially, we examined the precatalyst generated from CyR-Phos in the reaction of 2,6-dimethylchlorobenzene (**1a**) with 2-methylphenylboronic acid (**2a**) (Table 1). The ligand/Pd ratio was examined in a range from 1:1 to 5:1, and the best result was obtained at a ratio of 4:1 (Table 1, entries 1–4). However, when using precatalyst solution that had been stored in a freezer (ca. −20 °C) for 5 days, a significant drop in yield was observed (Table 1, entry 5). When the precatalyst solution was prepared in dioxane instead of THF, the decrease in yield after storage was improved but could not be completely prevented (Table 1, entries 6 and 7). In our previous work using R-Phos, the precatalyst could be used even after storage for several months without any loss of catalytic performance. To maintain the quality of the CyR-Phos precatalyst during storage, we further optimized the precatalyst and found that using an aryl

Received: September 20, 2013
Published: October 27, 2013

   dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513–11524

Table 1. Optimization of Precatalyst Based on CyR-Phos[a]



entry	Pd (mol %)	L:Pd	4-$BrC_6H_4CO_2Et$ (mol %)	storage (days)	yield (%)
1[b]	0.025	1:1		0	0
2[b]	0.025	3:1		0	78
3[b]	0.025	4:1		0	86
4[b]	0.025	5:1		0	48
5[b]	0.025	4:1		5	62
6[c]	0.025	4:1		0	76
7[c]	0.025	4:1		14	67
8[c]	0.025	4:1	0.5	0	96
9[c]	0.025	4:1	0.5	20	95
10[c,d]	0.01	4:1	0.2	5	87

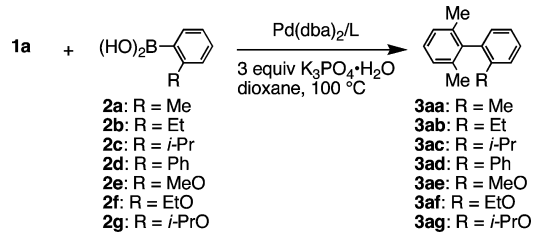
[a]All reactions were run with 1.0 mmol of **1a** and 1.5 equiv of **2a**. [b]Precatalyst solution was prepared in THF. [c]Precatalyst solution was prepared in dioxane. [d]2 h.

bromide additive permits the storage of the precatalyst. In addition, the yield of the catalytic reaction was substantially improved as compared to the reaction when the precatalyst was prepared without aryl bromide additive. Although we cannot presently explain the beneficial effects of aryl bromide on both the storage and activation of the precatalyst,[7] the reaction using the precatalyst prepared in the presence of ethyl 4-bromobenzoate, for example, went to completion (Table 1, entry 8) and the catalytic performance remained unchanged after 20 days (Table 1, entry 9). Using 0.01 mol % Pd, the reaction proceeded in 87% yield in 2 h, corresponding to a turnover number of 8,700 and a turnover frequency of 4,350 h^{-1} (Table 1, entry 10). To the best of our knowledge, these are the highest turnover number and turnover frequency reported for this sterically demanding Suzuki–Miyaura reaction.[3f,o,v]

With an efficient precatalyst in hand, we explored the substrate scope. Using 0.025 mol % of Pd, the reactions of **1a** with more sterically hindered *o*-alkyl- or *o*-aryl-substituted arylboronic acids **2b–d** gave the corresponding products **3ab–ad** in good to excellent yields (Table 2, entries 2–4). Also, a sterically diverse set of *o*-alkoxy-substituted arylboronic acids **2e–g** coupled with **1a** to provide the biphenyls **3ae–ag** in comparable yields under identical conditions (Table 2, entries 5–7). Though a higher catalyst loading (0.1 mol %) was required, R-Phos was also effective for the same substrate combinations (Table 2, entries 8–14).

The high catalytic performance regardless of the size and coordinating functional group of arylboronic acids motivated us to examine CyR-Phos and R-Phos in reactions of more sterically hindered aryl chlorides with the same set of arylboronic acids. In reactions of 2,6-diethylchlorobenzene (**1b**), the efficacy of CyR-Phos was maintained to afford the coupling products **3ba–bg** in excellent yields in <2 h with only 0.05 mol % Pd (Table 3, entries 1–7). In contrast, the catalyst generated from R-Phos required 20 times higher loading (1 mol %) to provide comparable outcomes from unfunctionalized arylboronic acids **2a–d** (Table 3, entries 8–11). When *o*-methoxy-substituted arylboronic acid **2e** was used as a coupling

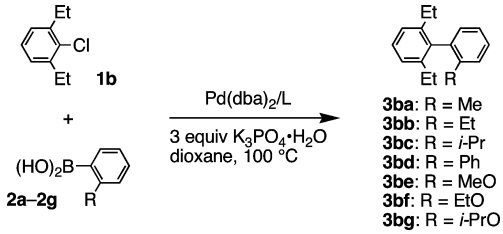
Table 2. Suzuki–Miyaura Reactions of 2,6-Dimethylchlorobenzene (1a) with *ortho*-Substituted Arylboronic Acids[a]



entry	$ArB(OH)_2$	L	Pd (mol %)	*t* (h)	product	yield (%)
1[b]	**2a**	CyR-Phos	0.025	1.5	**3aa**	96
2[b]	**2b**	CyR-Phos	0.025	1	**3ab**	96
3[b]	**2c**	CyR-Phos	0.025	1.5	**3ac**	76
4[b]	**2d**	CyR-Phos	0.025	1.5	**3ad**	100
5[b]	**2e**	CyR-Phos	0.025	2	**3ae**	88
6[b]	**2f**	CyR-Phos	0.025	2	**3af**	93
7[b]	**2g**	CyR-Phos	0.025	1.5	**3ag**	94
8[c]	**2a**	R-Phos	0.1	0.5	**3aa**	97
9[c]	**2b**	R-Phos	0.1	1.5	**3ab**	96
10[c]	**2c**	R-Phos	0.1	1	**3ac**	98
11[c]	**2d**	R-Phos	0.1	2	**3ad**	60
12[c]	**2e**	R-Phos	0.1	1.5	**3ae**	93
13[c]	**2f**	R-Phos	0.1	1.5	**3af**	100
14[c]	**2g**	R-Phos	0.1	1	**3ag**	60

[a]All reactions were run with 1.0 mmol of aryl chloride and 1.5 equiv of arylboronic acid. [b]0.025 mol % $Pd(dba)_2$, 0.1 mol % CyR-Phos, 0.5 mol % 4-$BrC_6H_4CO_2Et$. [c]0.1 mol % $Pd(dba)_2$, 0.3 mol % R-Phos.

Table 3. Suzuki–Miyaura Reactions of 2,6-Diethylchlorobenzene (1b) with *ortho*-Substituted Arylboronic Acids[a]



entry	$ArB(OH)_2$	L	Pd (mol %)	*t* (h)	product	yield (%)
1[b]	**2a**	CyR-Phos	0.05	2.5	**3ba**	93
2[b]	**2b**	CyR-Phos	0.05	1.5	**3bb**	85
3[b]	**2c**	CyR-Phos	0.05	1.5	**3bc**	94
4[b]	**2d**	CyR-Phos	0.05	3	**3bd**	93
5[b]	**2e**	CyR-Phos	0.05	2.5	**3be**	91
6[b]	**2f**	CyR-Phos	0.05	2.5	**3bf**	95
7[b]	**2g**	CyR-Phos	0.05	3.5	**3bg**	90
8[c]	**2a**	R-Phos	1	0.5	**3ba**	89
9[c]	**2b**	R-Phos	1	1.5	**3bb**	98
10[c]	**2c**	R-Phos	1	1	**3bc**	72
11[c]	**2d**	R-Phos	1	2	**3bd**	91
12[c]	**2e**	R-Phos	1	1.5	**3be**	14

[a]All reactions were run with 1.0 mmol of aryl chloride and 1.5 equiv of arylboronic acid. [b]0.05 mol % $Pd(dba)_2$, 0.2 mol % CyR-Phos, 1.0 mol % 4-$BrC_6H_4CO_2Et$. [c]1 mol % $Pd(dba)_2$, 3 mol % R-Phos.

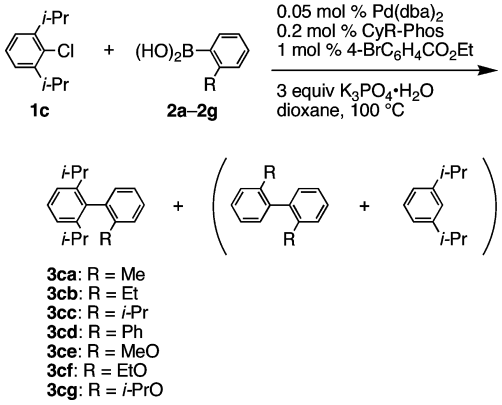
partner, the coupling product **3be** was obtained in only modest yield (Table 3, entry 12). Though we have no explanation for the remarkably detrimental effect of the coordinating methoxy

dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513–11524

group on the activity of R-Phos, the clear superiority of CyR-Phos over R-Phos for the highly hindered chloride **1b** is likely due to decreased steric demand of the dialkylphosphino group, which would increase the reactivity of the congested catalytic species.

CyR-Phos was also effective for coupling further hindered 2,6-diisopropylchlorobenzene (**1c**) with arylboronic acids **2a–g** using only the same low catalyst loading (Table 4, entries 1–7).

Table 4. Suzuki–Miyaura Reactions of 2,6-Diisopropylchlorobenzene (1c) with *ortho*-Substituted Arylboronic Acids[a]

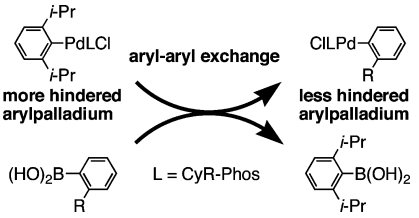


entry	$ArB(OH)_2$	t (h)	product	yield (%)
1	**2a**	4	**3ca**	64 (27, 14)[b]
2	**2b**	4	**3cb**	31 (22, 8)[b]
3	**2c**	4.5	**3cc**	27 (14, 12)[b]
4	**2d**	17	**3cd**	38 (39, 11)[b]
5	**2e**	3	**3ce**	83
6	**2f**	5.5	**3cf**	84
7	**2g**	4	**3cg**	69 (13, 5)[b]

[a]All reactions were run with 1.0 mmol of aryl chloride and 1.5 equiv of arylboronic acid. [b]Yields of homocoupling byproduct (left) and 1,3-diisopropylbenzene (right).

To the best of our knowledge, **1c** is the most hindered aryl chloride that has been successfully employed in the Suzuki–Miyaura reaction; to date, only two catalysts have been reported to be effective for this chloride.[4f,8] Also worth noting is that significant amounts of the homocoupling byproducts from arylboronic acids and 1,3-diisopropylbenzene, the dehalogenation product of **1c**, formed as the size of the boronic acids increased (Table 4, entries 1–4 and 7). We speculate that after the oxidative addition step, the resulting arylpalladium intermediate bearing two *o*-isopropyl substituents underwent the aryl–aryl exchange with arylboronic acid to give the mono-*ortho*-substituted arylpalladium complex and 2,6-diisopropylphenylboronic acid (Scheme 1); then, the former underwent the common transmetalation with another arylboronic acid to give the homocoupling byproduct with regeneration of the catalyst, and the latter underwent the protodeboronation to give the net dehalogenation product. The remarkable replacement of the common aryl–chloride exchange with the unusual aryl–aryl exchange in the reaction of relatively hindered boronic acids is likely due to the avoidance of forming the highly congested diarylpalladium intermediate.[9] The formation of the boronic acid-derived arylpalladium intermediate is also sterically favorable due to the significant

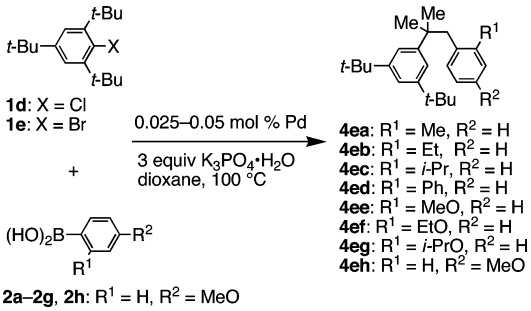
Scheme 1. Aryl–Aryl Exchange between Arylpalladium Intermediate and Arylboronic Acid



reduction of the steric congestion of the arylpalladium intermediate derived from the bulky aryl chloride **1c**.

In contrast to the excellent activity in the reactions of 2,6-dialkylchlorobenzenes **1a–c**, the catalyst could not mediate the coupling of the most sterically hindered 2,4,6-tri-*tert*-butylchlorobenzene (**1d**) even with 4-methoxyphenylboronic acid (**2h**), the less hindered coupling partner with no *ortho*-substituents (Table 5, entry 1). Fortunately, however, the

Table 5. C(sp^3)–H Arylation on *o*-*tert*-Butyl Substituent[a]



entry	ArX	$Ar'B(OH)_2$	product	yield (%)
1[b]	**1d**	**2h**		nr
2[b]	**1e**	**2h**	**4eh**	94
3[c]	**1e**	**2a**	**4ea**	100
4[c]	**1e**	**2b**	**4eb**	91
5[c]	**1e**	**2c**	**4ec**	82
6[c]	**1e**	**2d**	**4ed**	95
7[c]	**1e**	**2e**	**4ee**	80
8[c]	**1e**	**2f**	**4ef**	96
9[c]	**1e**	**2g**	**4eg**	99

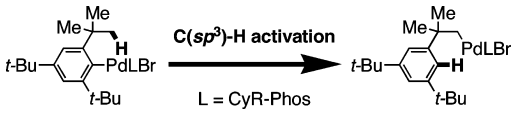
[a]All reactions were run with 1.0 mmol of aryl chloride and 1.5 equiv of arylboronic acid. [b]0.025 mol % $Pd(dba)_2$, 0.1 mol % CyR-Phos, 0.5 mol % 4-$BrC_6H_4CO_2Et$. [c]0.05 mol % $Pd(dba)_2$, 0.2 mol % CyR-Phos, 1.0 mol % 4-$BrC_6H_4CO_2Et$.

reaction of the bromide counterpart **1e** with **2h** proceeded to completion with only 0.025 mol % Pd (Table 5, entry 2). Though bromides are well-known as much more reactive halides compared with chlorides in palladium-catalyzed cross-coupling processes, the facile progress of the reaction highlights the excellent tolerance of the catalyst for sterically hindered aryl halides in the oxidative addition step. In addition, neither the Suzuki–Miyaura reaction nor the homocoupling side reaction, but rather the C(sp^3)–H arylation of the *o*-*tert*-butyl group took place exclusively.[10] The lack of any C(sp^2)–C(sp^2) bond-forming processes suggests that transmetalation between the bromide-derived arylpalladium intermediate and **2h** is completely inhibited by the steric hindrance of two large *o*-*tert*-butyl substituents. On the other hand, the tremendous congestion in the palladium complex allows either of the two *tert*-butyl substituents to stay continuously in close contact with Pd,

dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513–11524

which can facilitate the intramolecular activation of the inert C(sp^3)–H bond (Scheme 2). The resulting much less hindered

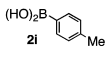
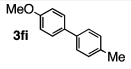
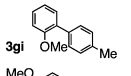
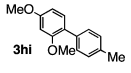
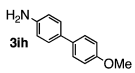
Scheme 2. Intramolecular C(sp^3)–H Activation in Bromide-Derived Arylpalladium Intermediate



alkylpalladium intermediate undergoes transmetalation with **2h** followed by reductive elimination to give the C(sp^3)–H arylation product **4eh**. Using 0.05 mol % Pd, the couplings of **1e** with various *ortho*-substituted arylboronic acids **2a–g** also gave the C(sp^3)–H arylation products **4ea–4eg** in excellent yields (Table 5, entries 3–8).

The ability of the catalyst to couple with aryl chlorides deactivated by electron-donating groups is also of great importance in palladium-catalyzed coupling reactions. Thus, we proceeded to assess the efficiency of CyR-Phos in the reactions of aryl chlorides containing electron-donating group(s) (Table 6). Using 0.025 mol % Pd, the reaction of

Table 6. Suzuki–Miyaura Reactions of Electronically Deactivated Aryl Chlorides[a]

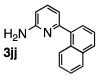
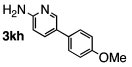
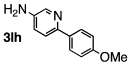
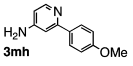
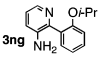
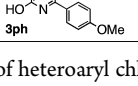
entry	ArCl	Ar'B(OH)$_2$	product	yield (%)
1[b]				99
2[b]		**2i**		84
3[b]		**2i**		19
4[c]	**1h**	**2i**	**3hi**	86
5[d]		**2h**		70

[a]All reactions were run with 1.0 mmol of aryl chloride, 1.5 equiv of arylboronic acid, and 3 equiv of $K_3PO_4·H_2O$ in dioxane at 100 °C. [b]0.025 mol % Pd(dba)$_2$, 0.1 mol % CyR-Phos, 0.5 mol % 4-BrC$_6$H$_4$CO$_2$Et. [c]0.25 mol % Pd(dba)$_2$, 1.0 mol % CyR-Phos. 5.0 mol % 4-BrC$_6$H$_4$CO$_2$Et. [d]0.1 mol % Pd(dba)$_2$, 0.4 mol % CyR-Phos, 2.0 mol % 4-BrC$_6$H$_4$*t*-Bu.

4-chloroanisole (**1f**) with 4-methylphenylboronic acid (**2i**) went to completion (Table 6, entry 1). The catalyst was also tolerant of a coordinating group at the *ortho* position (Table 6, entry 2). Although the reaction of 2,4-dimethoxychlorobenzene (**1h**) proceeded in only 19% yield due to strong deactivation by two methoxy groups, high yield was obtained at higher catalyst loading (Table 6, entries 3 and 4). Using 0.1 mol % Pd, the reaction of 4-chloroaniline (**1i**) with **2h** proceeded in 70% yield (Table 6, entry 5).

The high yield from the reaction of 4-chloroaniline (**1i**) raised the prospect that CyR-Phos would be effective for coupling other aryl and heteroaryl chlorides bearing an amino group. Nitrogen heteroaromatics are ubiquitous substructures in biologically active compounds and advanced materials.[11] However, in the Suzuki–Miyaura coupling of pyridyl and pyrimidyl chlorides bearing an unprotected amino group, substantial catalyst deactivation is often observed due to coordination with palladium.[12] To our delight, the use of CyR-Phos with 0.1 mol % Pd allowed for aminopyridyl or aminopyrimidyl chlorides to couple with arylboronic acids in high yield; the one exception was the most strongly basic coupling partner, 4-amino-2-chloropyridine (**1m**) (Table 7,

Table 7. Suzuki–Miyaura Reactions of Pyridyl and Pyrimidyl Chlorides Bearing Amino and Hydroxyl Groups[a]

entry	ArCl	Ar'B(OH)$_2$	product	yield (%)
1[b]				100
2[b]		**2h**		82
3[c]		**2h**		93
4[c]		**2h**		48
5[b]		**2g**		98
6[c]		**2a**		72
7[c]		**2h**		71

[a]All reactions were run with 1.0 mmol of heteroaryl chloride, 1.5 equiv of arylboronic acid, 0.1 mol % Pd(dba)$_2$, 0.4 mol % CyR-Phos, 2.0 mol % PhBr, and 3 equiv of $K_3PO_4·H_2O$ at 100 °C. [b]Reaction was run in *tert*-amyl alcohol. [c]Reaction was run in dioxane.

entries 1–6). As can be seen from the reactions using simple aryl chlorides, the catalytic activity was high for this substrate class, regardless of the steric character. In fact, 5-chloro-2,6-dimethyl-4-pyrimidinamine (**1o**), which possesses two bulky substituents *ortho* to the chlorine, coupled with **2a** to afford the corresponding tri-*ortho*-substituted heterobiaryl **3oa** in 72% yield (Table 7, entry 6). An unprotected hydroxypyridyl chloride (**1p**) was also well-tolerated in the catalytic system (Table 7, entry 7).

CONCLUSION

In summary, we have demonstrated that the palladium complex generated from CyR-Phos is an active, general, and long-lived catalyst for Suzuki–Miyaura reactions of aryl and heteroaryl chlorides deactivated by steric hindrance, electron richness, and coordinating functional groups. The excellent tolerance of the catalyst toward steric hindrance in the oxidative addition step could lead to the highly congested arylpalladium intermediate whose steric hindrance caused the common aryl–chloride exchange to be replaced by the unusual but sterically more

favorable aryl−aryl exchange in the subsequent transmetalation with boronic acid. In the reaction of arylbromide bearing two *o*-*tert*-butyl substituents, the close contact between the *tert*-butyl group and the palladium in the arylpalladium intermediate allowed intramolecular C(sp^3)−H activation followed by arylation with boronic acid in excellent yield. The precatalyst could be stored without any loss of catalytic performance through the use of an aryl bromide additive, which also significantly improved the yield of the coupling reaction. The superiority of CyR-Phos over R-Phos in forming tri-*ortho*-substituted biphenyls demonstrated that the dialkylphosphino substructure is an important control element for the efficiency of the ligands. Our ongoing efforts are directed toward applying CyR-Phos to additional palladium-catalyzed cross-coupling processes. The development of more effective ligands is also currently underway in our laboratory.

EXPERIMENTAL SECTION

General. All reactions were carried out under an atmosphere of argon in flame-dried glassware with a magnetic stir bar. Flash chromatography was performed with silica gel 60 (230−400 mesh). ^{1}H NMR spectra were recorded at 270.1 MHz, 399.9 MHz, 499.9 MHz, or 699.8 MHz. ^{13}C NMR were recorded at 100.6 MHz, 125.7 MHz, or 176.0 MHz. The ^{1}H chemical shifts were referenced to internal Me_4Si (δ 0.00 ppm). The ^{13}C chemical shifts were referenced to $CDCl_3$ (δ 77.0 ppm) or C_6D_6 (δ 128.0 ppm) relative to Me_4Si at δ 0.00 ppm. The ^{31}P chemical shifts were referenced to 85% H_3PO_4 (δ 0.00 ppm) as an external standard. Melting points are uncorrected. High-resolution mass spectra (HRMS) were measured using a Fourier transform mass spectrometer equipped with an electrospray ionization (ESI) or a double-focusing magnetic sector mass spectrometer equipped with electron impact (EI). All reagents were purchased and used without further purification. $K_3PO_4{\cdot}H_2O$ was finely ground prior to use. THF and dioxane used as solvents were distilled from sodium/benzophenone ketyl prior to use. *tert*-Amyl alcohol used as solvent for Suzuki−Miyaura reactions was purchased and used as received. Solvents for extraction and chromatography were HPLC grade.

Preparation of CyR-Phos: [Boranatodi(cyclohexyl)phosphino]cyclopentadiene. Cyclopentadiene (0.62 mL, 7.54 mmol) was dissolved in THF (16 mL) and cooled to 0 °C. At this temperature a *n*-hexane solution of *n*-BuLi (4.5 mL, 1.59 M, 3.15 mmol) was added, and the reaction mixture was stirred for 1 h. To the resulting cyclopentadienyl anion was added HMPA (5.0 mL, 28.7 mmol), and the mixture was stirred for 10 min at 0 °C. Then, Cy_2PCl (530 μL, 2.40 mmol) was added, and the reaction mixture was allowed to warm to room temperature. After being stirred for 3 h, the mixture was allowed to cool to −78 °C, and a THF solution of BH_3 (7.7 mL, 0.93 M, 7.16 mmol) was added and stirred for 30 min. The resulting mixture was allowed to warm to room temperature, quenched by 1 N HCl, diluted with $CHCl_3$, and washed twice with water and once with brine. The combined aqueous solutions were extracted with $CHCl_3$, and the combined organic solutions were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (1:1 CH_2Cl_2/*n*-hexane) to yield [boranatodi(cyclohexyl)phosphino]cyclopentadiene (573.9 mg, 2.08 mmol, 87%, ca. 64:36 mixture of regioisomers based on ^{1}H NMR spectroscopic analysis) as a white solid: ^{1}H NMR (499.9 MHz, $CDCl_3$) δ 0−1 (m, 3H), 1.1−1.4 (m, 10H), 1.6−2.0 (m, 22H), 3.17 (s, 0.73H), 3.19 (s, 1.27H), 6.55−6.60 (m, 0.7H), 6.63−6.67 (m, 0.64H), 6.77−6.80 (m, 0.64H), 7.12−7.18 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 25.9 (d, J = 1.4 Hz), 26.0 (d, J = 1.4 Hz), 26.5, 26.61, 26.63, 26.65, 26.67, 26.69, 26.72, 26.76, 26.77, 26.82, 26.85, 26.86, 43.5 (d, J = 12.2 Hz), 45.3 (d, J = 7.3 Hz), 131.3 (d, J = 53.7 Hz), 132.3 (d, J = 50.5 Hz), 132.4 (d, J = 5.5 Hz), 132.6 (d, J = 12.7 Hz), 134.5 (d, J = 7.0 Hz), 139.8 (d, J = 4.8 Hz), 146.6 (d, J = 8.7 Hz), 148.5 (d, J = 10.2 Hz) (observed complexity due to P−C splitting); ^{31}P NMR (202.3 MHz, $CDCl_3$) δ 21−22 (m); HRMS (EI) found 276.2178, calcd for $C_{17}H_{30}BP$ 276.2178.

CyR-Phos. [Boranatodi(cyclohexyl)phosphino]cyclopentadiene (313.8 mg, 1.14 mmol) was dissolved in THF (11 mL) and cooled to 0 °C. At this temperature a *n*-hexane solution of *n*-BuLi (0.68 mL, 1.63 M, 1.11 mmol) was added, and the reaction mixture was stirred for 1 h. To the resulting cyclopentadienyl anion was added a solution of the bromodicarbonyl ruthenium complex[5] (153.3 mg, 0.225 mmol) in THF (10 mL) at 0 °C, and the reaction mixture was allowed to warm to room temperature and then stirred for an additional 18 h. The mixture was quenched by saturated aqueous NH_4Cl, diluted with $CHCl_3$, and washed twice with water and once with brine. The combined aqueous solutions were extracted with $CHCl_3$, and the combined organic solutions were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (1:2 to 1:1 $CHCl_3$/*n*-hexane) to give the BH_3-protected title compound (150.1 mg, 0.183 mol, 81%) as a pale-yellow solid, which was dissolved in a solution of DABCO (524.9 mg, 4.68 mmol) in dioxane (9 mL) and then heated to 100 °C. After being stirred for 1 h, the mixture was allowed to cool to room temperature and concentrated under reduced pressure. The residue was purified by silica gel chromatography (AcOEt) to give the title compound (146.9 mg, 0.182 mmol, 81% for 2 steps) as a pale-yellow solid: mp = 124−126 °C; ^{1}H NMR (699.8 MHz, C_6D_6) δ 0.7−1.8 (m, 22H), 4.39 (s, 2H), 4.64 (s, 2H), 6.79 (ddt, J = 7.7 Hz, J = 7.0 Hz, J = 1.4 Hz, 1H), 6.85 (t, J = 7.7 Hz, 2H), 6.99−7.03 (m, 4H), 7.09 (dt, J = 7 Hz, J = 1.4 Hz, 2H), 7.14−7.16 (m, 2H), 7.19 (ddd, J = 8.4 Hz, J = 7.0 Hz, J = 1.4 Hz, 2H), 7.28−7.32 (m, 4H), 7.86 (dd, J = 8.4 Hz, J = 1.4 Hz, 2H), 8.15 (dd, J = 7.7 Hz, J = 0.7 Hz, 2H), 8.22 (d, J = 7.7 Hz, 2H); ^{13}C NMR (176.0 MHz, C_6D_6) δ 26.8 (d, J = 0.9 Hz), 27.57 (d, J = 11.1 Hz), 27.63 (d, J = 7.9 Hz), 30.8 (d, J = 4.0 Hz), 30.9, 33.7 (d, J = 15.3 Hz), 76.7 (d, J = 1.6 Hz), 78.1 (d, J = 10.7 Hz), 84.4 (d, J = 25.2 Hz), 84.6, 93.3, 99.4, 124.0, 125.9, 126.4, 126.5, 127.0, 127.2, 127.4, 128.3, 128.4, 131.2, 132.3, 132.7, 133.1, 135.3, 135.4, 137.3 (one aromatic sp^2 carbon missing due to overlap); ^{31}P NMR (283.3 MHz, C_6D_6) δ −9.8; HRMS (ESI) found 807.2685, calcd for $C_{52}H_{50}PRu$ $[M + H]^+$ 807.2688.

Preparation of Aryl Chloride: 2,6-Diethylchlorobenzene (1b).[4c] 2,6-Diethylaniline (2.224 g, 14.9 mmol) was dissolved in a mixture of HCl (12 N, 6.0 mL) and EtOH (16 mL) and cooled to 0 °C. The mixture was added to an aqueous solution (6 mL) of $NaNO_2$ (1.413 g, 20.5 mmol) and then stirred for 30 min. The resulting diazonium salt solution was added to an aqueous HCl solution (12 N, 20 mL) of CuCl (789.2 mg, 8.0 mmol) and heated to reflux with vigorous stirring for 20 min. The mixture was allowed to cool to room temperature, quenched by $NaHCO_3$, extracted with *n*-hexane, and washed twice with water and once with brine. The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (*n*-hexane) to yield the title compound (1.163 g, 6.896 mmol, 46%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.23 (t, J = 7.6 Hz, 6H), 2.78 (q, J = 7.6 Hz, 4H), 7.0−7.2 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1, 27.3, 126.4, 126.9, 133.5, 141.9; MS (EI) m/z (%) 170 (M^+ + 2, 21), 168 (M^+, 63), 155 (34), 153 (100), 133 (81); HRMS (EI) found 168.0706, calcd for $C_{10}H_{13}Cl_1$ 168.0706.

2,6-Diisopropylchlorobenzene (1c).[4f] 2,6-Diisopropylaniline (4.307 g, 24.3 mmol) was dissolved in a mixture of HCl (12 N, 10 mL) and EtOH (25 mL) and cooled to 0 °C. The mixture was added to an aqueous solution (10 mL) of $NaNO_2$ (2.299 g, 33.3 mmol) and then stirred for 60 min. The resulting diazonium salt solution was added to an aqueous HCl solution (12 N, 10 mL) of CuCl (1.345 g, 13.6 mmol) and heated to reflux with vigorous stirring for 50 min. The mixture was allowed to cool to room temperature, quenched by $NaHCO_3$, extracted with *n*-hexane, and washed twice with water and once with brine. The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (*n*-hexane) to yield the title compound (2.339 g, 11.89 mmol, 49%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.24 (d, J = 6.8 Hz, 12H), 3.49 (sept, J = 6.8 Hz, 2H), 7.1−7.2 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.9, 30.6, 123.9,

dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513−11524

126.6, 132.8, 146.0; MS (EI) m/z (%) 198 (M^++2, 9), 196 (M^+, 26), 183 (33), 181 (100); HRMS (EI) found 196.1020, calcd for $C_{12}H_{17}Cl_1$ 196.1019.

2,4,6-Tri-*tert*-butylchlorobenzene (1d).[13] 2,4,6-Tri-*tert*-butylaniline (1.496 g, 5.72 mmol) was dissolved in a mixture of HCl (12 N, 4.4 mL) and EtOH (10 mL) and cooled to 0 °C. The mixture was added to an aqueous solution (4 mL) of $NaNO_2$ (0.915 g, 13.26 mmol) and then stirred for 60 min. The resulting diazonium salt solution was added to an aqueous HCl solution (12 N, 15 mL) of CuCl (0.526 g, 5.31 mmol) and heated to reflux with vigorous stirring for 60 min. The mixture was allowed to cool to room temperature, quenched by $NaHCO_3$, extracted with *n*-hexane, and washed twice with water and once with brine. The organic solution was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel chromatography (*n*-hexane) to yield the title compound (0.524 g, 1.87 mmol, 33%) as a white solid: mp = 157−158 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.31 (s, 9H), 1.53 (s, 18H), 7.38 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 30.5, 31.4, 34.9, 37.2, 123.1, 131.3, 147.0, 147.8; MS (EI) m/z (%) 282 (M^++2, 12), 280 (M^+, 34), 267 (45), 265 (100); HRMS (EI) found 280.1960, calcd for $C_{18}H_{29}Cl_1$ 280.1958.

Representative Procedure for the Preparation of the Precatalyst Solution. A vial was charged with CyR-Phos (7.8 mg, 9.7 μmol), sealed with a screw cap with a PTFE/silicone septum, and then evacuated and backfilled with argon (3 cycles). To the vial was sequentially added 200 μL of a solution of $Pd(dba)_2$ (3.5 mg, 6.1 μmol) in dioxane (0.5 mL) and ethyl 4-bromobenzoate (12.4 mg, 54 μmol), and then the mixture was stored at room temperature for 3 h. The resulting solution was diluted with dioxane (1.8 mL) and then was used as the precatalyst solution.

General Procedure for Pd-Catalyzed Coupling of Aryl Halide with Arylboronic Acid. A flame-dried two-necked flask was charged with arylboronic acid and base, capped with a rubber septum, and then evacuated and backfilled with argon (3 cycles). To the flask was sequentially added aryl halide, the indicated solvent, and the indicated amount of a precatalyst solution via syringe through septum (aryl halides that were solids at room temperature were added during the initial charge, prior to the evacuation/backfill cycles), and then the reaction mixture was stirred at 100 °C for the indicated amount of time.

2,2′,6-Trimethylbiphenyl (3aa)[14] (Table 1, Entry 10). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (153.1 mg, 1.09 mmol), 2-methylphenylboronic acid (**2a**) (210.6 mg, 1.55 mmol), $K_3PO_4{\cdot}H_2O$ (719.8 mg, 3.13 mmol), a dioxane solution (88 μL, 1.23 mM, 0.11 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 in dioxane (2 mL) was stirred at 100 °C for 2 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (186.1 mg, 0.948 mmol, 87%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.95 (s, 6H), 1.97 (s, 3H), 7.00−7.30 (m, 7H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 19.4, 20.3, 126.0, 126.9, 127.0, 127.2, 128.8, 129.9, 135.5, 135.8, 140.5, 141.0.

2,6-Dimethyl-2′-ethylbiphenyl (3ab)[5b] (Table 2, Entry 2). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (142.7 mg, 1.02 mmol), 2-ethylphenylboronic acid (**2b**) (227.1 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (696.9 mg, 3.03 mmol), and a dioxane solution (200 μL, 1.22 mM, 0.24 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.0:22.5 ratio in dioxane (2 mL) was stirred at 100 °C for 60 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (206.8 mg, 0.983 mmol, 96%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.05 (t, J = 7.6 Hz, 3H), 1.96 (s, 6H), 2.28 (q, J = 7.6 Hz, 2H), 7.00 (d, J = 6.8 Hz, 1H), 7.05−7.40 (m, 6H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.5, 20.5, 25.7, 126.0, 126.9, 127.2, 128.2, 129.0, 136.0, 139.8, 140.9, 141.4 (one sp^2 carbon missing due to overlap); MS (EI) m/z (%) 210 (M^+, 77), 195 (100), 181 (38), 165 (50); HRMS (EI) found 210.1407, calcd for $C_{16}H_{18}$ 210.1409.

2,6-Dimethyl-2′-isopropylbiphenyl (3ac) (Table 2, Entry 3). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (140.0 mg, 1.00 mmol), 2-isopropylphenylboronic acid (**2c**) (243.9 mg, 1.49 mmol), $K_3PO_4{\cdot}H_2O$ (704.3 mg, 3.06 mmol), a dioxane solution (200 μL, 1.23 mM, 0.25 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 80 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (171.4 mg, 0.764 mmol, 76%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.10 (d, J = 6.8 Hz, 6H), 1.97 (s, 6H), 2.54 (sept, J = 6.8 Hz, 1H), 6.98 (d, J = 7.3 Hz, 1H), 7.03−7.28 (m, 4H), 7.28−7.44 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.7, 24.0, 29.8, 125.5, 125.8, 126.8, 127.2, 127.5, 129.0, 136.2, 139.0, 140.9, 146.3; MS (EI) m/z (%) 224 (M^+, 76), 209 (100), 181 (48); HRMS (EI) found 224.1565, calcd for $C_{17}H_{20}$ 224.1565.

2,6-Dimethyl-2′-phenylbiphenyl (3ad)[5b] (Table 2, Entry 4). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (140.3 mg, 1.00 mmol), 2-phenylphenylboronic acid (**2d**) (297.4 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (698.4 mg, 3.03 mmol), a dioxane solution (200 μL, 1.22 mM, 0.24 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.9:22.5 ratio in dioxane (2 mL) was stirred at 100 °C for 80 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (258.5 mg, 1.00 mmol, 100%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.93 (s, 6H), 6.95 (d, J = 7.3 Hz, 2H), 7.00−7.20 (m, 7H), 7.30−7.50 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.8, 126.5, 126.9, 127.1, 127.3, 127.4, 127.6, 128.7, 130.1, 130.3, 136.0, 138.9, 140.69, 140.74, 141.2; MS (EI) m/z (%) 258 (M^+, 100), 243 (49), 228 (24); HRMS (EI) found 258.1409, calcd for $C_{20}H_{18}$ 258.1409.

2,6-Dimethyl-2′-methoxybiphenyl (3ae)[5b] (Table 2, Entry 5). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (145.5 mg, 1.04 mmol), 2-methoxyphenylboronic acid (**2e**) (230.9 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (691.9 mg, 3.00 mmol), and a dioxane solution (200 μL, 1.23 mM, 0.25 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 120 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:5 AcOEt/*n*-hexane) to provide the title compound (193.6 mg, 0.912 mmol, 88%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 2.01 (s, 6H), 3.73 (s, 3H), 6.95−7.05 (m, 3H), 7.05−7.20 (m, 3H), 7.34 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.4, 55.2, 110.7, 120.6, 126.9, 128.3, 129.4, 130.5, 136.4, 138.1, 156.4 (one sp^2 carbon missing due to overlap); MS (EI) m/z (%) 212 (M^+, 100), 197 (36), 181 (46), 165 (32); HRMS (EI) found 212.1198, calcd for $C_{15}H_{16}O$ 212.1201.

2,6-Dimethyl-2′-ethoxybiphenyl (3af) (Table 2, Entry 6). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (144.3 mg, 1.03 mmol), 2-ethoxyphenylboronic acid (**2f**) (249.0 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (695.6 mg, 3.02 mmol), and a dioxane solution (200 μL, 1.23 mM, 0.25 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 100 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:5 AcOEt/*n*-hexane) to provide the title compound (216.5 mg, 0.957 mmol, 93%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.21 (t, J = 7.0 Hz,

3H), 2.02 (s, 6H), 3.99 (q, J = 7.0 Hz, 2H), 6.90−7.20 (m, 6H), 7.31 (ddd, J = 8.1 Hz, J = 6.8 Hz, J = 2.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.6, 20.4, 63.4, 112.1, 120.5, 126.7, 126.8, 128.2, 129.9, 130.7, 136.4, 138.4, 155.7; MS (EI) m/z (%) 226 (M^+, 100), 198 (38), 183 (83); HRMS (EI) found 226.1356, calcd for $C_{16}H_{18}O$ 226.1358.

2,6-Dimethyl-2′-isopropoxybiphenyl (3ag)[5b] (Table 2, Entry 7). Following the general procedure, a mixture of 2,6-dimethylchlorobenzene (**1a**) (141.0 mg, 1.00 mmol), 2-isopropoxyphenylboronic acid (**2g**) (310.3 mg, 1.72 mmol), $K_3PO_4{\cdot}H_2O$ (707.7 mg, 3.07 mmol), and a dioxane solution (200 μL, 1.22 mM, 0.24 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.0:22.5 ratio in dioxane (2 mL) was stirred at 100 °C for 80 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:9 AcOEt/n-hexane) to provide the title compound (226.0 mg, 0.940 mmol, 94%) as a colorless oil. ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.12 (d, J = 5.9 Hz, 6H), 2.02 (s, 6H), 4.32 (sept, J = 6.1 Hz, 1H), 6.92−7.18 (m, 6H), 7.29 (td, J = 7.3 Hz, J = 2.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.5, 22.0, 70.2, 114.7, 120.7, 126.7, 126.8, 128.1, 130.9, 131.1, 136.4, 138.6, 154.9; MS (EI) m/z (%) 240 (M^+, 61), 198 (99), 183 (100), 165 (25); HRMS (EI) found 240.1518, calcd for $C_{17}H_{20}O$ 240.1514.

2,6-Diethyl-2′-methylbiphenyl (3ba) (Table 3, Entry 1). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (172.8 mg, 1.02 mmol), 2-methylphenylboronic acid (**2a**) (207.4 mg, 1.53 mmol), $K_3PO_4{\cdot}H_2O$ (722.2 mg, 3.14 mmol), and a dioxane solution (400 μL, 1.25 mM, 0.50 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:23.2 ratio in dioxane (2 mL) was stirred at 100 °C for 150 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (n-hexane) to provide the title compound (212.8 mg, 0.949 mmol, 93%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.02 (t, J = 7.6 Hz, 6H), 1.96 (s, 3H), 2.17−2.31 (m, 4H), 7.07 (d, J = 6.8 Hz, 1H), 7.16 (d, J = 7.6 Hz, 2H), 7.17−7.30 (m, 4H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.1, 19.8, 26.3, 125.5, 127.0, 127.4, 129.70, 129.73, 135.9, 139.7, 139.8, 141.7 (one sp^2 carbon missing due to overlap); MS (EI) m/z (%) 224 (M^+, 100), 209 (58), 195 (56), 181 (44), 165 (55); HRMS (EI) found 224.1567, calcd for $C_{17}H_{20}$ 224.1565.

2,2′,6-Triethylbiphenyl (3bb) (Table 3, Entry 2). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (175.0 mg, 1.04 mmol), 2-ethylphenylboronic acid (**2b**) (228.0 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (714.7 mg, 3.10 mmol), and a dioxane solution (400 μL, 1.25 mM, 0.50 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:23.2 ratio in dioxane (2 mL) was stirred at 100 °C for 90 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (n-hexane) to provide the title compound (210.7 mg, 0.884 mmol, 85%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.03 (t, J = 7.6 Hz, 6H), 1.05 (t, J = 7.6 Hz, 3H), 2.17−2.30 (m, 6H), 7.04 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 7.6 Hz, 2H), 7.19−7.24 (m, 1H), 7.27−7.33 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.2, 15.1, 25.8, 26.6, 125.3, 125.4, 127.2, 127.4, 127.7, 129.8, 139.2, 139.6, 141.6, 141.9; MS (EI) m/z (%) 238 (M^+, 52), 209 (100), 181 (59), 165 (51); HRMS (EI) found 238.1723, calcd for $C_{18}H_{22}$ 238.1722.

2,6-Diethyl-2′-isopropylbiphenyl (3bc) (Table 3, Entry 3). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (163.3 mg, 0.97 mmol), 2-isopropylphenylboronic acid (**2c**) (249.4 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (696.1 mg, 3.02 mmol), and a dioxane solution (400 μL, 1.30 mM, 0.52 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.8:17.3 ratio in dioxane (2 mL) was stirred at 100 °C for 90 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (n-hexane) to provide the title compound (229.8 mg, 0.910 mmol, 94%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.06 (t, J = 7.6 Hz, 6H), 1.08 (d, J = 6.8 Hz, 6H), 2.16−2.33 (m, 4H), 2.53 (sept, J = 6.8 Hz, 1H), 7.02 (ddd, J = 7.6 Hz, J = 1.2 Hz, J = 0.4 Hz, 1H), 7.16 (d, J = 7.6 Hz, 2H), 7.20 (ddd, J = 7.6 Hz, J = 6.8 Hz, J = 1.6 Hz, 1H), 7.29 (dd, J = 8.0 Hz, J = 6.8 Hz, 1H), 7.32−7.41 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.2, 23.9, 26.6, 29.8, 125.20, 125.26, 125.3, 127.3, 127.5, 129.8, 138.4, 139.6, 142.1, 146.5; MS (EI) m/z (%) 252 (M^+, 87), 223 (59), 209 (69), 181 (100); HRMS (EI) found 252.1876, calcd for $C_{19}H_{24}$ 252.1878.

2,6-Diethyl-2′-phenylbiphenyl (3bd) (Table 3, Entry 4). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (168.2 mg, 1.00 mmol), 2-phenylphenylboronic acid (**2d**) (301.1 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (691.0 mg, 3.00 mmol), and a dioxane solution (400 μL, 1.25 mM, 0.50 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:23.2 ratio in dioxane (2 mL) was stirred at 100 °C for 170 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (n-hexane) to provide the title compound (266.7 mg, 0.931 mmol, 93%) as a white solid: mp = 61−62 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 0.98 (t, J = 7.6 Hz, 6H), 2.16−2.32 (m, 4H), 7.02 (d, J = 7.6 Hz, 2H), 7.05−7.08 (m, 2H), 7.10−7.17 (m, 3H), 7.17−7.21 (m, 2H), 7.37 (td, J = 7.2 Hz, J = 1.6 H, 1), 7.42−7.49 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.8, 26.5, 125.1, 126.5, 126.9, 127.3, 127.4, 127.5, 128.9, 123.0, 130.9, 138.4, 139.5, 140.8, 141.2, 141.9; MS (EI) m/z (%) 286 (M^+, 100), 271 (15), 257 (49), 241 (22), 229 (21), 165 (16); HRMS (EI) found 286.1723, calcd for $C_{22}H_{22}$ 286.1722.

2,6-Diethyl-2′-methoxybiphenyl (3be) (Table 3, Entry 5). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (175.1 mg, 1.04 mmol), 2-methoxyphenylboronic acid (**2e**) (229.4 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (695.1 mg, 3.02 mmol), a dioxane solution (400 μL, 1.30 mM, 0.52 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.8:17.3 ratio in dioxane (2 mL) was stirred at 100 °C for 150 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (0:1 to 1:0 AcOEt/n-hexane) to provide the title compound (227.4 mg, 0.946 mmol, 91%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.01 (t, J = 7.6 Hz, 6H), 2.22−2.38 (m, 4H), 3.72 (s, 3H), 6.96−7.02 (m, 2H), 7.05 (dd, J = 7.2 Hz, J = 1.6 Hz, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.28 (dd, J = 8.4 Hz, J = 7.2 Hz, 1H), 7.35 (ddd, J = 8.0 Hz, J = 7.2 Hz, J = 2.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.0, 26.7, 55.0, 110.4, 120.2, 125.3, 127.5, 128.3, 128.8, 131.1, 136.9, 142.5, 156.8; MS (EI) m/z (%) 240 (M^+, 100), 225 (18), 211 (74), 196 (25), 181 (33), 165 (39), 152 (21); HRMS (EI) found 240.1513, calcd for $C_{17}H_{20}O$ 240.1514.

2,6-Diethyl-2′-ethoxybiphenyl (3bf) (Table 3, Entry 6). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (169.6 mg, 1.01 mmol), 2-ethoxyphenylboronic acid (**2f**) (250.7 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (696.2 mg, 3.02 mmol), and a dioxane solution (400 μL, 1.30 mM, 0.52 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.8:17.3 ratio in dioxane (2 mL) was stirred at 100 °C for 150 min. The resulting reaction mixture was diluted with n-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/n-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:9 AcOEt/n-hexane) to provide the title compound (243.7 mg, 0.958 mmol, 95%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.01 (t, J = 7.6 Hz, 6H), 1.19 (t, J = 6.8 Hz, 3H), 2.22−2.38 (m, 4H), 3.98 (q, J = 6.8 Hz, 2H), 6.92−6.99 (m, 2H), 7.04 (dd, J = 7.6 Hz, J = 2.0 Hz, 1H), 7.13 (d, J = 7.6 Hz, 2H), 7.25 (t, J = 7.6 Hz, 1H), 7.31 (ddd, J = 8.4 Hz, J = 7.6 Hz, J = 2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.5, 15.1,

dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513−11524

26.7, 63.1, 111.5, 120.0, 125.1, 127.1, 128.2, 129.3, 131.3, 137.2, 142.5, 156.1; MS (EI) *m*/*z* (%) 254 (M^+, 100), 225 (100), 197 (64), 181 (26), 165 (21); HRMS (EI) found 254.1669, calcd for $C_{18}H_{22}O$ 254.1671.

2,6-Diethyl-2′-isopropoxybiphenyl (3bg) (Table 3, Entry 7). Following the general procedure, a mixture of 2,6-diethylchlorobenzene (**1b**) (167.7 mg, 0.99 mmol), 2-isopropoxyphenylboronic acid (**2g**) (272.1 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (695.6 mg, 3.02 mmol), and a dioxane solution (400 μL, 1.30 mM, 0.52 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.8:17.3 ratio in dioxane (2 mL) was stirred at 100 °C for 210 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (0:1 to 1:0 AcOEt/*n*-hexane) to provide 251.7 mg of a mixture of the title compound and isopropoxybenzene in a 89.3:10.7 ratio as a colorless oil, which corresponds to a 90% yield of the title compound (237.5 mg, 0.889 mmol). The title compound: ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.6 Hz, 6H), 1.13 (d, *J* = 6.0 Hz, 6H), 2.22−2.40 (m, 4H), 4.40 (sept, *J* = 6.0 Hz, 1H), 6.92−6.98 (m, 2H), 7.05 (dd, *J* = 7.2 Hz, *J* = 1.6 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.22−7.32 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.1, 21.9, 26.7, 69.4, 113.1, 120.0, 125.1, 127.1, 128.0, 130.1, 131.5, 137.4, 142.4, 155.2; MS (EI) *m*/*z* (%) 268 (M^+, 45), 226 (73), 197 (100); HRMS (EI) found 268.1828, calcd for $C_{19}H_{24}O$ 268.1827.

2,6-Diisopropyl-2′-methylbiphenyl (3ca) (Table 4, Entry 1). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (201.8 mg, 1.03 mmol), 2-methylphenylboronic acid (**2a**) (207.4 mg, 1.53 mmol), $K_3PO_4{\cdot}H_2O$ (692.1 mg, 3.01 mmol), and a dioxane solution (400 μL, 1.25 mM, 0.50 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.0:21.2 ratio in dioxane (2 mL) was stirred at 100 °C for 240 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (165.1 mg, 0.654 mmol, 64%) as a colorless oil, 2,2′-dimethylbiphenyl (38.1 mg, 0.209 mmol, 27%), and 1,3-diisopropylbenzene (23.6 mg, 0.145 mmol, 14%). The title compound: ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.02 (d, *J* = 6.8 Hz, 6H), 1.11 (d, *J* = 7.2 Hz, 6H), 1.99 (s, 3H), 2.45 (sept, *J* = 6.8 Hz, 2H), 7.05 (d, *J* = 6.8 Hz, 1H), 7.18−7.32 (m, 3H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.35 (dd, *J* = 7.6, *J* = 7.2 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.2, 23.4, 24.9, 30.3, 122.7, 125.4, 126.9, 127.7, 129.6, 129.8, 136.3, 138.4, 139.9, 146.5; MS (EI) *m*/*z* (%) 252 (M^+, 38), 237 (24), 195 (100), 179 (25), 167 (48), 165 (38); HRMS (EI) found 252.1878, calcd for $C_{19}H_{24}$ 252.1878.

2,6-Diisopropyl-2′-ethylbiphenyl (3cb) (Table 4, Entry 2). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (204.8 mg, 1.04 mmol), 2-ethylphenylboronic acid (**2b**) (226.1 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (690.9 mg, 3.00 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 240 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (86.6 mg, 0.325 mmol, 31%) as a colorless oil, 2,2′-diethylbiphenyl (34.5 mg, 0.164 mmol, 22%), and 1,3-diisopropylbenzene (13.1 mg, 0.081 mmol, 8%). The title compound: ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.01 (d, *J* = 6.8 Hz, 6H), 1.10 (t, *J* = 7.6 Hz, 6H), 1.12 (d, *J* = 6.8 Hz, 6H), 2.30 (q, *J* = 7.6 Hz, 2H), 2.46 (sept, *J* = 7.2 Hz, 2H), 7.03 (d, *J* = 7.2 Hz, 1H), 7.20−7.25 (m, 3H), 7.30−7.40 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.1, 23.2, 25.1, 25.7, 30.3, 122.6, 125.2, 127.1, 127.5, 127.7, 129.9, 138.2, 139.2, 141.9, 146.7; MS (EI) *m*/*z* (%) 266 (M^+, 46), 209 (58), 181 (100); HRMS (EI) found 266.2032, calcd for $C_{20}H_{26}$ 266.2035.

2,2′,6-Trisopropylbiphenyl (3cc) (Table 4, Entry 3). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (197.5 mg, 1.00 mmol), 2-isopropylphenylboronic acid (**2c**) (249.7 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (693.3 mg, 3.01 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 270 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (75.0 mg, 0.267 mmol, 27%) as a white solid, 2,2′-diisopropylbiphenyl (25.4 mg, 0.107 mmol, 14%) as a colorless oil, and 1,3-diisopropylbenzene (19.2 mg, 0.118 mmol, 12%). The title compound: mp = 59−60 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.00 (d, *J* = 6.8 Hz, 6H), 1.10 (d, *J* = 6.8 Hz, 6H), 1.15 (d, *J* = 7.2 Hz, 6H), 2.48 (sept, *J* = 6.8 Hz, 2H), 2.62 (sept, *J* = 7.2 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 7.15−7.25 (m, 3H), 7.30−7.45 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.0, 23.9, 25.4, 29.6, 30.3, 122.6, 125.1, 125.3, 127.4, 127.6, 129.9, 138.1, 138.3, 146.9, 147.0; MS (EI) *m*/*z* (%) 280 (M^+, 28) 237 (18), 223 (16), 195 (100), 181 (53); HRMS (EI) found 280.2186, calcd for $C_{21}H_{28}$ 280.2191.

2,6-Diisopropyl-2′-phenylbiphenyl (3cd) (Table 4, Entry 4). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (193.6 mg, 0.98 mmol), 2-phenylphenylboronic acid (**2d**) (297.2 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (693.9 mg, 3.01 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 17.5 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (117.1 mg, 0.372 mmol, 38%) as a white solid, 2,2′-diphenylbiphenyl (89.1 mg, 0.291 mmol, 39%) as a white solid, and 1,3-diisopropylbenzene (17.5 mg, 0.108 mmol, 11%). The title compound: mp = 129−133 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.8 Hz, 6H), 1.01 (d,, *J* = 6.8 Hz, 6H), 2.56 (sept, *J* = 6.8 Hz, 2H), 7.05−7.28 (m, 9H), 7.37 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 7.44 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 7.49 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.7, 25.4, 30.4, 122.5, 126.5, 126.7, 127.4, 127.5, 127.8, 129.3, 129.7, 131.0, 138.1, 138.4, 141.00, 141.01, 146.6; MS (EI) *m*/*z* (%) 314 (M^+, 84), 271 (82), 257 (100); HRMS (EI) found 314.2032, calcd for $C_{24}H_{26}$ 314.2035.

2,6-Diisopropyl-2′-methoxybiphenyl (3ce) (Table 4, Entry 5). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (193.6 mg, 0.984 mmol), 2-methoxyphenylboronic acid (**2e**) (231.0 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (699.7 mg, 3.04 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 180 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (218.3 mg, 0.813 mmol, 83%) as a white solid: mp = 50−51 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.06 (d, *J* = 6.8 Hz, 6H), 1.08 (d, *J* = 6.8 Hz, 6H), 2.55 (sept, *J* = 6.8 Hz, 2H), 3.71 (s, 3H), 6.96−7.06 (m, 3H), 7.21 (d, *J* = 7.6 Hz, 2H), 7.32−7.39 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.7, 24.2, 30.5, 55.0, 110.3, 120.2, 122.4, 127.8, 128.3, 129.0, 131.2, 135.6, 147.1, 157.1; MS (EI) *m*/*z* (%) 268 (M^+, 59), 225 (100), 211 (73); HRMS (EI) found 268.1827, calcd for $C_{19}H_{24}O$ 268.1827.

2,6-Diisopropyl-2′-ethoxybiphenyl (3cf) (Table 4, Entry 6). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (191.2 mg, 0.972 mmol), 2-ethoxyphenylboronic acid (**2f**) (251.4 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (692.6 mg, 3.01 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 330 min.

The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (229.4 mg, 0.812 mmol, 84%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.06 (d, J = 6.8 Hz, 6H), 1.08 (d, J = 6.8 Hz, 6H), 1.20 (t, J = 6.8 Hz, 3H), 2.56 (sept, J = 6.8 Hz, 2H), 3.99 (q, J = 6.8 Hz, 2H), 6.92−7.00 (m, 2H), 7.03 (dd, J = 7.6 Hz, J = 2.0 Hz, 1H), 7.20 (d, J = 7.6 Hz, 2H), 7.30−7.36 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 14.6, 23.8, 24.2, 30.5, 62.9, 111.1, 119.9, 122.2, 127.6, 128.1, 129.3, 131.3, 135.9, 147.1, 156.3; MS (EI) m/z (%) 282 (M^+, 78), 239 (70), 225 (49), 211 (34), 197 (100); HRMS (EI) found 282.1982, calcd for $C_{20}H_{26}O$ 282.1984.

2,6-Diisopropyl-2′-isopropoxybiphenyl (3cg) (Table 4, Entry 7). Following the general procedure, a mixture of 2,6-diisopropylchlorobenzene (**1c**) (193.8 mg, 0.985 mmol), 2-isopropoxyphenylboronic acid (**2g**) (278.0 mg, 1.54 mmol), $K_3PO_4{\cdot}H_2O$ (716.6 mg, 3.11 mmol), and a dioxane solution (400 μL, 1.20 mM, 0.48 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:25.8 ratio in dioxane (2 mL) was stirred at 100 °C for 240 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:30 AcOEt/*n*-hexane) to provide the title compound (200.4 mg, 0.676 mmol, 69%) as a white solid, 2,2′-diisopropoxybiphenyl (26.0 mg, 0.096 mmol, 13%) as a colorless oil, and 1,3-diisopropylbenzene (8.0 mg, 0. 049 mmol, 5%). The title compound: mp = 61.1−65.9 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.04 (d, J = 6.8 Hz, 6H), 1.09 (d, J = 6.8 Hz, 6H), 1.15 (d, J = 6.0 Hz, 6H), 2.56 (sept, J = 6.8 Hz, 2H), 4.46 (sept, J = 6.0 Hz, 1H), 6.90−6.98 (m, 2H), 7.02 (dd, J = 7.2 Hz, J = 1.6 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.28−7.38 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.9, 23.8, 24.4, 30.4, 68.8, 112.5, 119.8, 122.1, 127.4, 128.0, 130.0, 131.6, 136.1, 147.1, 155.2; MS (EI) m/z (%) 296 (M^+, 46), 254 (71), 239 (26), 211 (97), 197 (100), 169 (47); HRMS (EI) found 296.2140, calcd for $C_{21}H_{28}O$ 296.2140.

1-Methoxy-4-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4eh) (Table 5, Entry 2). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (325.4 mg, 1.00 mmol), 4-methoxyphenylboronic acid (**2h**) (230.4 mg, 1.52 mmol), $K_3PO_4{\cdot}H_2O$ (693.3 mg, 3.01 mmol), and a dioxane solution (200 μL, 1.30 mM, 0.26 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:3.8:22.7 ratio in dioxane (2 mL) was stirred at 100 °C for 9 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 to 1:0 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:2 $CHCl_3$/*n*-hexane) to provide the title compound (331.6 mg, 0.940 mmol, 94%) as a white solid: mp = 81−82 °C; ^{1}H NMR (699.8 MHz, $CDCl_3$) δ 1.30 (s, 18H), 1.31 (s, 6H), 2.76 (s, 2H), 3.74 (s, 3H), 6.67 (s, 4H), 7.10 (d, J = 1.4 Hz, 2H), 7.25 (t, J = 1.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.1, 31.6, 34.9, 39.1, 50.7, 55.0, 112.8, 119.3, 120.5, 131.1, 131.2, 147.7, 149.7, 157.8; MS (EI) m/z (%) 352 (M^+, 4), 231 (100); HRMS (EI) found 352.2765, calcd for $C_{25}H_{36}O$ 352.2766.

1-Methoxy-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4ea)[10a] (Table 5, Entry 3). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (325.3 mg, 1.00 mmol), 2-methylphenylboronic acid (**2a**) (202.9 mg, 1.49 mmol), $K_3PO_4{\cdot}H_2O$ (689.2 mg, 2.99 mmol), and a dioxane solution (460 μL, 1.11 mM, 0.51 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.6:22.3 ratio in dioxane (2 mL) was stirred at 100 °C for 8 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (336.1 mg, 0.999 mmol, 100%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.25 (s, 18H), 1.41 (s, 6H), 1.73 (s, 3H), 2.82 (s, 2H), 6.82 (dd, J = 7.2 Hz, J = 1.2 Hz, 1H), 6.95−7.07 (m, 3H), 7.01 (d, J = 2.0 Hz, 2H), 7.24 (t, J = 2.0 Hz, 1H); ^{13}C NMR (176.0 MHz, $CDCl_3$) δ 19.4, 28.5, 34.9, 39.7, 47.5, 119.5, 120.5, 124.7, 125.8, 130.1, 131.3, 137.3, 137.6, 147.2, 149.7; MS (EI) m/z (%) 336 (M^+, 3.1), 231 (100); HRMS (EI) found 336.2817, calcd for $C_{25}H_{36}$ 336.2817.

1-Ethoxy-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4eb) (Table 5, Entry 4). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (325.7 mg, 1.00 mmol), 2-ethylphenylboronic acid (**2b**) (225.4 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (717.1 mg, 3.11 mmol), and a dioxane solution (480 μL, 1.11 mM, 0.53 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:5.0:23.3 ratio in dioxane (2 mL) was stirred at 100 °C for 8 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (319.7 mg, 0.912 mmol, 91%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 0.97 (t, J = 7.6 Hz, 3H), 1.26 (s, 18H), 1.40 (s, 6H), 2.09 (q, J = 7.6 Hz, 2H), 2.84 (s, 2H), 6.80 (dd, J = 7.6 Hz, J = 1.2 Hz, 1H), 6.96−7.05 (m, 2H), 7.01 (d, J = 2.0 Hz, 2H), 7.01 (td, J = 7.6 Hz, J = 1.2 Hz, 1H), 7.24 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.1, 25.1, 28.5, 31.5, 34.9, 39.6, 46.7, 119.5, 120.5, 124.6, 126.1, 128.0, 131.4, 136.5, 143.5, 147.4, 149.7; MS (EI) m/z (%) 350 (M^+, 1.8), 231 (100); HRMS (EI) found 350.2973, calcd for $C_{26}H_{38}$ 350.2974.

1-Isopropyl-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4ec) (Table 5, Entry 5). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (326.0 mg, 1.00 mmol), 2-isopropylphenylboronic acid (**2c**) (246.7 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (689.8 mg, 3.00 mmol), and a dioxane solution (460 μL, 1.11 mM, 0.51 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.6:22.3 ratio in dioxane (2 mL) was stirred at 100 °C for 8 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (299.5 mg, 0.821 mmol, 82%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 0.94 (d, J = 6.8 Hz, 3H), 1.26 (s, 18H), 1.40 (s, 6H), 2.79 (sept, J = 6.8 Hz, 1H), 2.91 (s, 2H), 6.81 (d, J = 7.2 Hz, 1H), 6.95−7.00 (m, 1H), 7.05 (d, J = 2.0 Hz, 2H), 7.10−7.15 (m, 2H), 7.23 (t, J = 2.0 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 23.7, 28.7, 28.8, 31.9, 34.9, 39.5, 46.1, 119.6, 120.6, 124.4, 124.7, 126.2, 131.4, 135.7, 147.5, 147.8, 149.6; MS (EI) m/z (%) 364 (M^+, 1.2), 231 (100); HRMS (EI) found 364.3131, calcd for $C_{27}H_{40}$ 364.3130.

1-Phenyl-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4ed)[10a] (Table 5, Entry 6). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (324.8 mg, 1.00 mmol), 2-phenylphenylboronic acid (**2d**) (295.8 mg, 1.49 mmol), $K_3PO_4{\cdot}H_2O$ (697.1 mg, 3.03 mmol), and a dioxane solution (480 μL, 1.11 mM, 0.53 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.7:22.3 ratio in dioxane (2 mL) was stirred at 100 °C for 12 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (*n*-hexane) to provide the title compound (379.6 mg, 0.952 mmol, 95%) as a white solid: mp = 55−56 °C; ^{1}H NMR (699.8 MHz, $CDCl_3$) δ 1.07 (s, 6H), 1.26 (s, 18H), 2.99 (s, 2H), 6.79 (dd, J = 7.7 Hz, J = 0.7 Hz, 1H), 6.95 (d, J = 1.4 Hz, 2H), 7.11 (td, J = 7.7 Hz, J = 2.1 Hz 1H), 7.16−7.22 (m, 4H), 7.23 (t, J = 1.4 Hz, 1H), 7.31 (t, J = 7.7 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.0, 31.5, 34.9, 40.0, 46.4, 119.4, 120.4, 125.8, 126.3, 126.4, 127.9, 129.9, 130.1, 131.1, 136.5, 142.7, 143.3, 148.3, 149.7; MS (EI) m/z (%) 398 (M^+, 1.6), 231 (100); HRMS (EI) found 398.2974, calcd for $C_{30}H_{38}$ 398.2974.

1-Methoxy-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4ee) (Table 5, Entry 7). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (324.5 mg, 1.00 mmol), 2-methoxyphenylboronic acid (**2e**) (228.7 mg, 1.51 mmol),

dx.doi.org/10.1021/jo402089r | J. Org. Chem. 2013, 78, 11513−11524

$K_3PO_4·H_2O$ (705.0 mg, 3.06 mmol), and a dioxane solution (480 μL, 1.11 mM, 0.53 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:5.0:23.3 ratio in dioxane (2 mL) was stirred at 100 °C for 13 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (0:1 to 1:10 to 1:0 AcOEt/*n*-hexane) to provide the title compound (283.0 mg, 0.803 mmol, 80%) as a colorless oil. ^{1}H NMR (699.8 MHz, $CDCl_3$) δ 1.30 (s, 18H), 1.33 (s, 6H), 2.88 (s, 2H), 3.63 (s, 3H), 6.65 (dd, *J* = 7.0 Hz, *J* = 1.4 Hz, 1H), 6.72 (td, *J* = 7.0 Hz, *J* = 0.7 Hz 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 7.1−7.15 (m, 3H), 7.24 (t, *J* = 1.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 28.0, 31.6, 34.9, 39.5, 43.7, 54.9, 110.0, 119.3, 119.5, 120.4, 127.0, 127.7, 132.0, 148.4, 149.5, 158.0; MS (EI) *m*/*z* (%) 352 (M^+, 3.7), 231 (100); HRMS (EI) found 352.2765, calcd for $C_{25}H_{36}O$ 352.2766.

1-Ethoxy-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)propyl]-benzene (4ef) (Table 5, Entry 8). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (324.6 mg, 1.00 mmol), 2-ethoxyphenylboronic acid (**2f**) (249.3 mg, 1.50 mmol), $K_3PO_4·H_2O$ (715.7 mg, 3.11 mmol), and a dioxane solution (495 μL, 1.05 mM, 0.52 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:5.0:24.5 ratio in dioxane (2 mL) was stirred at 100 °C for 9 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (10:1 AcOEt/*n*-hexane) to provide the title compound (352.4 mg, 0.961 mmol, 96%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.31 (s, 18H), 1.38 (t, *J* = 6.8 Hz, 3H), 2.91 (s, 2H), 3.94 (q, *J* = 6.8 Hz, 2H), 6.66 (dd, *J* = 7.6 Hz, *J* = 2.0 Hz, 1H), 6.72 (td, *J* = 7.2 Hz, *J* = 1.2 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 7.12 (ddd, *J* = 8.4 Hz, *J* = 7.6 Hz, *J* = 2.0 Hz, 1H), 7.19 (d, *J* = 1.6 Hz, 2H), 7.26 (t, *J* = 1.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 15.0, 27.8, 31.6, 34.9, 39.6, 43.5, 63.1, 110.8, 119.3, 119.4, 120.3, 127.0, 127.7, 132.1, 149.0, 149.6, 157.5; MS (EI) *m*/*z* (%) 366 (M^+, 4.4), 231 (100); HRMS (EI) found 366.2923, calcd for $C_{26}H_{38}O$ 366.2923.

1-Isopropoxy-2-[2-methyl-2-(3,5-di-*tert*-butylphenyl)-propyl]benzene (4eg) (Table 5, Entry 9). Following the general procedure, a mixture of 2,4,6-tri-*tert*-butylbromobenzene (**1e**) (324.9 mg, 1.00 mmol), 2-isopropoxyphenylboronic acid (**2g**) (269.7 mg, 1.50 mmol), $K_3PO_4·H_2O$ (733.6 mg, 3.19 mmol), and a dioxane solution (480 μL, 1.05 mM, 0.50 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.7:23.3 ratio in dioxane (2 mL) was stirred at 100 °C for 13 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:30 to 1:40 AcOEt/*n*-hexane) to provide the title compound (374.9 mg, 0.985 mmol, 99%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 1.3 (m, 30H), 2.89 (s, 2H), 4.51 (sept, *J* = 6.0 Hz, 1H), 6.65−6.75 (m, 2H), 6.81 (d, *J* = 8.4, 1H), 7.11 (ddd, *J* = 7.6 Hz, *J* = 6.8 Hz, *J* = 2.0 Hz, 1H), 7.22 (d, *J* = 1.6 Hz, 2H), 7.26 (m, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 22.2, 27.8, 31.6, 34.9, 39.7, 43.6, 69.1, 112.0, 119.1, 119.3, 120.3, 126.8, 128.5, 132.4, 149.1, 149.6, 156.2; MS (EI) *m*/*z* (%) 380 (M^+, 3.9), 231 (100); HRMS (EI) found 380.3078, calcd for $C_{27}H_{40}O$ 380.3079.

4-Methyl-4′-methoxybiphenyl (3fi)[15] (Table 6, Entry 1). Following the general procedure, a mixture of 4-chloroanisole (**1f**) (143.0 mg, 1.00 mmol), 4-methylphenylboronic acid (**2i**) (204.0 mg, 1.50 mmol), $K_3PO_4·H_2O$ (694.7 mg, 3.02 mmol), and a dioxane solution (200 μL, 1.23 mM, 0.25 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 180 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:5 AcOEt/*n*-hexane) to provide the title compound (195.4 mg, 0.986 mmol, 99%) as a white solid: mp = 106−107 °C; ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.84 (s, 3H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.51 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 20.9, 55.0, 114.0, 126.4, 127.8, 129.3, 133.5, 136.1, 137.8, 158.8; MS (EI) *m*/*z* (%) 198 (M^+, 100), 183 (55), 155 (34); HRMS (EI) found 198.1043, calcd for $C_{14}H_{14}O$ 198.1045.

4-Methyl-2′-methoxybiphenyl (3gi)[3a] (Table 6, Entry 2). Following the general procedure, a mixture of 2-chloroanisole (**1g**) (160.5 mg, 1.13 mmol), 4-methylphenylboronic acid (**2i**) (204.5 mg, 1.49 mmol), $K_3PO_4·H_2O$ (697.0 mg, 3.03 mmol), and a dioxane solution (230 μL, 1.23 mM, 0.28 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.1:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 120 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:5 AcOEt/*n*-hexane) to provide the title compound (189.1 mg, 0.954 mmol, 84%) as a white solid: mp = 79−81 °C; ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.80 (s, 3H), 6.98 (d, *J* = 8.3 Hz, 1H), 7.03 (d, *J* = 7.3 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.28−7.36 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.1, 55.3, 111.0, 120.7, 128.3, 128.6, 129.3, 130.5, 130.7, 135.5, 136.4, 156.4; MS (EI) *m*/*z* (%) 198 (M^+, 100), 183 (48), 168 (39); HRMS (EI) found 198.1045, calcd for $C_{14}H_{14}O$ 198.1045.

4-Methyl-2′,4′-dimethoxybiphenyl (3hi) (Table 6, Entry 4). Following the general procedure, a mixture of 1-chloro-2,4-dimethoxybenzene (**1h**) (169.4 mg, 0.98 mmol), 4-methylphenylboronic acid (**2i**) (204.3 mg, 1.50 mmol), $K_3PO_4·H_2O$ (701.0 mg, 3.04 mmol), and a dioxane solution (2.0 mL, 1.25 mM, 2.5 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and ethyl 4-bromobenzoate in a 1.0:4.0:21.6 ratio in dioxane (2 mL) was stirred at 100 °C for 240 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (1:5 AcOEt/*n*-hexane), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:20 AcOEt/*n*-hexane) to provide the title compound (192.6 mg, 0.844 mmol, 86%) as a colorless oil. ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.79 (s, 3H), 3.85 (s, 3H), 6.53−6.58 (m, 2H), 7.17 (m, 3H), 7.39 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.0, 55.2, 55.3, 98.8, 104.4, 123.4, 128.6, 129.2, 131.0, 135.3, 135.9, 157.3, 160.0; MS (EI) *m*/*z* (%) 228 (M^+, 100), 213 (23), 198 (19); HRMS (EI) found 228.1150, calcd for $C_{15}H_{16}O_2$ 228.1150.

4-Amino-4′-methoxybiphenyl (3ih)[16] (Table 6, Entry 5). Following the general procedure, a mixture of 4-chloroaniline (**1i**) (133.4 mg, 1.05 mmol), 4-methoxyphenylboronic acid (**2h**) (231.0 mg, 1.52 mmol), $K_3PO_4·H_2O$ (700.4 mg, 3.04 mmol), and a dioxane solution (0.80 mL, 1.25 mM, 10 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and 1-bromo-4-*tert*-butylbenzene in a 1.0:4.0:25.6 ratio in dioxane (2 mL) was stirred at 100 °C for 370 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of alumina gel (acetone), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (2:1 $CHCl_3$/*n*-hexane) to provide the title compound (147.3 mg, 0.739 mmol, 70%) as a white solid: mp = 140−142 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 3.68 (brs, 2H), 3.83 (s, 3H), 6.74 (d, *J* = 8.8 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2 H), 7.36 (d, *J* = 8.8 Hz, 2 H), *J* = 7.45 (d, *J* = 8.8 Hz, 2 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.3, 114.0, 115.4, 127.3, 127.5, 131.2, 133.8, 145.3, 158.3; MS (EI) *m*/*z* (%) 199 (M^+, 100), 184 (89), 156 (40); HRMS (EI) found 199.0999, calcd for $C_{13}H_{13}N_1O$ 199.0997.

6-Naphthalen-1-yl-pyridin-2-ylamine (3jj) (Table 7, Entry 1). Following the general procedure, a mixture of 2-amino-6-chloropyridine (**1j**) (128.7 mg, 1.00 mmol), 1-naphtylboronic acid (**2j**) (259.4 mg, 1.51 mmol), $K_3PO_4·H_2O$ (708.3 mg, 3.08 mmol), and a dioxane solution (0.80 mL, 1.20 mM, 0.96 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and bromobenzene in a 1.0:4.1:22.9 ratio in *tert*-amyl alcohol (1.4 mL) was stirred at 100 °C for 70 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash

chromatography on silica gel (1:3 AcOEt/$CHCl_3$) to provide the title compound (220.1 mg, 1.00 mmol, 100%) as a white solid: mp = 99−101 °C; ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 4.56 (brs, 2H), 6.54 (d, J = 8.3 Hz, 1H), 6.91 (d, J = 7.3 Hz, 1H), 7.35−7.65 (m, 5H), 7.80−7.95 (m, 2H), 8.11 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 106.7, 114.6, 125.0, 125.5, 125.8, 125.9, 126.6, 127.9, 128.2, 130.9, 133.6, 137.7, 138.5, 157.1, 158.1; MS (EI) m/z (%) 220 (M^+, 56), 219 (100); HRMS (EI) found 220.1002, calcd for $C_{15}H_{12}N_2$ 220.1000.

5-(4-Methoxyphenyl)-pyridin-2-ylamine (3kh)[17] (Table 7, Entry 2). Following the general procedure, a mixture of 2-amino-5-chloropyridine (**1k**) (129.9 mg, 1.01 mmol), 4-methoxyphenylboronic acid (**2h**) (228.4 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (697.6 mg, 3.03 mmol), and a dioxane solution (0.80 mL, 1.20 mM, 0.96 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and bromobenzene in a 1.0:4.1:22.9 ratio in *tert*-amyl alcohol (1.4 mL) was stirred at 100 °C for 270 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (0:1 to 1:0 $CHCl_3$/AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (3:2 AcOEt/$CHCl_3$) to provide the title compound (166.1 mg, 0.830 mmol, 82%) as a white solid: mp = 173−174 °C; ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 3.84 (s, 3H), 4.47 (brs, 2H), 6.56 (d, J = 8.3 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 7.43 (d, J = 8.8 Hz, 2H), 7.62 (dd, J = 8.5 Hz, J = 2.5 Hz, 1H), 8.28 (d, J = 1.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.3, 108.5, 114.3, 127.1, 127.3, 130.9, 136.2, 146.0, 157.2, 158.8; MS (EI) m/z (%) 200 (M^+, 100); 185 (92); HRMS (EI) found 200.0950, calcd for $C_{12}H_{12}N_2O$ 200.0950.

6-(4-Methoxyphenyl)-pyridin-3-ylamine (3lh) (Table 7, Entry 3). Following the general procedure, a mixture of 5-amino-2-chloropyridine (**1l**) (128.5 mg, 1.00 mmol), 4-methoxyphenylboronic acid (**2h**) (228.3 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (691.4 mg, 3.00 mmol), and a dioxane solution (0.80 mL, 1.25 mM, 1.0 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and bromobenzene in a 1.0:4.1:20.8 ratio in dioxane (1.4 mL) was stirred at 100 °C for 5 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of alumina gel (acetone), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (3:1 AcOEt/*n*-hexane) to provide the title compound (185.5 mg, 0.926 mmol, 93%) as a white solid: mp = 109−110 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 3.70 (brs, 2H), 3.84 (s, 3H), 6.96 (dd, J = 9.2 Hz, 2 H), 7.03 (dd, J = 8.4 Hz, J = 2.8 Hz, 1H), 7.47 (dd, J = 8.4 Hz, J = 0.8 Hz, 1H), 7.83 (d, J = 8.8 Hz, 2H), 8.15 (dd, J = 2.8 Hz, J = 0.4 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.3, 105.6, 107.9, 113.8, 128.0, 132.4, 150.0, 153.3, 157.9, 160.1; MS (EI) m/z (%) 200 (M^+, 100), 185 (75), 157 (63); HRMS (EI) found 200.0950, calcd for $C_{12}H_{12}N_2O$ 200.0950.

6-(4-Methoxyphenyl)-pyridin-4-ylamine (3mh) (Table 7, Entry 4). Following the general procedure, a mixture of 4-amino-2-chloropyridine (**1m**) (129.7 mg, 1.01 mmol), 4-methoxyphenylboronic acid (**2h**) (227.2 mg, 1.50 mmol), $K_3PO_4{\cdot}H_2O$ (714.1 mg, 3.10 mmol), and a dioxane solution (0.80 mL, 1.25 mM, 1.0 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and 1-bromo-4-*tert*-butylbenzene in a 1.0:4.0:22.9 ratio in dioxane (1.4 mL) was stirred at 100 °C for 6 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of alumina gel (acetone), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (acetone) to provide the title compound (97.6 mg, 0.487 mmol, 48%) as a white solid: mp = 137−139 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 3.84 (s, 3H), 4.18 (brs, 2H), 6.44 (dd, J = 5.6 Hz, J = 2.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H), 6.96 (d, J = 8.8 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 8.27 (d, J = 5.6 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.1, 113.8, 119.9, 122.3, 127.0, 132.1, 136.7, 140.9, 147.5, 159.2; MS (EI) m/z (%) 200 (M^+, 100), 185 (46), 157 (28); HRMS (EI) found 200.0949, calcd for $C_{12}H_{12}N_2O$ 200.0950.

6-(2-Isopropoxyphenyl)-pyridin-5-ylamine (3 ng) (Table 7, Entry 5). Following the general procedure, a mixture of 3-amino-2-chloropyridine (**1n**) (129.4 mg, 1.01 mmol), 2-isopropoxyphenylboronic acid (**2g**) (279.1 mg, $K_3PO_4{\cdot}H_2O$ (721.4 mg, 3.13 mmol), and a *tert*-amyl alcohol solution (0.80 mL, 1.20 mM, 0.96 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and bromobenzene in a 1.0:4.1:23.8 ratio in *tert*-amyl alcohol (1.4 mL) was stirred at 100 °C for 70 min. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (AcOEt), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (1:2 AcOEt/$CHCl_3$) to provide the title compound (225.6 mg, 0.988 mmol, 98%) as a white solid: mp = 87−89 °C; ^{1}H NMR (270.1 MHz, $CDCl_3$) δ 1.19 (d, J = 6.1 Hz, 6 H), 3.93 (brs, 2H), 4.38 (sept, J = 6.1 Hz, 1H), 6.95−7.20 (m, 4H), 7.35 (ddd, J = 8.0 Hz, J = 7.3 Hz, J = 1.7 Hz, 1H), 7.44 (dd, J = 7.6 Hz, J = 1.5 Hz, 1H), 8.14 (dd, J = 4.4 Hz, J = 1.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 21.6, 71.8, 115.7, 121.7, 122.1, 122.4, 129.1, 129.8, 131.7, 139.0, 141.0, 144.0, 154.4; MS (EI) m/z (%) 228 (M^+, 21), 213 (36), 185 (100), 169 (57); HRMS (EI) found 228.1263, calcd for $C_{14}H_{16}N_2O$ 228.1263.

2,6-Dimethyl-5-(2-methylphenyl)-pyrimidin-4-ylamine (3oa)[12d] (Table 7, Entry 6). Following the general procedure, a mixture of 5-chloro-2,6-dimethyl-4-pyrimidinamine (**1o**) (158.6 mg, 1.01 mmol), 2-methylphenylboronic acid (**2a**) (205.8 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (700.4 mg, 3.04 mmol), and a dioxane solution (0.80 mL, 1.25 mM, 1.0 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and 1-bromo-4-*tert*-butylbenzene in a 1.0:4.1:22.4 ratio in dioxane (1.4 mL) was stirred at 100 °C for 6 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (acetone), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (7:1 acetone/$CHCl_3$) to provide the title compound (155.1 mg, 0.727 mmol, 72%) as a white solid: mp = 204−206 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 2.07 (s, 3H), 2.11 (s, 3H), 2.53 (s, 3H), 4.65 (brs, 2H), 7.11 (d, J = 6.4 Hz, 1H), 7.28−7.35 (m, 3H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 19.2, 21.7, 25.5, 113.5, 126.8, 128.5, 129.8, 130.7, 133.6, 137.1, 160.9, 162.5, 165.7; MS (EI) m/z (%) 213 (M^+, 80), 198 (100); HRMS (EI) found 213.1265, calcd for $C_{13}H_{15}N_3$ 213.1266.

2-Hydroxy-6-(4-methoxyphenyl)pyridine (3ph) (Table 7, Entry 7). Following the general procedure, a mixture of 6-chloro-2-hydroxypyridine (**1p**) (131.6 mg, 1.02 mmol), 4-methoxyphenylboronic acid (**2h**) (229.9 mg, 1.51 mmol), $K_3PO_4{\cdot}H_2O$ (705.8 mg, 3.06 mmol), and a dioxane solution (0.80 mL, 1.20 mM, 0.96 μmol) of the precatalyst composed of $Pd(dba)_2$, CyR-Phos, and 1-bromo-4-*tert*-butylbenzene in a 1.0:4.1:19.2 ratio in dioxane (1.4 mL) was stirred at 100 °C for 6.5 h. The resulting reaction mixture was diluted with *n*-hexane (5 mL), filtered through a thin pad of silica gel (acetone), and concentrated under reduced pressure. The crude material obtained was purified by flash chromatography on silica gel (7:1 acetone/$CHCl_3$) to provide the title compound (145.0 mg, 0.721 mmol, 71%) as a white solid: mp = 199−201 °C; ^{1}H NMR (399.9 MHz, $CDCl_3$) δ 3.86 (s, 3H), 6.42 (dd, J = 7.2 Hz, J = 1.2 Hz, 1H), 6.49 (dd, J = 8.8 Hz, J = 0.8 Hz, 1H), 7.01 (d, J = 9.2 Hz, 2H), 7.46 (dd, J = 8.8 Hz, J = 7.2 Hz, 1H), 7.66 (d, J = 8.8 Hz, 2H), 11.2−12.7 (brs, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 55.4, 103.9, 114.6, 117.7, 125.9, 128.0, 141.4, 146.7, 161.1, 165.1; MS (EI) m/z (%) 201 (M^+, 100), 173 (26), 158 (58), 130 (21); HRMS (EI) found 201.0790, calcd for $C_{12}H_{11}N_1O_2$ 201.0790.

■ ASSOCIATED CONTENT

Supporting Information

Full spectroscopic data including ^{1}H NMR, ^{13}C NMR, and ^{31}P NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported financially by a Grant-in-Aid for Scientific Research (21550100) from MEXT.

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