Highly Active Palladium Catalysts for Suzuki Coupling Reactions

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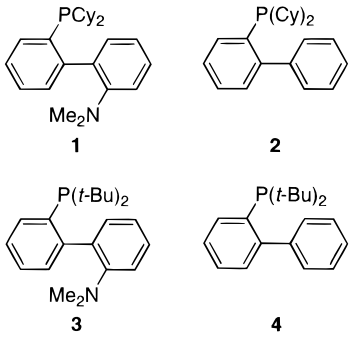
Abstract: Mixtures of palladium acetate and *o*-(di-*tert*-butylphosphino)biphenyl (**4**) catalyze the room-temperature Suzuki coupling of aryl bromides and aryl chlorides with 0.5−1.0 mol % Pd. Use of *o*-(dicyclohexylphosphino)biphenyl (**2**) allows Suzuki couplings to be carried out at low catalyst loadings (0.000001−0.02 mol % Pd). The process tolerates a broad range of functional groups and substrate combinations including the use of sterically hindered substrates. This is the most active catalyst system in terms of reaction temperature, turnover number, and steric tolerance which has been reported to date.

The palladium-catalyzed cross coupling of aryl halides with organoboron reagents has become one of the most widely utilized methods for the formation of sp^2-sp^2 carbon−carbon bonds.[1] However, most protocols for Suzuki coupling do not effectively transform aryl chlorides, which are the cheapest and most readily available aryl halides.[1,2] The few existing methods for the palladium-catalyzed Suzuki coupling of aryl chloride substrates usually only function well for electron deficient substrates.[3a−f,4] Methods for the nickel-catalyzed Suzuki coupling of aryl chlorides have been reported which are more general than the protocols which use palladium catalysts, but do not work well for very hindered substrates.[3g,h,5] Room-temperature Suzuki couplings of aryl halides are rare, usually require toxic additives such as thallium hydroxide, and do not work for aryl chloride substrates.[6]

We have recently reported that the aminophosphine ligand 2-(dimethylamino)-2′-dicyclohexylphosphinobiphenyl (**1**) promotes the palladium-catalyzed amination and room-temperature Suzuki coupling of aryl chlorides.[7] Although palladium catalysts supported by this ligand were sufficiently active to promote room-temperature Suzuki coupling reactions of aryl chlorides, this ligand required four steps to prepare from commercially available starting materials.

Related studies directed toward the development of improved catalysts for palladium-catalyzed C−O bond forming reactions led to the discovery that di-*tert*-butylphosphino-aminobiphenyl ligand **3** was a highly efficient ligand for the coupling of aryl halides with phenols or NaO*t*Bu.[8] In some cases catalysts derived from the desamino derivative (*o*-biphenyl)P(*t*-Bu)$_2$ (**4**) were found to be of comparable activity to those from **3**.



Further studies involving ligands **2**−**4** revealed that catalysts supported by **4** were substantially more reactive than catalysts supported by **1** in Suzuki coupling reactions of aryl bromides and chlorides carried out at room temperature, and functioned efficiently for a wide variety of substrates with 0.5−1.0 mol % Pd.[9] Use of **2** as a ligand was successful for the Suzuki coupling of hindered substrates and provided for efficient reactions at

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(3) (a) Shen, W. *Tetrahedron Lett.* **1997**, *38*, 5575−5578. (b) Beller, M.; Fischer, H.; Herrmann, W. A.; Öfele, K.; Brossmer, C. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1848−1849; (c) Bumagin, N. A.; Bykov. V. V. *Tetrahedron* **1997**, *53*, 14437-14450. (d) Mitchell, M. B.; Wallbank, P. J. *Tetrahedron Lett.* **1991**, *32*, 2273−2276. (e) Firooznia, F.; Gude, C.; Chan, K.; Satoh, Y. *Tetrahedron Lett.* **1998**, *39*, 3985−3988. (f) Cornils, B. *Org. Process. Res. Dev.* **1998**, *2*, 121−127. (g) Indolese, A. F. *Tetrahedron Lett.* **1997**, *38*, 3513−3516. (h) Saito, S.; Oh-tani, S.; Miyaura, N. *J. Org. Chem.* **1997**, *62*, 8024−8030.

(4) (a) Fu has recently reported the Suzuki coupling of electron-rich aryl chlorides using palladium complexes with P(*t*-Bu)$_3$ as the supporting ligand. Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387−3388. (b) Guran has reported the Suzuki coupling of electron-rich aryl chlorides using an electron-rich, chelating aryl dialkyl phosphine. See: Bei, X.; Crevier, T.; Guran, A. S.; Jandeleit, B.; Powers, T. S.; Turner, H. W.; Uno, T.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40*, 3855−3858. (c) Suzuki couplings of aryl chlorides catalyzed by palladium carbene complexes have been reported. See: Herrmann, W. A.; Reisinger, C.-P.; Spiegler, M. *J. Organomet. Chem.* **1998**, *557*, 93−96. Electron-rich aryl chlorides are effectively coupled if the proper carbene ligand is chosen. See: Zhang, C.; Huang, J.; Trudell, M. L.; Nolan, S. P. *J. Org. Chem.* **1999**, *64*, 3804−3805.

(5) Genêt has recently reported a biphasic system for the nickel-catalyzed Suzuki coupling of aryl chlorides. In this report he described the synthesis of 2,6,2′-methyl-4′-acetylbiphenyl in 67% yield using 10 mol % (dppe)-$NiCl_2$ and 50 mol % of a sulfonated triphenylphosphine ligand. See: Galland, J.-C.; Savignac, M.; Genêt, J.-P. *Tetrahedron Lett.* **1999**, *40*, 2323−2326.

(6) (a) Campi, E. M.; Jackson, W. R.; Marcuccio, S. M.; Naeslund, C. G. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2395. (b) Anderson, J. C.; Namli, H.; Roberts, C. A. *Tetrahedron* **1997**, *53*, 15123−15134. (c) Uenishi, J.-i.; Beau, J.-M.; Armstrong, R. W.; Kishi, Y. *J. Am. Chem. Soc.* **1987**, *109*, 4756−4758.

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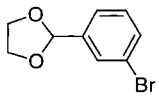
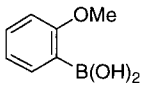
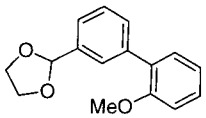
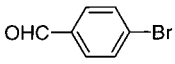
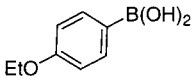
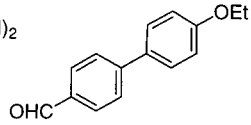
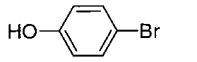
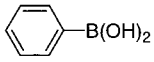
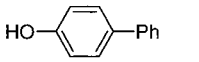
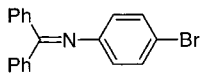
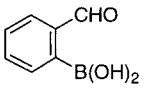
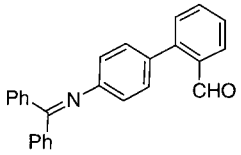
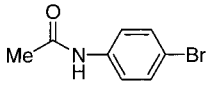
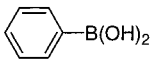
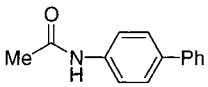
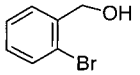
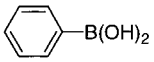
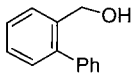
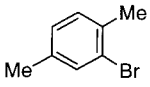
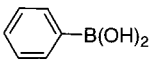
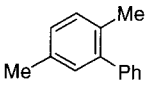
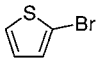
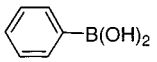
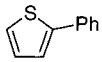
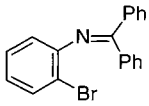
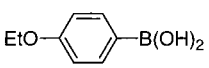
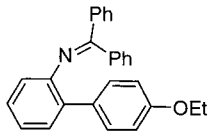
Table 1. Suzuki Coupling of Aryl Bromides[a]

Entry	Halide	Boronic Acid	Product	Ligand	Time (h)	Yield (%)
1				**4** $(ArO)_3P$[b]	2.5 2.5	86[c] 81[c]
2				**4** $(ArO)_3P$[b]	2 2	90 82
3				**4**	12	90[d]
4				**4**	20	89
5				**4**	11	88[d]
6				**4**	11	83[d]
7				**4** **4** **2**	40 12 22	82 94[e] 93
8				**4**	3	98
9				**2**	17	87[f,g]

[a] Reaction conditions: 1.0 equiv aryl bromide, 1.5 equiv boronic acid, 3.0 equiv KF, 1 mol% $Pd(OAc)_2$, cat ligand (2L/Pd) THF (1 mL/mmol aryl bromide, rt; reaction times have not been mimimized. Yields in Tables 1−4 represent isolated yields (average of two or more experiments) of compounds estimated to be ≥95% pure as judged by ^{1}H NMR and GC analysis (known compounds) and combustion analysis (new compounds). [b] ArO_3P = Tris(2,4-di-*tert*-butylphenyl)phosphite. [c] The reaction was conducted with 0.5 mol% Pd(OAc)2. [d] The reaction was conducted at 50 °C. [e] The reaction was conducted at 45 °C. [f] The reaction was conducted at 80 °C. [g] K_3PO_4 (2.0 equiv) used in place of KF.

very low catalyst loadings.[9] Of note is that **2** and **4** are prepared in high yield in a single step and are now commercially available.[10] Moreover, they are air stable, crystalline compounds which require no special handling. Herein we report detailed studies on the effectiveness of catalysts based on ligands **2** and **4** in Suzuki coupling reactions.

Results

Room-Temperature Suzuki Coupling of Aryl Halides. The reaction of a wide variety of aryl halides and boronic acids was examined using conditions optimized for room-temperature Suzuki coupling; the results are shown in Tables 1 and 2. A catalyst composed of $Pd(OAc)_2$/**4** efficiently promotes the room-temperature Suzuki coupling of both electron-rich and -poor aryl bromides (Table 1) and chlorides (Table 2). As is usually the case in Suzuki coupling reactions conducted under non-aqueous conditions,[1,11] a wide variety of functional groups are tolerated, and the catalyst is also active for heterocyclic halide substrates. Aryl halides with ortho substituents are usually efficiently coupled, although heating was occasionally required for reactions to proceed to completion. Reactions of ortho-substituted halides were often more efficient if **2** was used in place of **4** (see below). Cross-coupling of chloropyridine derivatives, or aryl halides containing acidic protons were slower at room temperature, and heating was required for reactions to proceed to completion in <24 h. The coupling of an aryl chloride with an alkyl 9-BBN derivative[12] (generated in situ) was effected at 65 °C (Table 2, entry 11).

During the course of our studies, we examined several different bases for the Suzuki coupling reactions. For room-temperature reactions, KF or CsF[11] were found to be the most effective of these. Other bases such as K_3PO_4, alkali metal carbonates, and sodium ***tert***-butoxide were substantially less effective at room-temperature, and alkali metal acetates failed to promote the reaction. Reactions conducted at room temper-

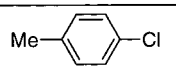
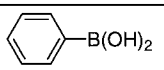
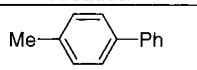
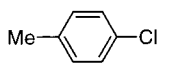
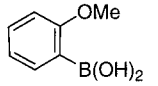
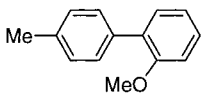
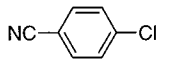
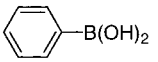
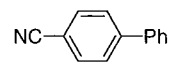
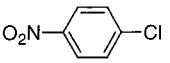
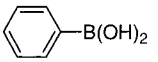
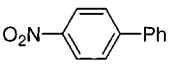
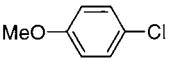
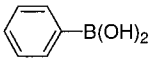
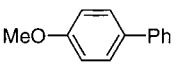
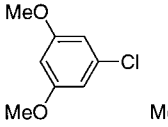
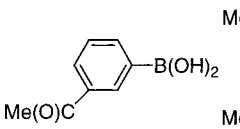
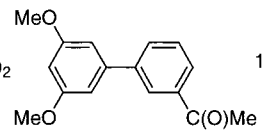
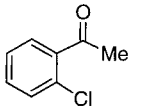
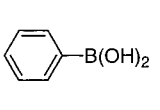
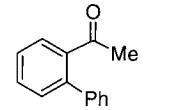
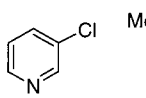
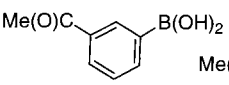
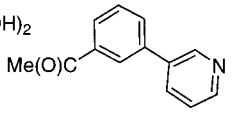
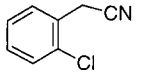
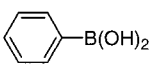
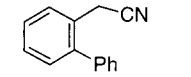
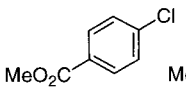
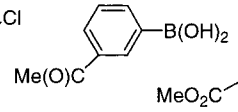
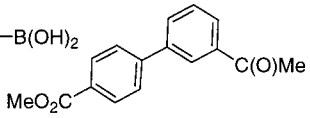
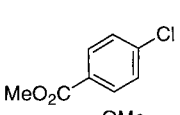
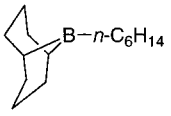
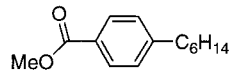
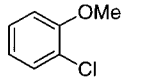
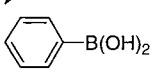
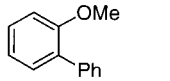
(9) (a) Portions of this work have been previously communicated. See: Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1999**, *38*, 2413−2416. (b) The **4**/$Pd(OAc)_2$ catalyst system has also been shown to be effective for room-temperature catalytic amination of aryl chlorides; see ref 9a.

(10) Ligands **2** and **4** are now commercially available from Strem Chemical Co.

(11) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095−6097.

(12) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314−321.

Table 2. Suzuki Coupling of Aryl Bromides[a]

Entry	Halide	Boronic Acid	Product	mol% Pd	Time (h)	Yield (%)
1				1 0.5	6 19	95 97
2				1	24	95
3				1	2	88
4				1 0.2	4 8	98 98
5				1 1.5	6 21	93[b] 92
6				1	7	90
7				1	2.5	93
8				1	9	94[c]
9				1	20	91
10				1	2	91
11				1/2	20	83[d]
12				1	24	96

[a] Reaction conditions: 1.0 equiv aryl chloride, 1.5 equiv boronic acid, 3.0 equiv KF, cat $Pd(OAc)_2$, cat **4** (2L/Pd) THF (1 mL/mmol aryl bromide, rt; reaction times have not been mimimized. [b] Reaction conducted at 45 °C. [c] The reaction was conducted at 50 °C. [d] The reaction was conducted at 65 °C.

ature were most efficient in THF or dioxane. Use of DME or CH_3CN as solvent led to slower reactions, while reactions run in toluene or NMP gave very low conversions. Alcohols (MeOH, EtOH, *i*-PrOH) were poor solvents for the room-temperature Suzuki coupling, and their use led to reduction of the starting aryl halide.[13]

The correct combination of solvent and base was extremely important. While KF was ineffective in toluene, it was the most efficient promoter of room-temperature Suzuki coupling reactions in THF. Furthermore, while K_3PO_4 was less useful than KF for reactions in THF, reactions could be run at very low catalyst loadings using K_3PO_4 in toluene solvent at 100 °C (see below). Reactions conducted with low catalyst loadings were much less efficient in oxygenated solvents, such as THF, DME, or dioxane when K_3PO_4 was employed as the base. Use of biphasic solvent systems generally gave inferior results compared to reactions run without added water.

With respect to precatalyst, $Pd(OAc)_2$ was more effective than $Pd_2(dba)_3$; catalysts derived from the latter did not catalyze room-temperature couplings of aryl chlorides for the systems examined. The use of $Pd_2(dba)_3$ for reactions of aryl bromides at low catalyst loadings gave better results than $Pd(OAc)_2$ in THF at 65 °C, although $Pd(OAc)_2$ was a superior palladium source for reactions conducted in toluene at 100 °C.

Reactions of 5-chloro-1,3-dimethoxybenzene with phenylboronic acid at room-temperature proceeded more rapidly as the amount of boronic acid and KF added to the reaction mixture was increased; 21 ± 1% conversion was obtained after 1 h with 1.5 equiv boronic acid and 3.0 equiv KF while 32 ± 2% conversion was observed after the same period of time when 3.0 equiv boronic acid and 6.0 equiv KF was employed (after 4 h 66 ± 2% and 96 ± 3% conversion were observed, respectively). This trend suggests that transmetalation may be

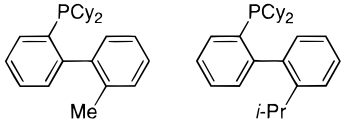
(13) Primary and secondary alkoxides are known to reduce aryl halides in the presence of palladium catalysts. Zask, A.; Helquist, P. *J. Org. Chem.* **1978**, *43*, 1619−1620.

the rate-limiting step for this substrate combination. However, it is possible that the rate-limiting step in the catalytic cycle may change when other substrates or reaction conditions are used.

A recent report described the use of a cyclometalated tris-(2,4-di-*tert*-butylphenyl)phosphite palladium complex as a highly active catalyst for the Suzuki coupling of aryl bromides.[14] The authors reported that the cyclometalated complex was sufficiently active to promote the room-temperature Suzuki coupling of 4-bromoacetophenone with phenylboronic acid, and speculated that the palladacycle was probably being cleaved in situ to a noncyclometalated catalyst.[14] We examined the use of mixtures of palladium acetate and tris(2,4-di-*tert*-butylphenyl)-phosphite as a catalyst under our reaction conditions and found that this system gave results comparable to those obtained with **4**/$Pd(OAc)_2$ in room-temperature Suzuki couplings of aryl bromides (Table 1, entries 1−2), but was unreactive toward aryl chlorides. Even at 100 °C, the coupling of 4-chlorotoluene with phenylboronic acid catalyzed by 1 mol % palladium acetate and 2 mol % tris(2,4-di-*tert*-butylphenyl)phosphite proceeded only to 5% conversion.

Synthesis of Biaryls Containing More Than One Ortho Substituent. Although examples of Suzuki coupling to form very hindered biphenyls from aryl iodides or bromides have been reported,[6b,15] reactions of this type are often problematic.[1,6b,15a] In some cases the use of certain bases (TlOH,[6b] $Ba(OH)_2$,[15a] or K_3PO_4[15a]), or solvent combinations (e.g., toluene/water/ethanol, 3/3/1)[15e] have been reported to give improved results, although the generality of these protocols is not clear. To the best of our knowledge, only one example of the synthesis of biphenyls bearing three ortho substituents from aryl chloride substrates has been previously reported.[5]

Using our conditions, substrates with more than one ortho substituent were substantially less reactive than other aryl halides, and the **4**/$Pd(OAc)_2$ catalyst system was usually not very effective for reactions of these types of substrates. However, catalysts employing ligands **1**, **2**, **5**, or **6** functioned well for reactions of 2,6-disubstituted halides, 2,6-disubstituted boronic acids, and the coupling of *o*-substituted halides with *o*-substituted boronic acids. Ligands **1**, **5**, and **6** were equally effective for these reactions, while **2** provided catalysts which were slightly less efficient (Table 3, entries 7−8). The best results in reactions of hindered substrates were usually obtained with K_3PO_4 as the base in toluene solvent. While L/Pd ratios of 2/1 were usually employed, occasionally it was found that use of a 3−4/1 ratio was beneficial.



5 **6**

While reactions which formed biaryls containing three ortho substituents were fairly efficient, reactions which formed tetra-ortho substituted biaryls were problematic and typically proceeded to <40% conversion.[16] Surprisingly, use of an increased quantity of catalyst did not give improved results.

Suzuki Coupling at Low Catalyst Loading. Studies to minimize the quantity of catalyst necessary further demonstrated the high activity of catalysts based on the dialkylphosphino(*o*-biphenyl) ligands. When **4** was used as the supporting ligand, reactions of electronically neutral aryl bromides proceeded to completion with 0.025−0.05 mol % $Pd_2(dba)_3$ at 65 °C in THF, or with 0.1 mol % $Pd(OAc)_2$ in toluene at 100 °C in <24 h; the activated aryl chloride 4-chloroacetophenone was coupled with phenylboronic acid in 92% yield using 0.02 mol % Pd (Table 4, entry 6). Generally the best results were obtained with K_3PO_4 as the stoichiometric base in toluene solvent.

Higher turnover numbers were achieved when ligand **2** was employed in place of ligand **4**. Reactions of unactivated aryl bromides proceeded to completion with 0.005 mol % Pd (Table 4, entries 1−3), while the coupling of 4-chlorotoluene proceeded to 99% conversion (93% isolated yield) with 0.05 mol % Pd (Table 4, entry 5). Tris(2,4-di-*tert*-butylphenyl)phosphite proved to be less effective than **2** for the coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid when a catalyst loading of 0.001 mol % Pd was employed (Table 4, entry 2); the reaction catalyzed by Pd/**2** proceeded to an average of 92% conversion (93% average GC yield) while the Pd/phosphite catalyst system afforded an average conversion of 43% (44% average GC yield). Interestingly, the reaction of 1-bromo-4-*tert*-butylbenzene with *o*-tolylboronic acid proceeded to 89% conversion (88% GC yield) using the phosphite ligand (Table 4, entry 3).

Remarkably low catalyst loadings could be used for the cross-coupling of 4′-bromoacetophenone with phenylboronic acid. Previous reports have described catalyst systems which provide 74 000 or 1 000 000 turnovers for this reaction at 135 °C.[3b,14] We were able to reproducibly obtain 100 000 000 turnovers in <24 h at 100 °C using the (*o*-biphenyl)P(*t*-Bu)$_2$ catalyst system for this reaction; a control experiment conducted in the absence of a phosphine ligand showed that 100 000 turnovers could be obtained using $Pd(OAc)_2$ in the absence of added ligand as the catalyst for this reaction. These exceptionally high turnover numbers were only obtained for this substrate combination suggesting that it is not a useful benchmark to test new catalysts in Suzuki couplings.

Discussion

Our results demonstrate that catalysts supported by ligands **2** or **4** are substantially more active for Suzuki coupling than catalysts based on triarylphosphines or trialkylphosphines which have been previously described.[1] The efficiency of catalysts based on **2** or **4** is most likely due to the combination of a number of factors. The electronic properties of the ligand are certainly of importance, as most triarylphosphines are not sufficiently electron-rich to promote the oxidative addition of aryl chlorides, particularly at room temperature.[2,17] However, previous studies have shown that electron-rich trialkylphosphines such as PCy_3 are rather inefficient ligands for the Suzuki coupling of electron-rich aryl halides;[3a,e] although these electron-

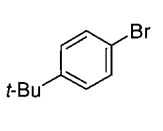
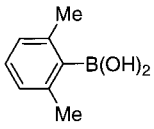
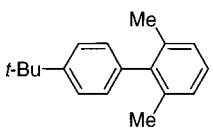
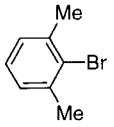
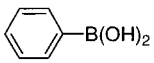
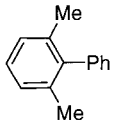
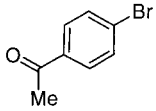
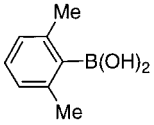
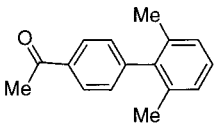
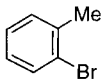
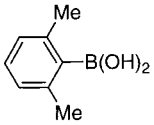
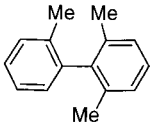
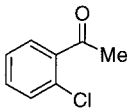
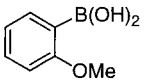
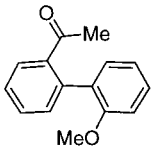
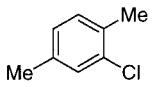
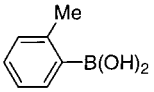
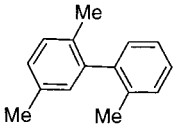
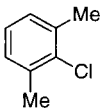
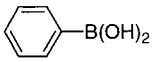
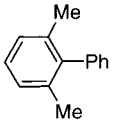
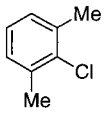
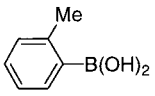
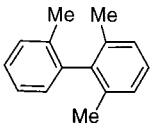
(14) Albisson, D. A.; Bedford, R. B.; Lawrence, S. E.; Scully, P. N. *J. Chem. Soc., Chem. Commun.* **1998**, 2095−2096.

(15) (a) Bringmann, G.; Götz, R.; Keller, P. A.; Walter, R.; Boyd, M. R.; Lang, F.; Garcia, A.; Walsh, J. J.; Tellitu, I.; Bhaskar, K. V.; Kelly, T. R. *J. Org. Chem.* **1998**, *63*, 1090−1097. (b) Zhang, H.; Kwong, F. Y.; Tian, Y.; Chan, K. S. *J. Org. Chem.* **1998**, *63*, 6886−6890. (c) Johnson, M. G.; Foglesong, R. J. *Tetrahedron Lett.* **1997**, *38*, 7001−7002. (d) Hoye, T. R.; Chen, M. *J. Org. Chem.* **1996**, *61*, 7940−7942. (e) Bahl, A.; Grahn, W.; Stadler, S.; Feiner, F.; Bourhill, G.; Bräuchle, C.; Reisner, A.; Jones, P. G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1485−1488. (f) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207−210. (g) Katz, H. E. *J. Org. Chem.* **1987**, *52*, 3932−3934.

(16) No catalyst has been reported which is effective for Suzuki coupling reactions to form biaryls with four ortho substituents; to the best of our knowledge, only one isolated yield (12%) has been for the synthesis of a tetrasubstituted biaryl (using Suzuki coupling) has been reported. See ref 15c.

(17) Herrmann, W. A.; Broβmer, C.; Priermeier, T.; Öfele, K. *J. Organomet. Chem.* **1994**, *481*, 97−108.

Table 3. Suzuki Coupling of Sterically Hindered Substrates[a]

Entry	Halide	Boronic Acid	Product	Ligand	Temp (°C)	Time (h)	Yield (%)
1				**1**	100	16	97
2				**4** **2**	65 rt	19 13	81[b,c] 92[b,c]
3				**4**	80	16	87[d]
4				**1**	100	20	86
5				**4**	65	6	90
6				**2**	80	15	96
7				**1** **2**	100 100	22 22	91 85[e]
8				**6** **2**	100 100	3 17	92 88[f]

[a] Reaction conditions: 1.0 equiv aryl chloride, 1.5 equiv boronic acid, 2.0 equiv K_3PO_4, 1 mol % $Pd(OAc)_2$, cat ligand (4L/Pd) toluene (3 mL/mmol halide); reaction times have not been mimimized. [b] KF (3.0 equiv) used in place of K_3PO_4. [c] Ratio of L/Pd = 2/1. [d] The reaction was conducted with 2 mol % $Pd(OAc)_2$. [e] Of two runs, one proceeded to 93% conversion, the other proceeded to 97% conversion. [f] Of two runs, one proceeded to 97% conversion.

rich ligands facilitate oxidative addition,[18] they also decrease the rate of reductive elimination processes.[19] In contrast, Fu has shown that tBu$_3$P is an effective ligand for the Suzuki coupling of aryl chlorides.[4a] These findings reflect that the combination of both steric bulk and electronics is important (see below). The higher efficiency of t-Bu$_3$P relative to Cy$_3$P has previously been documented in aryl amination processes by the Tosoh group.[20]

Ligands **2** and **4** possess a fine balance of steric and electronic properties which allow for significantly accelerated oxidative addition while facilitating the other steps (transmetalation, reductive elimination) in the catalytic cycle. The basic phosphine group promotes oxidative addition, and binds tightly to the metal (relative to a triarylphosphine) to prevent precipitation of the catalyst. We believe that the ortho-phenyl moiety may provide a stabilizing interaction between the aromatic π-system and one of the metal d-orbitals,[21] and increases the steric bulk around the metal, which promotes reductive elimination and favors monophosphine palladium species.[22,23] This interaction also causes the aryl group of the substrate to be oriented perpen-

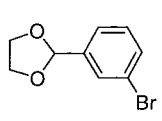
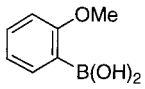
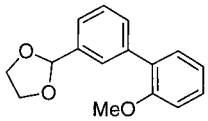
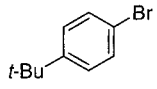
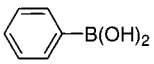
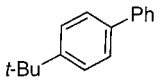
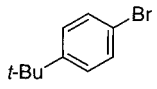
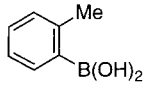
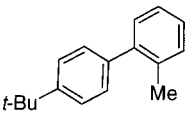
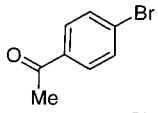
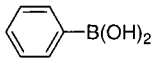
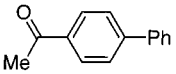
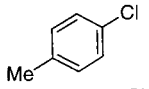
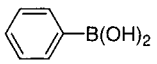
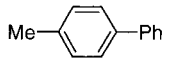
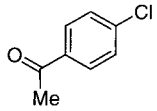
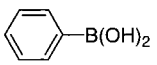
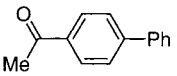
(18) (a) It is well-known that the use of electron-rich phosphine ligands accelerates the rate of oxidative addition of aryl halides to Pd(0). See: Spessard, G. O.; Meissler, G. L. *Organometallic Chemistry;* Prentice Hall: Upper Saddle River, New Jersey, 1996; pp 171−175. (b) In his pioneering studies, Milstein demonstrated oxidative addition of aryl chlorides to Pd(dippp)$_2$ (dippp = 1,3-bis(diisopropylphosphino)propane) at 38 °C. Portnoy, M.; Milstein, D. *Organometallics* **1993**, *12*, 1665−1673.

(19) Hegedus, L. S. *Transition Metals in The Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, CA, 1994; Chapter 2.

(20) (a) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617−620. (b) Yamamoto, T.; Nishiyama, M.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 2367−2370.

(21) Metal-π interactions have been observed in other palladium complexes. (a) Ossor, H.; Pfeffer, M.; Jastrzebski, J. T. B. H.; Stam, C. H. *Inorg. Chem.* **1987**, *26*, 1169−1171. (b) Falvello, L. R.; Fornies, J.; Navarro, R.; Sicilia, V.; Tomas, M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 891−893. (c) Sommovigo, M.; Pasquali, M.; Leoni, P.; Braga, D.; Sabatino, P. *Chem. Ber.* **1991**, *124*, 97−99. (d) Li, C.-S.; Cheng, C.-H.; Liao, F.-L.; Wang, S.-L. *J. Chem. Soc., Chem. Commun.* **1991**, 710−712. (e) Kannan, S.; James, A. J.; Sharp, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 215−216.

Table 4. Suzuki Coupling of Aryl Bromides[a]

Entry	Halide	Boronic Acid	Product	mol% Pd	Ligand	Time (h)	Yield (%)
1				0.005	**2**	18	87
2				0.1	**4**	20	96[b,c,d]
				0.05	**4**	24	94[b,c,d,e]
				0.02	**4**	26	92
				0.005	**2**	16	94
				0.001	**2**	20	92 (GC)[g]
				0.001	ArO_3P	20	43 (GC)[h,i]
				0.005	ArO_3P	24	54 (GC)[i,k]
3				0.1	**4**	25	94[b,c,d]
				0.005	**2**	20	96
				0.005	ArO_3P	24	88 (GC)[i,l]
4				0.001	**4**	19	96[b]
				0.001	–	19	100 (GC)
				0.000001	**4**	24	91
5				0.1	**4**	25	95
				0.05	**2**	25	93[f]
6				0.02	**4**	23	92

[a] Reaction conditions: 1.0 equiv aryl bromide, 1.5 equiv boronic acid, 2.0 equiv K_3PO_4, cat $Pd(OAc)_2$, cat ligand (2L/Pd) toluene (3 mL/mmol halide), 100 °C; reaction times have not been mimimized. All reactions proceed to completion unless otherwise noted. [b] $Pd_2(dba)_3$ used in place of $Pd(OAc)_2$. [c] THF used in place of toluene. [d] Reaction conducted at 65 °C. [e] CsF (3.0 equiv) used in place of K_3PO_4. [f] Reaction proceeded to 99% conversion. [g] Reaction proceeded to 99% (average) conversion. [h] Reaction proceeded to 44% (average) conversion. [i] ArO_3P = tris(2,4-di-*tert*-butylphenyl)phosphite. [j] Of two experiments, one proceeded to only 99% conversion. [k] The reaction proceeded to 52% (average) conversion. [l] The reaction proceeded to 89% (average) conversion.

dicular to the coordination plane which should be the most stereoelectronically favorable conformation for reductive elimination.[24]

Room-temperature Suzuki coupling reactions catalyzed by Pd/**4** were faster than those catalyzed by Pd/**2**. However, ligands **1**, **2**, **5**, and **6** were more effective for the Suzuki coupling of hindered substrates. Presumably this latter set of ligands are more efficient than **4** because their smaller size allows for relatively facile transmetalation to the $L_nPd(Ar)X$ intermediate when sterically encumbered aryl halides or boronic acids are used; the decreased steric properties of the ligand allows for the transformation of larger substrates. The ability of the electron-rich ligands to prevent precipitation of the palladium also may contribute to their efficiency in reactions of hindered substrates.

In general, **2** gave better results at low catalyst loading than were obtained with **4**. The larger *o*-(di-*tert*-butylphosphino)-biphenyl ligand (**4**) may tend to dissociate from the metal more readily than the smaller *o*-(dicyclohexylphosphino)biphenyl ligand (**2**) to form unligated palladium complexes which are unstable and lead to the precipitation of the metal. Therefore, catalysts based on the smaller dicyclohexylphosphino moiety are more stable than those based on larger ligands and thus allow for higher turnover numbers in reactions run at low catalyst loadings.

The fact that significantly higher turnover numbers are obtained with the electron-rich dialkyl(biphenyl)phosphine ligands than with less electron-rich phosphine or phosphite ligands is due in part to the basic nature of **2** and **4**. These ligands bind to the metal more tightly than triarylphosphine derivatives and may help to increase catalyst lifetime by keeping the metal in solution for extended periods of time. Although steric influences on coordination number are important for reactivity,[22] the basic phosphine is necessary to promote the oxidative addition step in the catalytic cycle.[2,18] This is highlighted by the results obtained with the tris(2,4-di-*tert*-butylphenyl)phosphite ligand. While the steric bulk of the phosphite ligand may lead to pathways favoring the more reactive L_1 palladium complexes, it is not as electron-rich as **1**−**6**, and is ineffective as a ligand for Suzuki coupling reactions of aryl chloride substrates.

Conclusion

In conclusion, we have developed a new, highly active catalyst system for Suzuki coupling of aryl halides based on ligands **2** and **4**, which are easily prepared in one step and are commercially available.[10] While the use of **4** generally gives faster reaction rates in room-temperature Suzuki couplings, **2**

(22) Monophosphine palladium complexes have been demonstrated to be catalytically active intermediates in other palladium-catalyzed processes. Oxidative addition, transmetalation, and reductive elimination often proceed at higher rates if coordinatively unsaturated intermediates are accessible. See: (a) Farina, V. *Comprehensive Organometallic Chemistry*, 2nd ed.; Pergamon Press: Oxford, 1995; Vol. 12, pp 161−240. (b) Hartwig, J. F. *Synlett* **1997**, 329−340 and references therein.

(23) A detailed mechanistic study on both Suzuki coupling and catalytic amination will be reported separately.

(24) Biaryl-forming reductive elimination from Pt(II) has been postulated to occur via a transition state in which both arenes are perpendicular to the coordination plane. See: Braterman, P. S.; Cross, R. J.; Young, G. B. *J. Chem. Soc., Dalton Trans. 1* **1977**, 1892−1897.

is more effective for hindered substrates and operates more efficiently at low catalyst loadings. Of great importance is that with the use of ligands **2**−**6** the rate of oxidative addition is greatly enhanced, while the rate of the other steps of the catalytic cycle are probably also increased. Thus, their use avoids the common pitfall in which speeding up the rate of one step slows that of another, resulting in little or no increase in the overall rate of the reaction. Our current view is that the success of these ligands is due to a combination of (1) their electron-richness, to enhance the rate of oxidative addition and keep the palladium in solution and (2) their steric bulk, to enhance the rate of reductive elimination and to maximize the quantity of L_1Pd complexes, increasing the rate of transmetalation. We also believe that the presence of the *o*-biphenyl moiety is important, helping to confer air stability to the ligand, enhancing the rate of reductive elimination as well as stabilizing the catalyst by interacting with the Pd. Further studies concerning the effectiveness of this class of ligands for other palladium-catalyzed reactions, as well as mechanistic studies to determine the factors responsible for the high activities of these catalysts are currently underway.

Experimental Section

General. All reactions were carried out under an argon atmosphere in oven-dried glassware. Elemental analyses were performed by E & R Microanalytical Laboratory Inc., Parsippany, NJ, or by Atlantic Microlabs Inc, Norcross, GA. Toluene was distilled under nitrogen from molten sodium. THF was distilled under argon from sodium benzophenone ketyl. DME was purchased anhydrous from Aldrich Chemical Co. and was used without further purification. Unless stated otherwise, commercially obtained materials were used without purification. Aryl halides were purchased from Aldrich Chemical Co. except for 4-chloroacetophenone and 2-bromoisopropylbenzne which were purchased from Fluka Chemical Co., 2-bromobiphenyl which was purchased from Lancaster Synthesis Inc., and *N*-(diphenylmethylene)-4-bromoaniline[25] which was prepared according to a previously published procedure.[25] Dicyclohexylchlorophosphine, palladium acetate, and *n*-butyllithium were purchased from Strem Chemical Co. Boronic acids were purchased from Aldrich Chemical company and were used without further purification. Trimethyl borate, triisopropyl borate, 9-BBN, di-*tert*-butylchlorophosphine, potassium fluoride, and 1-hexene were purchased from Aldrich Chemical Co. Tribasic potassium phosphate was purchased from Fluka Chemical Co. Sodium carbonate was purchased from Mallinckrodt Chemical Co. Tetrakis(triphenylphosphine)palladium was prepared according to a literature procedure,[26] or purchased from Strem Chemical company. 2-(*N*,*N*-Dimethylamino)-2′-(dicyclohexylphosphino)biphenyl (**1**) was prepared according to the previously published procedure.[7] 2,6-Dimethylphenylboronic acid was prepared according to a literature procedure[27] which was modified such that *n*-butyllithium and triisopropyl borate were used in place of *s*-butyllithium and trimethyl borate. IR spectra reported in this paper were obtained by placing neat samples directly on the DiComp probe of an ASI REACTIR in situ IR instrument. Yields in Tables 1 and 2 refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ^{1}H NMR, and GC analysis or combustion analysis. Entries 1[7] and 5[7] from Table 2 have been previously reported by this group and were characterized by comparison of their ^{1}H NMR spectra to those of samples prepared prior to this work; their purity was confirmed by GC analysis. The procedures described in this section are representative, and thus the yields may differ from those given in Tables 1-4.

***o*-(Dicyclohexylphosphino)biphenyl (2)**.[9] An oven-dried round-bottomed flask equipped with a magnetic stirbar and a rubber septum was allowed to cool to room temperature under an argon purge. The flask was charged with 2-bromobiphenyl (0.69 mL, 4.0 mmol) and THF (10 mL), and cooled to −78 °C in a dry ice/acetone bath. *n*-Butyllithium in hexanes (1.6 M, 2.75 mL, 4.4 mmol) was added dropwise with stirring. The resulting yellow solution was stirred at −78 °C for 45 min, during which time a yellow precipitate formed. A solution of dicyclohexylchlorophosphine (1.16 g, 5.0 mmol) in THF (2 mL) was added to the mixture dropwise at −78 °C, and the resulting solution was stirred at −78 °C for 15 min. The solution was then warmed to 0 °C in an ice water bath and allowed to warm slowly to room temperature overnight (14 h). The reaction was quenched with saturated aqueous ammonium chloride (10 mL), diluted with ether (50 mL), and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (20 mL). The combined organic layers were washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered, and concentrated to give a colorless oil. Methanol (5 mL) was added, and a white precipitate formed. The material was then recrystallized from hot methanol (two crops of crystals were collected) to afford 994 mg (71%) of a white solid, mp 103 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62−7.51 (m, 1H), 7.40−7.10 (m, 8H), 1.95−1.45 (m, 13H), 1.35−0.95 (m, 9H); ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.7; ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.7, 150.4, 142.9, 142.8, 134.1, 133.8, 132.8, 130.61, 130.55, 130.5, 130.2, 1301, 128.1, 127.3, 127.14, 127.05, 126.7, 126.4, 34.7, 34.5, 30.5, 30.2, 29.3, 29.1, 27.3, 27.2, 27.1, 26.4 (observed complexity due to P−C splitting; definitive assignments have not yet been made); IR (neat, cm^{-1}) 2916, 1441, 749. Anal. Calcd for $C_{24}H_{31}P$: C, 82.25; H, 8.92. Found: C, 82.18; H, 9.04.

2-(Di-*tert*-butylphosphino)biphenyl (4).[8,9] An oven-dried round-bottomed flask equipped with a magnetic stirbar and a rubber septum was allowed to cool to room temperature under an argon purge. The flask was charged with magnesium turnings (617 mg, 25.4 mmol) and a small crystal of iodine. The flask was purged with argon, and a solution of 2-bromobiphenyl (5.38 g, 23.1 mmol) in THF (40 mL) was added. The mixture was heated to reflux with stirring for 2 h and then allowed to cool to room temperature. The septum was removed, and anhydrous copper(I) chloride (2.40 g, 24.2 mmol) was added. The flask was capped with the septum and purged with argon for 2 min. Di-*tert*-butylchlorophosphine (5.0 g, 27.7 mmol) was added via syringe, and the mixture was heated to reflux with stirring for 8 h. The mixture was cooled to room temperature and diluted with 1:1 hexanes/ether (200 mL). The resulting suspension was filtered, and the solids were washed with hexanes (60 mL). The solid material was transferred to a flask containing 1:1 hexane/ethyl acetate (150 mL) and water (100 mL) and 30% aqueous ammonium hydroxide (60 mL) were added. The resulting slurry was stirred at room temperature for 5 min then transferred to a separatory funnel. The layers were separated, and the organic phase was washed with brine (100 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The resulting solid was recrystallized from methanol (2 crops of crystals were collected) to afford 4.46 g (67%) of a white solid, mp 86−86.5 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95−7.85 (m, 1H), 7.40−7.21 (m, 8H), 1.15 (d, 18H, J = 11.6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 18.7; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.4, 150.9, 143.6, 143.5, 135.6, 135.2, 135.0, 130.5, 130.4, 130.1, 128.3, 127.0, 126.7, 126.5, 126.2, 126.0, 125.6, 32.7, 32.4, 30.8, 30.6 (observed complexity due to P−C splitting; definitive assignments have not yet been made); IR (neat, cm^{-1}) 2956, 1459, 1362, 1173; Anal. Calcd for $C_{20}H_{27}P$: C, 80.50; H, 9.12. Found: C, 80.67; H, 9.36.

2-Dicyclohexylphosphino-2′-methylbiphenyl (5). A flame-dried flask was cooled to room temperature under an argon purge and charged with tetrakis(triphenylphosphine)palladium (425 mg, 0.37 mmol), sodium carbonate (3.9 g, 36.8 mmol), and *o*-tolylboronic acid (1.0 g, 7.36 mmol). The flask was purged with argon and a degassed mixture of DME (60 mL), water (18 mL), and ethanol (3 mL) was added to the flask via cannula. 1-Bromo-2-iodobenzene (1.13 mL, 8.83 mmol) was added to the flask via syringe and the mixture was heated to 90 °C for 42 h. The mixture was cooled to room temperature, diluted with ether (50 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with aqueous sodium hydroxide (3 × 75 mL). The organic layer was concentrated in vacuo, and the crude material was dissolved in 1:1 ether/dichloromethane (200 mL), washed with brine (50 mL), dried over anhydrous sodium sulfate,

(25) Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 4960−4976.
(26) Hegedus, L. S. In *Organometallics in Synthesis*; Schlosser, M., Ed.; John Wiley and Sons: West Sussex, England, 1994; p 448.
(27) Schoevarrs, A. M.; Kruizinga, W.; Zijlstra, R. W. J.; Veldman, N.; Spek, A. L.; Feringa, B. L. *J. Org. Chem.* **1997**, *62*, 4943−4948.

filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford 1.57 g of 2-bromo-2′-methylbiphenyl which contained ∼5% of 2-bromoiodobenzene as judged by GC analysis. This material was used without further purification.

An oven-dried Schlenk flask was cooled to room temperature under an argon purge and charged with 2-bromo-2′-methylbiphenyl (682 mg, 2.76 mmol) and THF (7 mL). The mixture was cooled to −78 °C with stirring and *n*-butyllithium (1.6 M, 1.9 mL, 3.04 mmol) was added dropwise. The mixture was stirred at −78 °C for 70 min, and then a solution of dicyclohexylchlorophosphine (803 mg, 3.45 mmol) in THF (2 mL) was added dropwise at −78 °C via syringe. The mixture was stirred at −78 °C for 20 min, warmed to 0 °C and stirred for 20 min, and then warmed to room temperature and stirred for 18 h. The mixture was quenched with saturated aqueous ammonium chloride (5 mL), diluted with ether (50 mL), and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (20 mL). The combined organic layers were washed with brine (30 mL), dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude material was crystallized from ethanol to afford 754 mg (65% overall yield) of the title compound as a white solid, mp 107−109 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.56 (s, br, 1H), 7.37−7.30 (m, 2H), 7.28−7.10 (m, 4 H), 7.06 (d, 1H, J = 7.3 Hz), 2.06 (s, 3H), (1.99−1.80 (m, 1H), 1.80−1.45 (m, 11H), 1.40−0.85 (m, 10H); ^{31}P NMR (121 MHz, $CDCl_3$) δ −10.97; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 149.5, 142.4, 142.3, 135.5, 134.5, 134.2, 132.5, 130.7, 130.0, 129.9, 129.3, 128.2, 127.2, 126.3, 124.5, 35.4, 35.2, 33.2, 33.0, 30.8, 30.6, 30.0, 29.8, 29.7, 29.6, 28.8, 28.7, 27.6, 27.44, 27.39, 27.2, 27.0, 26.4, 26.3, 20.7, 20.6 (observed complexity due to P−C splitting; definitive assignments have not yet been made); IR (neat, cm^{-1}) 2927, 1445, 1177, 1007, 766. Anal. Calcd for $C_{25}H_{33}P$: C, 82.38; H, 9.13. Found: C, 82.11; H, 9.21.

2-Dicyclohexylphosphino-2′-isopropylbiphenyl (6). An oven-dried flask was cooled to room temperature under an argon purge and charged with 2-bromoisopropyl benzene (4.0 g, 20.0 mmol) and THF (80 mL). The solution was cooled to −78 °C and a solution of *n*-butyllithium in hexanes (1.65 M, 12.7 mL, 21.0 mmol) was added dropwise. The mixture was stirred at −78 °C for 1 h and then transferred via cannula to a separate flask containing a solution of triisopropyl borate (9.2 mL, 40.0 mmol) in THF (40 mL) under argon which had been cooled to −78 °C. The reaction mixture was stirred at −78 °C for 15 min, and then warmed to room temperature and allowed to stir overnight (14 h). Aqueous HCl (1 M, 250 mL) was added, and the mixture was stirred at room temperature for 15 min. The mixture was basified to pH 14 with aqueous NaOH (6 M), and the mixture was transferred to a separatory funnel. The mixture was extracted with ether (100 mL), and the organic layer was discarded. The aqueous phase was acidified to ∼pH 7 with aqueous HCl (1 M) and was extracted with ether (2 × 150 mL). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was precipitated from ether/pentane to give 2-isopropylphenylboronic acid (2.4 g) which was used without further purification.

An oven-dried flask was charged with the crude 2-isopropylphenylboronic acid (2.4 g), tetrakis(triphenylphosphine) palladium (840 mg, 0.61 mmol, 5 mol %), and K_3PO_4 (4.6 g, 21.9 mmol). The flask was purged with argon, and then DMF (100 mL) and 2-bromoiodobenzene (1.88 mL, 14.6 mmol) were added via syringe. The mixture was heated to 100 °C for 48 h, and then cooled to room temperature, diluted with ether (200 mL) and water (100 mL), and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (200 mL). The combined organic layers were washed with aqueous NaOH (1 M), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to give 2-bromo-2′-isopropylbiphenyl (1.5 g). The crude material was used without further purification.

An oven-dried flask was cooled to room temperature under an argon purge and charged with the crude 2-bromo-2′-isopropylbiphenyl (1.1 g, 4.0 mmol), and THF (10 mL). The mixture was cooled to −78 °C, and a solution of *n*-butyllithium in hexanes (1.6 M, 2.8 mL, 4.4 mmol) was added dropwise. The mixture was stirred at −78 °C for 1 h, and then a solution of dicyclohexylchlorophosphine (1.16 g, 5.0 mmol) in THF (2 mL) under argon was added dropwise. The mixture was stirred at −78 °C for 15 min and then warmed to room temperature and stirred for 20 h. Aqueous ammonium chloride (10 mL) was added, and the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The layers were separated, and the aqueous layer was extracted with ether (20 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude material was crystallized from ethanol to afford 877 mg (∼11% overall yield from 2-isopropylbromobenzene) of a white crystalline solid, mp 104 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.58 (s, br, 1H), 7.36−7.10 (m, 6H), 7.00 (d, 1H, J = 7.5 Hz), 2.65 (p, 1H, J = 6.8 Hz), 1.99−1.85 (m, br, 1H), 1.75−1.45 (m, 11H), 1.28−0.85 (m, 17H); ^{31}P NMR (121 MHz, $CDCl_3$) δ −12.75; ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.9, 149.5, 146.2, 141.15, 141.07, 134.9, 134.7, 132.7, 132.6, 130.9, 130.4, 130.3, 127.9, 127.6, 126.3, 124.7, 124.3, 35.8, 35.6, 33.9, 33.7, 30.9, 30.8, 30.3, 30.0, 29.9, 29.7, 29.6, 29.5, 28.9, 28.8, 27.6, 27.5, 27.4, 27.3, 27.2, 27.0, 26.5, 26.4, 25.3, 22.6 (observed complexity due to P−C splitting; definitive assignments have not yet been made); IR (neat, cm^{-1}) 2921, 1443, 1003, 753. Anal. Calcd for $C_{27}H_{37}P$: C, 82.61; H, 9.50. Found: C, 82.35; H, 9.55.

***N*-(Diphenylmethylene)-2-bromoaniline** An oven-dried flask was charged with 2-bromoaniline (10.32 g, 60.0 mmol), benzophenone (10.93 g, 60.0 mmol), 5 Å molecular sieves (150 g), and toluene (300 mL); the mixture was heated to 100 °C with stirring under an argon atmosphere for 36 h. The mixture was cooled to room temperature, filtered, and concentrated in vacuo to afford a yellow solid which was recrystallized from methanol to afford 16.58 g (82%) of a yellow solid, mp 103−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, 2H, J = 7.0 Hz), 7.50−7.40 (m, 4H), 7.28−7.16 (m, 5H), 7.05−6.99 (m, 1H), 6.80−6.74 (m, 1H), 6.53 (d, 1H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 150.1, 138.7, 135.9, 132.3, 131.0, 129.5, 128.8, 128.5, 128.2, 127.8, 127.4, 121.1, 115.2; IR (neat, cm^{-1}) 3056, 1615, 1447, 1275, 1025. Anal. Calcd for $C_{19}H_{14}BrN$: C, 67.87; H, 4.20. Found: C, 67.76; H, 4.24.

General Procedure for the Suzuki Coupling of Aryl Halides Using KF as Base.

An oven-dried resealable Schlenk flask was evacuated and backfilled with argon[28] and charged with $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 1.0 mol %), ligand **4** (6.0 mg, 0.020 mmol, 2.0 mol %), the boronic acid (1.5 mmol), and potassium fluoride (174 mg, 3.0 mmol). The flask was evacuated and backfilled with argon, and THF (1 mL) and the aryl halide (1.0 mmol) were added through a rubber septum (aryl halides which were solids at room temperature were added prior to the second evacuation/backfill cycle). The flask was sealed with a Teflon screwcap, and the reaction mixture was stirred at room temperature until the starting aryl chloride had been completely consumed as judged by GC analysis. The reaction mixture was diluted with ether (30 mL) and poured into a separatory funnel. The mixture was washed with aqueous NaOH (1 M, 20 mL), and the aqueous layer was extracted with ether (20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

Suzuki Coupling of Aryl Bromides

2-Methoxy-3-(1,3-dioxolane)-biphenyl. The coupling of 2-(3-bromophenyl)-1,3-dioxolane with 2-methoxyphenylboronic acid was effected using the general procedure with 0.5 mol % $Pd(OAc)_2$ and 1.0 mol % **4** to afford 215 mg (84%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.55−7.50 (m, 1H), 7.43−7.40 (m, 2H), 7.38−7.28 (m, 2H), 7.06−6.96 (m, 2H), 5.59 (s, 1H), 4.17−4.01 (m, 4H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 138.5, 137.6, 130.8, 130.3, 130.2, 128.6, 127.8, 127.5, 124.8, 120.7, 111.1, 103.7, 65.1, 55.4; IR (neat, cm^{-1}) 2887, 1598, 1239, 1100, 753. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.92; H, 6.49.

(28) Reactions in which argon purges were used instead of the evacuation/backfill cycles (at all points required in the procedure) gave similar results.

2-Methoxy-3-(1,3-dioxolane)biphenyl. (Phosphite ligand was used). The coupling of 2-(3-bromophenyl)-1,3-dioxolane with 2-methoxyphenylboronic acid was effected using the general procedure with 0.5 mol % $Pd(OAc)_2$ and 1.0 mol % tris(2,4-di-*tert*-butylphenyl)phosphite to afford 211 mg (82%) of the title compound as a colorless oil.

4-Formyl-4′-ethoxybiphenyl. The coupling of 4-bromobenzaldehyde with 4-ethoxyphenylboronic acid was effected using the general procedure with 0.5 mol % $Pd(OAc)_2$ and 1.0 mol % **4** to afford 203 mg (90%) of the title compound as a white solid, mp 102−103 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.92 (d, 2H, J = 8.4 Hz), 7.72 (d, 2H, J = 8.3 Hz), 7.58 (d, 2H, J = 8.8 Hz), 6.99 (d, 2H, J = 8.8 Hz), 4.10 (q, 2H, J = 7.1 Hz), 1.45 (t, 3H, J = 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.7, 159.5, 146.7, 134.7, 131.8, 130.2, 128.4, 126.9, 115.0, 63.6, 14.7; IR (neat, cm^{-1}) 2984, 1679, 1602, 1185, 822. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 80.02; H, 6.47.

4-Formyl-4′-ethoxybiphenyl. The coupling of 4-bromobenzaldehyde with 4-ethoxyphenylboronic acid was effected using the general procedure with 0.5 mol % $Pd(OAc)_2$ and 1.0 mol % tris(2,4-di-*tert*-butylphenyl)phosphite to afford 178 mg (79%) of the title compound as a white solid.

4-Phenylphenol.[29] The coupling of 4-bromophenol with phenylboronic acid was effected using the general procedure with a reaction temperature of 50 °C to afford 152 mg (89%) of the title compound as a white solid, mp 146−147 °C (lit. mp 165 °C).[29] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.6−6.8 (m, 9H), 4.88 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.0, 140.7, 134.0, 129.4, 128.7, 128.4, 126.7, 115.6; IR (neat, cm^{-1}) 3350, 1262, 1116, 834, 757. Anal. Calcd for $C_{12}H_{10}O$: C, 84.68; H, 5.92. Found: C, 84.96; H, 5.64.

2-Formyl-4′-diphenylketiminebiphenyl. The coupling of *N*-(diphenylmethylene)-4-bromoaniline[25] with 2-formylphenylboronic acid was effected using the general procedure (carried out on a 2 mmol scale) to afford 647 mg (90%) of the title compound as a yellow powder, mp 96−98 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.88 (s, 1H), 7.98 (d, 1H, J = 8.0 Hz), 7.79 (d, 2H, J = 7.3 Hz), 7.59 (t, 1H, J = 7.3 Hz), 7.39−7.50 (m, 6H), 7.30 (d, 2H, J = 5.9 Hz), 7.17 (d, 4H, J = 7.8 Hz), 6.84 (d, 2H, J = 7.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.5, 168.8, 151.3, 145.7, 139.3, 135.9, 133.6, 133.4, 132.2, 130.9, 130.6, 130.3, 129.4, 129.3, 128.8, 128.2, 127.9, 127.4, 127.3, 121.0; IR (neat, cm^{-1}) 3059, 2845, 2747, 1691, 1595, 1472, 1445, 1392. Anal. Calcd for $C_{26}H_{19}NO$: C, 86.40; H, 5.30. Found: C, 86.43; H, 5.09.

***N*-Acetyl-4-aminobiphenyl**.[30] The coupling of 4′-bromoacetanilide with phenylboronic acid was effected using the general procedure with a reaction temperature of 50 °C to afford 188 mg (89%) of the title compound as a white solid, mp 150−153 °C (lit. mp 171 °C).[30] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.7−7.3 (m, 9H), 2.19 (s, 3H), 2.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 140.4, 137.1, 131.9, 128.8, 127.5, 127.1, 126.8, 120.3, 24.5; IR (neat, cm^{-1}) 3308, 3192, 1660, 1606, 1454, 1490, 1405, 1370, 1324. Anal. Calcd for $C_{14}H_{13}NO$: C, 79.59; H, 6.20. Found: C, 79.49; H, 6.00.

2-Phenylbenzyl alcohol.[31] The coupling of 2-bromobenzyl alcohol with phenylboronic acid was effected using the general procedure with a reaction temperature of 50 °C to afford 162 mg (88%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5−7.2 (m, 9H), 4.54 (s, 2H), 2.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.1, 140.6, 137.9, 130.0, 129.0, 128.3, 128.2, 127.6, 127.5, 127.2; IR (neat, cm^{-1}) 3350, 3061, 1478, 1451, 1193, 1007, 749. Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.94; H, 6.91.

2,5-Dimethylbiphenyl.[32] The coupling of 2-bromo-*p*-xylene with phenylboronic acid was effected using the general procedure with a reaction temperature of 45 °C to afford 171 mg (94%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4−7.0 (m, 8H), 2.34 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0, 141.7, 135.1, 132.1, 130.5, 130.2, 129.2, 128.0, 127.9, 126.6; IR (neat, cm^{-1}) 3026, 2922, 1490, 1444, 811, 776, 703. Anal. Calcd for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 92.11; H, 7.86.

2,5-Dimethylbiphenyl.[32] (Reaction was run at room temperature). The coupling of 2-bromo-*p*-xylene with phenylboronic acid was effected using the general procedure to afford 149 mg (82%) of the title compound as a colorless oil.

2,5-Dimethylbiphenyl.[32] **(**Reaction was run at room temperature, ligand 2 was used). The coupling of 2-bromo-*p*-xylene with phenylboronic acid was effected using the general procedure with ligand **2** to afford 175 mg (96%) of the title compound as a colorless oil.

2-Phenylthiophene.[33] The coupling of 2-bromothiophene with phenylboronic acid was effected using the general procedure to afford 159 mg (99%) of the title compound as a white solid, mp 34−35 °C (lit. mp 34−36 °C).[33] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69 (d, 2H, J = 7.2 Hz), 7.44 (dd, 2H, J = 7.8 Hz, 7.2 Hz), 7.44 (t, 1H, J = 7.8 Hz), 7.37 (d, 1H, J = 3.8 Hz), 7.33 (d, 1H, J = 5.0 Hz), 7.13 (dd, 1H, J = 5.0 Hz, 3.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 134.3, 128.8, 128.0, 127.4, 125.9, 124.7, 123.0; IR (neat, cm^{-1}) 3076, 1596, 1488, 1446, 1426, 1334, 1257, 1074, 852, 824, 757, 690. Anal. Calcd for $C_{10}H_8S$: C, 74.96; H, 5.03. Found: C, 75.06; H, 5.00.

2,6-Dimethylbiphenyl.[34] The coupling of 2-bromo-*m*-xylene with phenylboronic acid was effected using the general procedure with a reaction temperature of 65 °C to afford 149 mg (82%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5−7.0 (m, 8H), 2.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 141.0, 136.0, 129.0, 128.4, 127.2, 127.0, 126.6. IR (neat, cm^{-1}) 3057, 3022, 1463, 1444, 768; Anal. Calcd for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 91.92; H, 8.00.

2,6-Dimethylbiphenyl.[34] **(**Reaction was run at room temperature, ligand **2** was used). The coupling of 2-bromo-*m*-xylene with phenylboronic acid was effected using the general procedure with ligand **2** to afford 168 mg (92%) of the title compound as a colorless oil.

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4-Methylbiphenyl.[7] The coupling of 4-chlorotoluene with phenylboronic acid was effected using the general procedure to afford 161 mg (96%) of the title compound as a white solid, mp 42−45 °C (lit. mp 44−46 °C).[7]

4-Methylbiphenyl.[7] The coupling of 4-chlorotoluene with phenylboronic acid was effected using the general procedure with 0.5 mol % $Pd(OAc)_2$ and 1.0 mol % **4** to afford 161 mg (96%) of the title compound as a white solid.

2-Methoxy-4′-methylbiphenyl.[7] The coupling of 4-chlorotoluene with 2-methoxyphenyl boronic acid was effected using the general procedure to afford 188 mg (95%) of the title compound as a white solid, mp 71−72 °C (lit. mp 74−75 °C).[7] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, 1H, J = 8.3 Hz), 7.3−6.9 (m, 7H), 3.81 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 136.6, 135.5, 130.8, 130.6, 129.4, 128.7, 128.3, 120.7, 111.1, 55.5, 21.2; IR (neat, cm^{-1}) 3022, 1598, 1486, 1463, 1258, 1235, 1031, 818, 753. Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 85.02; H, 7.33.

4-Cyanobiphenyl.[35] The coupling of 4-chlorobenzonitrile with phenylboronic acid was effected using the general procedure to afford 156 mg (87%) of the title compound as a white solid, mp 86−87 °C (lit. mp 82−84 °C).[35] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76−7.68 (m, 4H), 7.60−7.58 (m, 2H), 7.52−7.43 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 139.1, 132.5, 129.0, 128.6, 127.6, 127.4, 118.9, 110.8; IR (neat, cm^{-1}) 2227, 1605, 1485, 768. Anal. Calcd for $C_{13}H_9N$: C, 87.12; H, 5.06. Found: C, 87.04; H, 5.06.

4-Nitrobiphenyl.[36] The coupling of 4-chloronitrobenzene with phenylboronic acid was effected using the general procedure with 0.2 mol % $Pd(OAc)_2$ and 0.4 mol % **4** to afford 196 mg (98%) of the title compound as a yellow solid, mp 102−103 °C (lit. mp 114−114.5 °C).[36]

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^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (d, 2H, J = 8.5 Hz), 7.73 (d, 2H, J = 8.5 Hz), 7.63 (d, 2H, J = 7.6 Hz), 7.52−7.44 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 147.0, 138.7, 129.1, 128.9, 127.8, 127.3, 124.1; IR (neat, cm $^{-1}$)1594, 1513, 1447, 1351, 1104, 1077. Anal. Calcd for $C_{12}H_9NO_2$: C, 72.35; H, 4.55. Found: C, 72.63; H, 4.20.

4-Nitrobiphenyl.[36] (1.0 mol % Pd used). The coupling of 4-chloronitrobenzene with phenylboronic acid was effected using the general procedure to afford 196 mg (98%) of the title compound as a yellow solid.

4-Methoxybiphenyl.[7] The coupling of 4-chloroanisole with phenylboronic acid was effected using the general procedure and a reaction temperature of 45 °C to afford 163 mg (88%) of the title compound as a white solid, mp 77−78.5 °C (lit. mp 83−84 °C).[7]

4-Methoxybiphenyl.[7] The coupling of 4-chloroanisole with phenylboronic acid was effected using the general procedure with 1.5 mol % $Pd(OAc)_2$ and 3.0 mol % **4** to afford 170 mg (92%) of the title compound as a white solid.

3-Acetyl-3′,5′-dimethoxybiphenyl. The coupling of 5-chloro-1,3-dimethoxybenzene with 3-acetylphenylboronic acid was effected using the general procedure to afford 232 mg (91%) of the title compound as a white solid, mp 73−74 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.92 (d, 1H, J = 7.5 Hz), 7.75 (d, 1H, J = 7.5 Hz), 7.50 (t, 1H, J = 7.5 Hz), 6.73 (s, 2H), 6.48 (s, 1H), 3.84 (s, 6H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 161.0, 142.2, 141.5, 137.4, 131.7, 128.9, 127.4, 126.8, 105.4, 99.5, 55.3, 26.6; IR (neat, cm^{-1}) 3006, 2937, 1459, 1402, 1349, 1266, 1204, 1155. Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.07; H, 5.94.

2-Acetylbiphenyl.[37] The coupling of 2-chloroacetophenone with phenylboronic acid was effected using the general procedure (carried out on a 2 mmol scale) to afford 369 mg (94%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50−7.57 (m, 2H), 7.33−7.44 (m, 7H), 2.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.8, 140.8, 140.7, 140.4, 130.7, 130.2, 128.8, 128.8, 128.6, 127.8, 127.4, 30.4; IR (neat, cm^{-1}) 3058, 3024, 1687, 1594, 1471, 1449, 1354, 1269, 1233. Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16. Found: C, 85.76; H, 6.39.

3-(3-Acetylphenyl)pyridine. The coupling of 3-chloropyridine with 3-acetylphenylboronic acid was effected using the general procedure with a reaction temperature of 50 °C to afford 181 mg (92%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.88 (d, 1H, J = 2.3 Hz), 8.64 (d, 1H, J = 4.7 Hz), 8.18 (s, 1H), 8.00 (d, 1H, J = 7.7 Hz), 7.92 (d, 1H, J = 8.0 Hz), 7.79 (d, 1H, J = 7.7 Hz), 7.60 (t, 1H, J = 7.8 Hz), 7.43−7.39 (m, 1H), 2.67 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 149.0, 148.2, 138.4, 138.3, 135.7, 134.4, 131.5, 129.3, 127.9, 126.8, 123.6, 26.6; IR (neat, cm^{-1}) 3034, 1683, 1239, 791. Anal. Calcd for $C_{13}H_{11}NO$: C, 79.17; H, 5.62. Found: C, 79.12; H, 5.62.

2-Cyanomethylbiphenyl.[38] The coupling of 2-chlorobenzyl cyanide with phenylboronic acid was effected using the general procedure to afford 177 mg (92%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.53 (m, 1H), 7.48−7.38 (m, 5H), 7.30−7.26 (m, 3H), 3.63 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.8, 139.9, 130.4, 128.9, 128.6, 128.2, 127.7, 118.1, 22.0; IR (neat, cm^{-1}) 3061, 2250, 1482, 749. Anal. Calcd for $C_{14}H_{11}N$: C, 87.01; H, 5.74. Found: C, 87.25; H, 5.60.

4-Carbomethoxy-3′-acetylbiphenyl. The coupling of methyl-4-chlorobenzoate with 3-acetylphenylboronic acid was effected using the general procedure to afford 229 mg (90%) of the title compound as a white solid, mp 109−110 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.12 (d, 2H, J = 8.3 Hz), 7.96 (d, 1H, J = 7.8 Hz), 7.82 (d, 1H, J = 6.5 Hz), 7.68 (d, 2H, J = 8.8 Hz), 7.57 (t, 1H, J = 7.7 Hz), 3.94 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 166.6, 144.3, 140.3, 137.7, 131.5, 130.1, 129.3, 129.1, 127.9, 126.9, 126.8, 52.0, 26.6; IR (neat, cm^{-1}) 3003, 1722, 1679, 1293, 1111, 768. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.96; H, 5.27.

Methyl-(4-*n*-hexyl)benzoate. An oven-dried Schlenk flask was charged with 9-BBN (146 mg, 1.2 mmol) in a nitrogen-filled glovebox. The flask was capped with a rubber septum and removed from the glovebox. THF (2 mL) was added, the suspension was cooled to 0 °C, and 1-hexene (0.175 mL, 1.4 mmol) was added via syringe. The mixture was stirred at 0 °C for 5 min, warmed to room temperature, and stirred overnight (∼14 h). The solution was then transferred via cannula to a separate oven-dried Schlenk flask which had been cooled to room temperature under an argon purge and charged with methyl 4-chlorobenzoate (171 mg, 1.0 mmol), potassium fluoride (174 mg, 3.0 mmol), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 1 mol %), **2** (7.0 mg, 0.02 mmol, 2 mol %), and THF (1 mL). The mixture was heated to 65 °C with stirring until the starting aryl chloride had been completely consumed as judged by GC analysis (20 h). The mixture was cooled to room temperature, diluted with ethyl acetate (30 mL), and transferred to a separatory funnel. The mixture was washed with aqueous NaOH (2 M, 20 mL) and washed with brine (20 mL). The organic layer was concentrated in vacuo, and the crude material was purified by flash chromatography on silica gel to afford 186 mg (84%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, 2H, J = 8.2 Hz), 7.24 (d, 2H, J = 8.2 Hz), 3.90 (s, 3H), 2.65 (t, 2H, J = 7.7 Hz), 1.69−1.57 (m, 2H), 1./60−1.25 (m, 6H), 0.88 (t, 3H, J = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 148.5, 129.6, 128.4, 127.6, 51.9, 36.0, 31.6, 31.1, 28.9, 22.6, 14.0; IR (neat, cm^{-1}) 2928, 2856, 1724, 1436, 1278, 1109. Anal. Calcd for $C_{14}H_{20}O$: C, 76.33; H, 9.15. Found: C, 76.57; H, 9.43.

2-Methoxybiphenyl.[39] The coupling of 2-chloroanisole with phenylboronic acid was effected using the general procedure to afford 181 mg (98%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, 2H, J = 8.0 Hz), 7.46 (t, 2H, J = 8.0 Hz), 7.40−7.35 (m, 3H), 7.08 (t, 1H, J = 7.4 Hz), 7.03 (d, 1H, J = 8.6 Hz), 3.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.4, 138.5, 130.8, 130.7, 129.5, 128.6, 127.9, 126.9, 120.8, 111.2, 55.5; IR (neat, cm^{-1}) 3059, 3025, 2955, 2833, 1597, 1584, 1504, 1483, 1463, 1430, 1260, 1236, 1180, 1123, 1056, 1028, 1009, 754, 732, 699. Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.43; H, 6.68.

General Procedure for the Suzuki Coupling of Aryl Halides Using K_3PO_4 as Base

An oven-dried resealable Schlenk flask was evacuated and backfilled with argon and charged with $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 1.0 mol %), ligand **4** (6.0 mg, 0.020 mmol, 2.0 mol %), the boronic acid (1.5 mmol), and K_3PO_4 (425 mg, 2.0 mmol). The flask was evacuated and backfilled with argon, and toluene (3 mL) and the aryl halide (1.0 mmol) were added through a rubber septum (aryl halides which were solids at room temperature were added prior to the second evacuation/backfill cycle). The flask was sealed with a Teflon screwcap, and the reaction mixture was heated to 65 °C with stirring until the starting aryl halide had been completely consumed as judged by GC analysis. The reaction mixture was then cooled to room temperature, diluted with ether (30 mL), and poured into a separatory funnel. The mixture was washed with aqueous NaOH (1 M, 20 mL), and the aqueous layer was extracted with ether (20 mL). The combined organic layers were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

2-(Diphenylketimine)-4′-ethoxybiphenyl. The coupling of *N*-(diphenylmethylene)-2-bromoaniline with 4-ethoxyphenylboronic acid was effected using the general procedure with ligand **2** and a reaction temperature of 80 °C to afford 328 mg (87%) of the title compound as a yellow solid, mp 97−98 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.64 (d, 2H, J = 6.7 Hz), 7.49−7.30 (m, 3H), 7.20−6.90 (m, 8H), 6.86 (d, 1H, J = 7.9 Hz), 6.77 (d, 2H, J = 6.8 Hz), 6.65 (d, 2H, J = 7.0 Hz), 3.99 (q, 2H, J = 7.0 Hz), 1.39 (t, 3H, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 157.4, 148.9, 139.3, 136.3, 132.2, 131.0, 130.3, 129.8, 129.1, 128.7, 128.2, 128.0, 127.3, 126.9, 63.2, 14.8; IR (neat, cm^{-1}) 2983, 1607, 1470, 1243, 1052. Anal. Calcd for $C_{27}H_{23}NO$: C, 85.91; H, 6.14. Found: C, 85.81; H, 6.08.

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2,6-Dimethyl-4′-*tert*-butylbiphenyl. The coupling of 1-bromo-4-*tert*-butylbenzene with 2,6-dimethylphenylboronic acid was effected using the general procedure (carried out on a 0.5 mmol scale) with 4 mol % **1** as the supporting ligand and a reaction temperature of 100 °C to afford 114 mg (96%) of the title compound as a white solid, mp 71−73 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, 2H, J = 8.2 Hz), 7.19−7.08 (m, 3H), 7.08 (d, 2H, J = 8.2 Hz), 2.05 (s, 6H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 141.9, 137.8, 136.3, 128.6, 127.2, 126.8, 125.1, 34.5, 31.4, 20.9; IR (neat, cm^{-1}) 3034, 2952, 2864, 1507, 1462, 1397, 1362, 1113, 1002, 835, 768. Anal. Calcd for $C_{18}H_{22}$: C, 90.70; H, 9.30. Found: C, 91.05; H, 9.02.

2,6-Dimethyl-4′-acetylbiphenyl. The coupling of 4′-bromoacetophenone with 2,6-dimethylphenylboronic acid was effected using the general procedure (carried out on a 0.5 mmol scale) with 2 mol % $Pd(OAc)_2$ and 4 mol % **4** and a reaction temperature of 80 °C to afford 98 mg (87%) of the title compound as a white solid, mp 64−65 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13 (d, 2H, J = 8.2 Hz), 7.36 (d, 2H, J = 8.2 Hz), 7.29−7.20 (m, 3H), 2.75 (s, 3H), 2.11 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.8, 146.4, 140.6, 135.6, 135.5, 129.4, 128.6, 127.5, 127.4, 26.6, 20.7; IR (neat, cm^{-1}) 2998, 2947, 1679, 1602, 1398, 1354, 1265,1109, 1004, 956, 776. Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.98; H, 6.93.

2,6-Dimethyl-2′-methylbiphenyl.[34] The coupling of 2-bromotoluene with 2,6-dimethylphenylboronic acid was effected using the general procedure (carried out on a 0.5 mmol scale) with **1** as the supporting ligand and a reaction temperature of 100 °C to afford 88 mg (90%) of the title compound as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.24 (m, 3H), 7.22−7.12 (m, 3H), 7.06−7.03 (m, 1H), 2.00 (s, 3H), 1.98 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.0, 140.4, 135.8, 135.5, 129.9, 128.7, 127.1, 126.9, 126.8, 126.0, 20.4, 19.4; IR (neat, cm^{-1}) 3060, 1583, 1462, 1120, 760. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.57; H, 8.20.

2,6-Dimethyl-2′-methylbiphenyl.[34] The coupling of 2-chloro-*m*-xylene with *o*-tolylboronic acid was effected using the general procedure with **6** as the supporting ligand and a reaction temperature of 100 °C to afford 180 mg (92%) of the title compound as a colorless oil.

2,6-Dimethyl-2′-methylbiphenyl.[34] The coupling of 2-chloro-*m*-xylene with *o*-tolylboronic acid was effected using the general procedure with **2** as the supporting ligand and a reaction temperature of 100 °C to afford 174 mg (89%) of the title compound as a colorless oil.

2-Methoxy-2′-acetylbiphenyl. The coupling of 2-chloroacetophenone with 2-methoxyphenyl boronic acid was effected using the general procedure to afford 201 mg (89%) of the title compound as a white solid, mp 83 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, 1H, J = 7.7 Hz), 7.54−7.49 (m, 1H), 7.42−7.26 (m, 4H), 7.06 (t, 1H, J = 7.3 Hz), 6.92 (d, 1H, J = 8.2 Hz), 3.73 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.2, 155.8, 140.7, 136.7, 131.1, 130.8, 130.5, 129.9, 129.3, 127.3, 127.1, 121.0, 110.6, 55.0, 28.8; IR (neat, cm^{-1}) 3003, 1695, 1243, 757. Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.89; H, 6.02.

2,5-Dimethyl-2′-methylbiphenyl. The coupling of 2-chloro-*p*-xylene with *o*-tolylboronic acid was effected using the general procedure with **2** as the supporting ligand and a reaction temperature of 80 °C to afford 185 mg (94%) of the title compound a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.04 (m, 6H), 6.93 (s, 1H), 2.33 (s, 3H), 2.06 (s, 3H), 2.00 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7, 141.4, 135.8, 134.9, 132.6, 129.9, 129.7, 129.6, 129.2, 127.8, 127.0, 125.5, 20.9, 19.8, 19.3; IR (neat, cm^{-1}) 3041, 2921, 1482, 1032, 810. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.68; H, 8.17.

2,6-Dimethylbiphenyl.[34] The coupling of 2-chloro-*m*-xylene with phenylboronic acid was effected using the general procedure with **1** as the supporting ligand and a reaction temperature of 100 °C to afford 164 mg (90%) of the title compound as a colorless oil.

2,6-Dimethylbiphenyl.[34] The coupling of 2-chloro-*m*-xylene with phenylboronic acid was effected using the general procedure with **2** as the supporting ligand and a reaction temperature of 100 °C to afford 135 mg (85%) of the title compound as a colorless oil. A small amount of the starting aryl chloride (7%) was not consumed during the course of the reaction.

General Procedure for the Suzuki Coupling of Aryl Halides at Low Catalyst Loadings (≤0.1 mol % Pd)

An oven-dried resealable Schlenk flask was evacuated and backfilled with argon and charged with the boronic acid (1.5 mmol) and K_3PO_4 (2.0 mmol). The flask was evacuated and backfilled with argon, and THF (1.5 mL) and the aryl halide (1.0 mmol) were added through a rubber septum. A separate flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol) and ligand **4** (4.5 mmol, 0.015 mmol) and was purged with argon. THF (1 mL) was added, the mixture was stirred for 1 min at room temperature, and then 100 μL of this solution (0.1 mol % Pd, 0.15 mol % ligand **4**) was added to the Schlenk flask followed by additional THF (1.5 mL). The septum was removed, the flask was sealed with a Teflon screwcap, and the mixture was stirred at room temperature for 2 min and then heated to 65 °C with stirring until the starting aryl bromide had been completely consumed as judged by GC analysis. The reaction mixture was then cooled to room temperature, diluted with ether (20 mL), and poured into a separatory funnel. The mixture was washed with aqueous NaOH (1 M, 20 mL), and the layers were separated. The aqueous layer was extracted with ether (20 mL), and the combined organic extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was then purified by flash chromatography on silica gel.

4-*tert*-Butylbiphenyl.[39] (0.1 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure to afford 199 mg (95%) of a glassy solid, mp 47−49 °C (lit. mp 51−52 °C).[39b] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58−7.51 (m, 4H), 7.46−7.38 (m, 4H), 7.30−7.26 (m, 1H), 1.34 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 141.1, 138.3, 128.7, 127.0, 126.9, 126.8, 125.7, 34.5, 31.4; IR (neat, cm^{-1}) 2961, 1486, 834, 764. Anal. Calcd for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.42; H, 8.69.

4-*tert*-Butylbiphenyl.[39] (0.05 mol % Pd, CsF as base). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with CsF (3.0 mmol) as the base and a 50 μL of a catalyst solution composed of $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol), ligand **4** (4.5 mmol, 0.015 mmol), in THF (1 mL) to afford 202 mg (96%) of a glassy solid.

4-*tert*-Butylbiphenyl.[39] (0.02 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 80 °C, and 20 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **4** (6.0 mg, 0.02 mmol), and THF (2 mL) to afford 196 mg (93%) of a glassy solid.

4-*tert*-Butylbiphenyl.[39] (0.005 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **2** (7.0 mg, 0.02 mmol), and THF (10 mL) to afford 198 mg (94%) of a glassy solid.

4-*tert*-Butylbiphenyl.[39] (0.001 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 10 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **2** (7.0 mg, 0.02 mmol), and THF (10 mL). When the reaction was no longer progressing, the mixture was cooled to room temperature, and dodecane (0.23 mL) was added as an internal standard; GC analysis showed 93% conversion (96% GC yield).

4-*tert*-Butylbiphenyl.[39] (0.001 mol % Pd, K_3PO_4 as base, phosphite ligand). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 10 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), tris(2,4-di-*tert*-butylphenyl)phosphite (13.0 mg, 0.02 mmol), and THF (10 mL). When the reaction was no longer progressing, the mixture was cooled to room-temperature and dodecane (0.23 mL) was added as an internal standard; GC analysis showed 40% conversion (42% GC yield).

4-*tert*-Butylbiphenyl[39] (0.005 mol % Pd, K_3PO_4 as base, phosphite ligand). The coupling of 1-bromo-4-*tert*-butylbenzene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution

composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), tris(2,4-di-*tert*-butylphenyl)phosphite (13.0 mg, 0.02 mmol), and THF (10 mL). When the reaction was no longer progressing, the mixture was cooled to room-temperature and dodecane (0.23 mL) was added as an internal standard; GC analysis showed 47% conversion (49% GC yield).

2-Methyl-4′-*tert*-butylbiphenyl (0.1 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with *o*-tolylboronic acid was effected using the general procedure with 100 μL of a catalyst solution composed of $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol), ligand **4** (4.5 mmol, 0.015 mmol), and THF (1 mL) to afford 210 mg (94%) of a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, 2H, J = 8.2 Hz), 7.27−7.22 (m, 6H), 2.29 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.5, 141.9, 139.0, 135.4, 130.3, 129.9, 128.8, 127.0, 125.7, 124.9, 34.5, 31.4, 20.5; IR (neat, cm^{-1}) 2961, 1482, 1112, 838. Anal. Calcd for $C_{17}H_{20}$: C, 91.01; H, 8.99. Found: C, 91.11; H, 9.21.

2-Methyl-4′-*tert*-butylbiphenyl (0.005 mol % Pd, K_3PO_4 as base). The coupling of 1-bromo-4-*tert*-butylbenzene with *o*-tolylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **2** (7.0 mg, 0.02 mmol), and THF (10 mL) to afford 216 mg (96%) of a glassy solid.

2-Methyl-4′-*tert*-butylbiphenyl (0.005 mol % Pd, K_3PO_4 as base, phosphite ligand). The coupling of 1-bromo-4-*tert*-butylbenzene with *o*-tolylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), tris-(2,4-di-*tert*-butylphenyl)phosphite (13.0 mg, 0.02 mmol), and THF (10 mL). When the reaction was no longer progressing, the mixture was cooled to room-temperature and dodecane (0.23 mL) was added as an internal standard; GC analysis showed 87% conversion (84% GC yield).

2-Methoxy-3-(1,3-dioxolane)biphenyl (0.005 mol % Pd, K_3PO_4 as base). The coupling of 2-(3-bromophenyl)-1,3-dioxolane with *o*-methoxyphenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **2** (7.0 mg, 0.02 mmol), and THF (10 mL) to afford 223 mg (87%) of a glassy solid. See above for NMR data.

4-Acetylbiphenyl[32] (0.02 mol % Pd, K_3PO_4 as base, from the aryl chloride). The coupling of 4-chloroacetophenone with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 100 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **4** (6.0 mg, 0.02 mmol), and THF (5 mL) to afford 178 mg (91%) of the title compound as a white solid, mp 120−121 °C (lit. mp 109−110 °C).[32] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, 2H, J = 8.6 Hz), 7.71−7.62 (m, 4H), 7.50−7.40 (m, 3H), 2.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5, 145.7, 139.8, 135.9, 128.9, 128.8, 128.2, 127.2, 127.1, 26.5; IR (neat, cm^{-1}) 2999, 1679, 764. Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16. Found: C, 85.62; H, 6.07.

4-Acetylbiphenyl[32] (0.001 mol % Pd, K_3PO_4 as base, from the aryl bromide). The coupling of 4-bromoacetophenone with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 50 μL of a catalyst solution prepared as follows: a flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol) and ligand **4** (4.5 mg, 0.015 mmol) and was purged with argon. THF (5 mL) was added, and the mixture was stirred for 1 min at room temperature. Then 50 μL of this solution (0.01 mol % Pd, 0.02 mol % **4**) was added to a second flask containing 1 mL of THF. The title compound was obtained as a white solid (187 mg, 95%).

4-Acetylbiphenyl.[32] (0.000001 mol % Pd, K_3PO_4 as base, from the aryl bromide). The coupling of 4-bromoacetophenone with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 10 μL of a catalyst solution prepared as follows: in 20 mL of THF in a flask in an argon-filled glovebox were dissolved $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and ligand **4** (12.0 mg, 0.04 mmol). A portion of this solution (10 μL, 0.00001 mmol Pd, 0.001 mol % Pd, 0.002 mol % **4**) was added to a second flask containing THF (10 mL). The title compound was obtained as a white solid (176 mg, 90%).

4-Acetylbiphenyl[32] (0.001 mol % Pd, no ligand). The coupling of 4-bromoacetophenone with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 10 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol) and THF (10 mL). When the aryl halide had been completely consumed, the mixture was cooled to room temperature, and dodecane (0.23 mL) was added as an internal standard; the GC yield was determined to be 101%.

4-Methyl biphenyl[27] (0.1 mol % Pd, ligand 4). The coupling of 4-chlorotoluene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 100 μL of a catalyst solution composed of $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), ligand **4** (12.0 mg, 0.04 mmol), and THF (2 mL) to afford 161 mg (96%) of the title compound.

4-Methyl biphenyl[27] (0.05 mol % Pd, ligand 5). The coupling of 4-chlorotoluene with phenylboronic acid was effected using the general procedure with toluene solvent, a reaction temperature of 100 °C, and 100 μL of a catalyst solution composed of $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), ligand **2** (7.0 mg, 0.02 mmol), and THF (2 mL) to afford 158 mg (94%) of the title compound.

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