JOC*Note*

Efficient Stille Cross-Coupling Reaction Using Aryl Chlorides or Bromides in Water

Christian Wolf* and Rachel Lerebours

Department of Chemistry, Georgetown University, Washington, D.C. 20057

cw27@georgetown.edu

Received May 23, 2003

Abstract: An efficient Stille cross-coupling reaction using a variety of aryl halides in neat water has been developed. Employing palladium−phosphinous acid catalyst $[(t\text{-Bu})_2P(OH)]_2PdCl_2$ allows formation of biaryls from aryl chlorides and bromides in good to high yields. Functional groups such as ketones and nitriles are tolerated, and organic cosolvents are not required. The air stability and solubility in water of the palladium complexes used in this study facilitate operation of the coupling reaction and product isolation. The feasibility of catalyst recycling has also been demonstrated.

Palladium-catalyzed cross-coupling reactions utilizing aryl halides and triflates has become a widely used strategy for the formation of new carbon−carbon bonds and in particular for the synthesis of biaryls. The recent development of highly active transition-metal complexes provides new opportunities for employing less reactive halides including unactivated (electron-rich) aryl chlorides in Suzuki, Negishi, Hiyama, Kumada, Stille, and Heck reactions.[1,2] The replacement of expensive, toxic, and flammable organic solvents by water is highly desirable for reducing costs and for developing environmentally benign synthetic reactions that facilitate catalyst recycling. Various examples of aqueous C−C bond formations including Suzuki,[3] Buchwald−Hartwig,[4] Sonogashira,[5] Stille,[6] and Heck reactions[3c,7] have been reported.[8] However, many methods developed to date require organic cosolvents and are restricted to aryl bromides or iodides but are not compatible with less reactive aryl chlorides. Because of its versatility, Stille coupling has enjoyed widespread popularity and use in the synthesis of biphenyls since the biaryl structure exhibits a common motif in pharmaceuticals and other biologically active compounds.

We report herein an efficient aqueous C−C bond formation procedure employing commercially available, water-soluble palladium−phosphinous acid complexes $[(t\text{-Bu})_2P(OH)]_2PdCl_2$ (POPd), $[[(t\text{-Bu})_2P(OH)(t\text{-Bu})_2PO)]\text{-}PdCl]_2$ (POPd1), and $[(t\text{-Bu})_2P(OH)PdCl_2]_2$ (POPd2) in the coupling reaction of aryl chlorides or bromides and phenyltrimethylstannane, Figure 1.[9] The introduction of palladium−phosphinous acids to aqueous organic catalysis using inexpensive aryl chlorides and bromides is expected to provide another entry for the development of coupling procedures utilizing water as the solvent.

Initial catalyst screening and optimization of the Stille coupling using phenyltrimethyltin, **1**, and 4-chloro-2-methylquinoline, **2**, revealed superior catalytic activity of POPd over POPd1 and POPd2, Scheme 1. 2-Methyl-4-phenylquinoline, **3**, was obtained in 91% yield using 6 mol % POPd as the catalyst in the presence of dicyclohexylmethylamine. The stability to air of palladium−phosphinous acid complexes POPd, POPd1, and POPd2 greatly facilitates catalyst handling and operation of the Stille reaction because working under an inert atmosphere is not required. Notably, employing POPd in 1:1

(1) For a recent review see: Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 4176−4211.

(2) (a) Riermeier, T. H.; Zapf, A.; Beller, M. *Top. Catal.* **1997**, *4*, 301−309. (b) Shirakawa, E.; Yamasaki, K.; Hiyama, T. *Synthesis* **1998**, 1544−1549. (c) Littke, A. F.; Fu, G. C. *J. Org. Chem.* **1999**, *64*, 10−11. (d) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147−168. (e) Shiota, T.; Yamamori, T. *J. Org. Chem.* **1999**, *64*, 453−457. (f) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1999**, *38*, 2411−2412. (g) Zhang, C. M.; Huang, J. K.; Trudell, M. L.; Nolan, M. L. *J. Org. Chem.* **1999**, *64*, 3804−3805. (h) Mowery, M. E.; DeShong, P. *Org. Lett.* **1999**, *1*, 2137−2140. (i) Bei, X.; Turner, H. W.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40*, 3855−3858. (j) Bei, X.; Turner, H. W.; Weinberg, W. H.; Guram, A. S. *J. Org. Chem.* **1999**, *64*, 6797−6803. (k) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550−9561. (l) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889−9890. (m) Bohm, V. P. W.; Herrmann, W. A. *Chem.−Eur. J.* **2000**, *6*, 1017−1025. (n) Gruber, A. S.; Zim, D.; Ebeling, G.; Monteiro, A. l.; Dupont, J. *Org. Lett.* **2000**, 1287−1290. (o) Morales-Morales, D.; Redon, R.; Yung, C.; Jensen, C. M. *Chem. Commun.* **2000**, 1619−1620. (p) Bohm, V. P. W.; Weskamp, T.; Gstottmayr, C. W. K.; Herrmann, W. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 1602−1604. (q) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009−3066. (r) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020−4028. (s) Zapf, A.; Ehrentraut, A.; Beller, M. *Angew. Chem., Int. Ed.* **2000**, *39*, 4153−4155. (t) Stambuli, J. P.; Stauffer, S. R.; Shaughnessy, K. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 2677−2678. (u) Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 2719−2724. (v) Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.* **2001**, *123*, 6989−7000. (w) Whitcombe, N. J.; Hii, K. K.; Gibson, S. E. *Tetrahedron* **2001**, *57*, 7449−7476. (x) Yin, J. J.; Rainka, M. P.; Zhang, X. X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 1162−1163. (y) Bedford, R. B.; Cazin, C. S. J.; Hazelwood, S. L. *J. Chem Soc., Chem. Commun.* **2002**, 2608−2609. (z) Bedford, R. B.; Cazin, C. S. J.; Hazelwood, S. L. *J. Chem Soc., Chem. Commun.* **2002**, 2610−2611.

(3) (a) Badone, D.; Baroni, M.; Cardamone, R.; Ielmini, A.; Guzzi, U. *J. Org. Chem.* **1997**, *62*, 7170−7173. (b) Uozomi, Y.; Danjo, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 3384−3388. (c) Gelpke, A. E. S.; Veerman, J. J. N.; Goedheijt, M. S.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Hiemstra, H. *Tetrahedron* **1999**, *55*, 6657−6670. (d) Paetzold, E.; Oehme, G. *J. Mol. Catal. A: Chem.* **2000**, *152*, 69−76. (e) LeBlond, C. R.; Andrews, A. T.; Sun, Y.; Sowa, J. R. *Org. Lett.* **2001**, *3*, 1555−1557. (f) Shaughnessy, K. H.; Booth, R. S. *Org. Lett.* **2001**, *3*, 2757−2759. (g) Dupuis, C.; Adiey, K.; Charruault, L.; Michelet, V.; Savignac, M.; Genet, J.-P. *Tetrahedron Lett.* **2001**, *42*, 6523−6526. (h) Ueda, M.; Nishimura, M.; Miyaura, N. *Synlett* **2000**, 856−858. (i) Botella, L.; Najera, C. *Angew. Chem.* **2002**, *41*, 179−181. (j) Alonso, D. A.; Najera, C.; Pacheco, M. A. *J. Org. Chem.* **2002**, *67*, 5588−5594. (k) Bedford, R. B.; Blake, M. E.; Butts, C. P.; Holder, D. *Chem. Commun.* **2003**, 466−467. (l) Leadbeater, N. E.; Marco, M. *J. Org. Chem.* **2003**, *68*, 888−892.

(4) Wuellner, G.; Jaensch, H.; Kannenberg, S.; Schubert, F.; Boche, G. *Chem. Commun.* **1998**, 1509−1510.

(5) (a) Amatore, C.; Blart, E.; Genet, J. P.; Jutand, A.; Lemaire-Audoire, S.; Savignac, M. *J. Org. Chem.* **1995**, *60*, 6829−39. (b) Hessler, A.; Stelzer, O.; Dibowski, H.; Worm, K.; Schmidtchen, F. P. *J. Org. Chem.* **1997**, *62*, 2362−2369. (c) Lopez-Deber, M. P.; Castedo, L.; Granja, J. R. *Org. Lett.* **2001**, *3*, 2823−2826.

(6) (a) Roshchin A. I.; Bumagin, N. A.; Beletskaya, I. P. *Tetrahedron Lett.* **1995**, *36*, 125−128. (b) Rai, R.; Aubrecht, K. B.; Collum, D. B. *Tetrahedron Lett.* **1995**, *36*, 3111−3114 (c) Kang, S.-K.; Baik, T.-G.; Song, S.-Y. *Synlett* **1999**, *3*, 327−329.

(7) Genet, J. P.; Blart, E.; Savignac, M. *Synlett* **1992**, 715−717.

(8) (a) Genet, P. J.; Savignac, M. *J. Organomet. Chem.* **1999**, *576* (1−2), 305−317. (b) Takami, K.; Yorimitsu, H.; Shinokubo, H.; Matsubara, S.; Oshima, K. *Org. Lett.* **2001**, *3*, 1997−1999. (c) Murata, M.; Shimazaki, R.; Watanabe, S.; Masuda, Y. *Synthesis* **2001**, 2231−2233.

(9) (a) Li, G. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 1513−1516. (b) Li, G. Y.; Zheng, G.; Noonan, A. F. *J. Org. Chem.* **2001**, *66*, 8677−8681. (c) Li, G. Y. *J. Org. Chem.* **2002**, *67*, 3643−3650.

10.1021/jo0347056 CCC: $25.00
Published on Web 08/23/2003

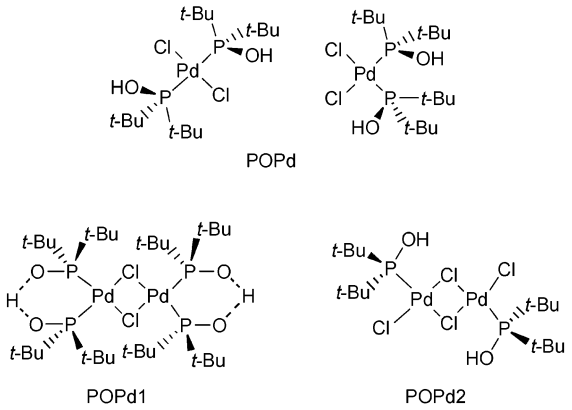
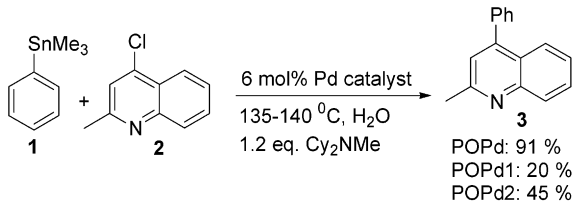


FIGURE 1. Structures of POPd, POPd1, and POPd2.

SCHEME 1. Stille Coupling of 1 and 2 in Water

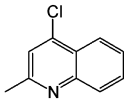
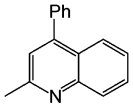
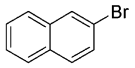
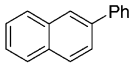
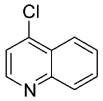
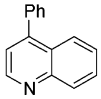
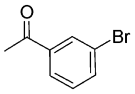
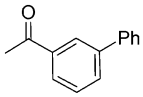
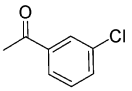
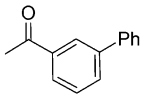
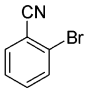
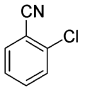
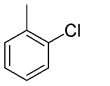
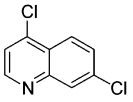
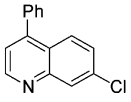
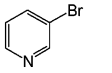
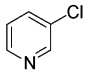
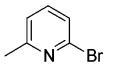
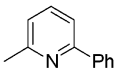


water/DMF or decreasing the reaction temperature to 100 °C resulted in significantly lower yields of coupling product **3**, i.e., 57% and 40%.[10]

We were pleased to find that POPd exhibits catalytic activity toward a variety of aryl chlorides and bromides, Table 1. Biaryl formation requires subsequent oxidative addition of aryl halides to the Pd complex, transmetalation, and reductive elimination to complete the catalytic cycle, Figure 2.[11] The usefulness of aryl chlorides in coupling reactions following this general mechanism is limited because of their reluctance to undergo oxidative addition to many Pd catalysts. However, our results show that POPd combines solubility and stability in water with high catalytic activity.

In general, employing aryl bromides in the Stille coupling affords better yields than employing aryl chlorides. Comparison of the results obtained for the formation of 3-phenylacetophenone, **6**, 2-phenylbenzonitrile, **7**, and 3-phenylpyridine, **10**, reveals that the replacement of aryl chlorides by their corresponding aryl bromides provides higher yields, entries 4−7, 10, and 11. Noteworthy, functional groups such as nitriles and ketones are tolerated, and 4,7-dichloroquinoline, an important precursor of antimalarial drugs derived from chloroquine,[12] was selectively converted to 7-chloro-4-phenylquinoline, **9**.[13] Although the development of new antimalarial drugs exhibiting a 7-chloroquinolyl pharmacophore such as chloroquine has recently attracted increasing attention,[14] only a few studies utilizing chloroquinolines in cross-coupling reactions have been reported to date.[15] The high selectivity of POPd greatly facilitates the preparation of chloroquine-derived drugs because it allows one to employ 4,7-dichloroquinoline as an inexpensive starting material in contrast to synthetic

TABLE 1. Stille Cross-Coupling of Aryl Halides in Water[a]

entry	aryl halide	product	yield (%)
1		 **3**	91
2		 **4**	80
3		 **5**	80
4		 **6**	91
5		 **6**	88
6		 **7**	87
7		 **7**	62
8		 **8**	60
9		 **9**	76[b]
10		 **10**	96
11		 **10**	61
12		 **11**	61

[a] All reactions were carried out with 6 mol % POPd and 1.2 equiv of Cy_2NMe and **1**, respectively, in water at 135−140 °C using a closed vessel. [b] Formation of 4-chloro-7-phenylquinoline was not observed.

(10) Attempts to increase yields of the optimized POPd-catalyzed coupling reaction using equimolar additives of TBAF or TBAB were not successful.

(11) Chlorotrimethylstannane easily hydrolyzes in water to form trimethylsilanol and hydrochloric acid, which was neutralized by dicyclohexylmethylamine, Cy_2NMe.

(12) (a) De, D.; Byers, L. D.; Krogstad, D. J. *J. Hetercycl. Chem.* **1997**, *34*, 315−320. (b) O'Neill, P. M.; Willock, D. J.; Hawley, S. R.; Bray, P. G.; Storr, R. C.; Ward, S. A.; Park, B. K. *J. Med. Chem.* **1997**, *40*, 437−448. (c) O'Neill, P. M.; Bray, P. G.; Hawley, S. R.; Ward, S. A.; Park, B. K. *Pharmacol. Ther.* **1998**, *77*, 29−58. (d) De, D.; Krogstad, F. M.; Byers, L. D.; Krogstad, D. J. *J. Med. Chem.* **1998**, *41*, 4918−4926. (e) Raynes, K. J.; Stocks, P. A.; O'Neill, P. M.; Park, B. K.; Ward, S. A. *J. Med. Chem.* **1999**, *42*, 2747−2751.

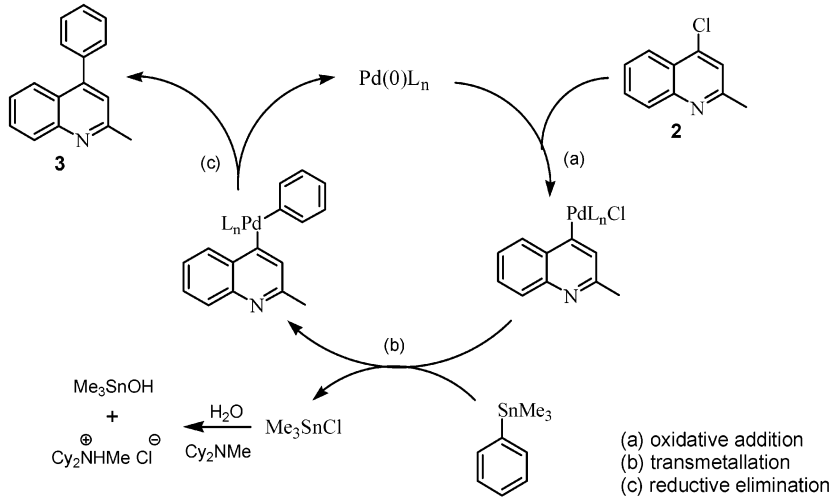


FIGURE 2. Aqueous Stille coupling.

strategies involving multiple-step ring construction of the 4-substituted 7-chloroquinoline moiety. To further investigate the potential of our aqueous Stille coupling protocol, we chose to scale-up the POPd-catalyzed cross-coupling of stannane **1** and 2-bromonaphthalene. Employing 1.0 g (5.0 mmol) of the aryl bromide provided 2-phenylnaphthalene, **4**, in 79% yield, which is in excellent agreement with a yield of 80% obtained when the reaction was performed on a 0.5 mmol scale.

Stille cross-coupling is frequently used as a key step in the synthesis of pharmaceuticals. Simple catalyst isolation and recycling are important features of a synthetic methodology with practicable industrial applications. We therefore chose to recycle POPd for the cross-coupling of 3-bromopyridine, **12**, and phenyltrimethylstannane, **1**, Figure 3. After completion of each reaction, the mixture was extracted with diethyl ether to collect coupling product 3-phenylpyridine, **10**. The separated aqueous solution was then reloaded with the same amounts of **1** and **12** as in the previous cycle. We obtained biaryl **10** in 95−96% yield after the first two coupling reactions but found that the catalytic performance of the recycled POPd slightly diminished after each step. Results obtained after the first two runs were in excellent agreement, but yields decreased in the following reactions to 90% and finally to 84% after the fourth run. Nevertheless, our recycling experiments demonstrate that POPd-catalyzed Stille coupling in water greatly facilitates product isolation and purification because coupling products can easily be separated by extraction from the water-soluble catalyst.

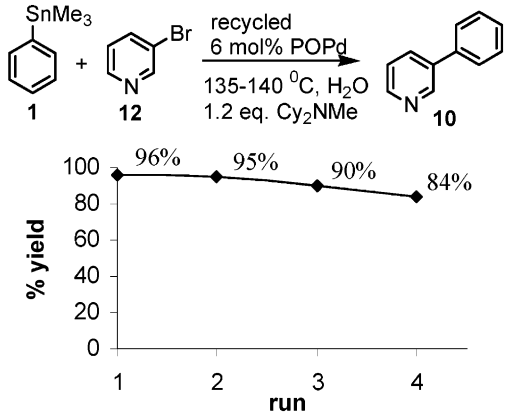


FIGURE 3. Synthesis of biaryl **10** using recycled POPd.

In conclusion, we have developed an efficient aqueous Stille cross-coupling reaction that allows formation of biaryls from a variety of aryl halides in good to high yields. Our methodology does not require organic cosolvents and utilizes air-stable and water-soluble palladium−phosphinous acid complexes, which greatly facilitates operation of the coupling reaction, product isolation, and catalyst recycling. Efforts to further expand the scope of POPd, POPd1, and POPd2 to aqueous coupling reactions that avoid the use of toxic stannanes are in progress in our laboratory.

Experimental Section

General Procedures. All chemicals were of reagent grade. Reactions were carried out using a high-pressure vessel (i.d. 31.7 cm) made of 4.0 mm Pyrex 7740 heavy wall glass and equipped with a 4 mm bore valve and an Aegis backing O-ring. Flash chromatography was carried out on Kieselgel 60, particle size 0.032−0.063 mm. NMR spectra were obtained at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR) using $CDCl_3$ as the solvent. Chemical shifts are reported in parts per million relative to the peak for TMS. 2-Methylbiphenyl, **8**, is commercially available.

Stille Coupling. A mixture of POPd (16.0 mg, 6 mol %), aryl halide derivative (0.6 mmol), phenyltrimethylstannane (0.7 mmol), and Cy_2NMe (120 mg, 0.61 mmol) was stirred in 5 mL of deionized water at 140 °C using a closed vessel. After 24 h, the reaction mixture was allowed to cool to room temperature and extracted with Et_2O. The combined organic layers were

(13) We found that esters and aldehydes are not stable under the coupling reaction conditions reported herein. Employing methyl 4-chlorobenzoate in the Stille coupling resulted in extensive hydrolysis, and 4-phenylbenzoic acid was obtained in 60% yield. The cross-coupling of 4-bromobenzaldehyde and phenyltrimethyltin gave 45% 4-phenylbenzyl alcohol and 45% 4-phenylbenzoic acid, which is probably a result of Cannizzaro disproportionation.

(14) Ridley, R. G. *Nature* **2002**, *415*, 686−693.

(15) (a) Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *Synthesis* **1987**, 693−696. (b) Godard, A.; Fourquez, J. M.; Tamoin, R.; Marsais, F.; Queguiner, G. *Synlett* **1994**, 235−236. (c) Ciufolini, M. A.; Mitchell, J. W.; Roschangar, F. *Tetrahedron Lett.* **1996**, *37*, 8281−8284. (d) Shiota, T.; Yamamori, T. *J. Org. Chem.* **1999**, *64*, 453−457. (e) Legros, J.-Y.; Primault, G.; Fiaud, J.-C. *Tetrahedron* **2001**, *57*, 2507−2514.

washed with brine and dried over $MgSO_4$, and the solvents were removed under vacuum. The residue was purified by flash chromatography on silica gel as indicated below.

2-Methyl-4-phenylquinoline, 3. Purification by chromatography on silica gel using hexanes/diethyl ether/triethylamine, 50:50:1. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.78 (s, 3H), 7.23 (s, 1H), 7.43 (ddd, J = 1.4, J = 7.6, J = 8.5, 1H), 7.47−7.51 (m, 5H), 7.69 (ddd, J = 1.4 Hz, J = 7.6 Hz, J = 8.4 Hz, 1H), 7.86 (dd, J = 1.4 Hz, J = 8.4 Hz, 1H), 8.08 (dd, J = 1.4 Hz, J = 8.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.4, 122.1, 125.0, 125.5, 125.6, 128.2, 128.5, 128.9, 129.2, 129.5, 138.0, 148.2, 148.3, 158.3. Anal. Calcd for $C_{16}H_{13}N$: C, 87.64; H, 5.98; N, 6.39. Found: C, 87.52; H, 5.82; N, 6.35.

2-Phenylnaphthalene, 4.[16] Purification by chromatography on silica gel using hexanes/dichloromethane, 10:1. ^{1}H NMR ($CDCl_3$): δ 7.37 (m, 1H), 7.45−7.50 (m, 4H), 7.71−7.76 (m, 3H), 7.81−7.91 (m, 3H), 8.03 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 126.0, 126.2, 126.4, 126.7, 127.8, 127.9, 128.1, 128.7, 128.9, 129.3, 133.1, 134.1, 138.9, 141.5.

4-Phenylquinoline, 5.[17] Purification by chromatography on silica gel using hexanes/ethyl acetate/triethylamine, 100:10:1. ^{1}H NMR (75 MHz, $CDCl_3$): δ 7.34 (d, J = 4.4 Hz, 1H), 7.50−7.52 (m, 6H), 7.73 (dd, J = 7.0 Hz, J = 8.2 Hz, 1H), 7.92 (d, J = 7.0 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 8.95 (d, J = 4.4 Hz, 1H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 121.5, 126.1, 126.8, 128.6, 128.8, 129.5, 129.7, 130.0, 138.2, 148.7, 148.8, 150.0.

3-Acetylbiphenyl, 6.[18] Purification by chromatography on silica gel using hexanes/dichloromethane, 1:1. ^{1}H NMR ($CDCl_3$): δ 2.99 (s, 1H), 7.38−7.63, (m, 6H); 7.80 (ddd, J = 0.8 Hz, J = 3.0 Hz, J = 7.7 Hz, 1H), 7.93 (ddd, J = 0.6 Hz, J = 2.8 Hz, J = 7.7 Hz, 1H), 8.18 (dd, J = 0.6 Hz, J = 3.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 27.1, 127.2, 127.4, 128.0, 129.1, 129.2, 131.9, 137.9, 140.0, 142.0, 194.0.

2-Cyanobiphenyl, 7.[19] Purification by chromatography on silica gel using hexanes/diethyl ether, 5:1. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42−7.59 (m, 7H), 7.65 (ddd, J = 1.4 Hz, J = 7.7 Hz, J = 7.7 Hz, 1H), 7.77 (dd, J = 0.8 Hz, J = 7.7 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 111.5, 118.9, 127.7, 128.9, 130.3, 133.0, 133.9, 138.3, 145.7.

7-Chloro-4-phenylquinoline, 9. Purification by chromatography on silica gel using hexanes/dichloromethane/triethylamine, 100:50:1. ^{1}H NMR ($CDCl_3$): δ 7.35 (d, J = 4.3 Hz, 1H), 7.40−7.55 (m, 6H), 7.91 (d, J = 9.1 Hz, 1H), 8.09 (d, J = 1.9 Hz, 1H), 8.98 (d, J = 4.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 121.7, 125.4, 127.5, 127.8, 128.9, 129.6, 135.4, 137.7, 147.0, 148.7, 149.3, 151.2. Anal. Calcd for $C_{15}H_{10}NCl$: C, 75.16; H, 4.21; N, 5.84. Found: C, 74.78; H, 4.13; N, 5.57.

3-Phenylpyridine, 10.[20] Purification by chromatography on silica gel using hexanes/ethyl acetate, 5:1. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33−7.51 (m, 4H), 7.56−7.61 (m, 2H), 7.88 (ddd, J = 0.6 Hz, J = 1.7 Hz, J = 7.8 Hz, 1H), 8.59 (dd, J = 1.7 Hz, J = 4.7 Hz, 1H), 8.85 (dd, J = 0.9 Hz, J = 2.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 123.7, 127.3, 128.3, 129.3, 134.5, 136.8, 138.1, 148.5, 148.6.

2-Phenyl-6-methylpyridine, 11.[21] Purification by chromatography on silica gel using hexanes/diethyl ether/triethylamine, 50:50:1. ^{1}H NMR (75 MHz, $CDCl_3$): δ 2.63 (s, 3H), 6.98 (d, J = 7.7 Hz, 1H), 7.30−7.35 (m, 4H), 7.47 (dd, J = 7.4 Hz, J = 8.0 Hz, 1H), 7.98−8.01 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ 25.1, 117.8, 121.8, 127.2, 128.9, 137.0, 157.1, 158.5.

Acknowledgment. We thank Combiphos Catalysts, Inc., New Jersey (www.combiphos.com), for POPd, POPd1, and POPd2.

JO0347056

(16) Choudary, B. M.; Madhi, S.; Chowdari, N. S.; Kantam, M. L.; Sreedhar, B *J. Am. Chem. Soc.* **2002**, *124*, 14127−14136.
(17) Karikomi, M.; Tsukada, H.; Toda, T. *Heterocycles* **2001**, *55*, 1249−1252.
(18) Rao, M. L. N.; Shimada, S.; Yamazaki, O.; Tanaka, M. *J. Organomet. Chem.* **2002**, *659*, 117−120.
(19) Riguet, E.; Alami, M.; Cahiez, G. *J. Organomet. Chem.* **2001**, *624*, 376−379.
(20) Littke, A. F.; Schwarz, L.; Fu, G. C. *J. Am. Chem. Soc.* **2002**, *124*, 6343−6348.
(21) Padwa, A.; Akiba, M.; Cohen, L. A.; MacDonald, J. G. *J. Org. Chem.* **1983**, *48*, 695−703.