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An Improved Preparation of Arylboronates: Application in One-Pot Suzuki Biaryl Synthesis†

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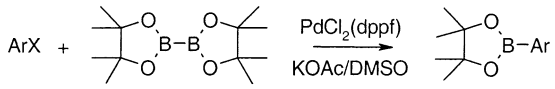
Abstract: We have developed a modification of the Miyaura arylboronate synthesis[1a] by substituting a ligandless palladium catalyst for $PdCl_2$(dppf). Palladium acetate, free of ligand, was found highly effective for such coupling reactions. This modified procedure is advantageous over the original Miyaura synthesis in ease of workup, catalyst removal, and low catalyst cost. Furthermore, the boronates formed in this manner can be used directly for Suzuki coupling reactions in a one-pot fashion. The biaryl products have improved impurity profiles and reduced heavy metal contamination.

Arylboronates are playing an increasingly prominent role in Suzuki cross-coupling reactions as important alternatives to arylboronic acids, especially when the corresponding boronic acids are not readily available.[2] The $PdCl_2$(dppf)-catalyzed cross-coupling reaction of bis(pinacolato)diboron with arylhalides, first reported by Miyaura and co-workers, is a convenient method for the synthesis of arylboronates (Scheme 1).[1a] In contrast to the more traditional organometallic approach,[3] the Miyaura procedure enables facile access to boronic acid derivatives in the presence of sensitive functionalities such as ester, ketone, cyano, or nitro groups. We have found, however, in the course of a large-scale synthesis of a lead drug candidate, that the use of $PdCl_2$(dppf) as a catalyst is not optimal. The quality of the arylboronates and subsequent Suzuki coupling products are often compromised by coloration and high residual heavy metal content. Large-scale chromatography is often needed for purification and high catalyst cost also makes this procedure undesirable as a manufacturing process. In this paper, we wish to report an improved synthesis of arylboronates by substituting a ligandless palladium catalyst for $PdCl_2$(dppf). Palladium acetate, a much cheaper palladium catalyst,[4a] is highly effective for such coupling reactions. Furthermore, the boronates prepared in this manner can be used directly for Suzuki coupling reactions in a one-pot fashion. The resultant biaryl products have improved impurity profiles and reduced heavy metal contamination.

SCHEME 1. Miyaura One-step Arylboronate Synthesis Catalyzed by $PdCl_2$(dppf)[1]



In their pioneering study, Miyaura and co-workers reported that potassium acetate was essential for the palladium(0)-catalyzed aryl halide/diboron coupling reaction. They thus proposed the presence of an acetoxopalladium(II) intermediate in the catalytic cycle.[1a] We speculated that palladium acetate would be equally capable of catalyzing the coupling reaction by facilitating the formation of this key intermediate, thus rendering $PdCl_2$(dppf) unnecessary.

The coupling reaction between arylhalides and bis(pinacolato)diboron was carried out in DMF at 80 °C under argon with 3 mol % of palladium acetate (unless otherwise specified) and 3 equiv of potassium acetate. Under these conditions, arylbromides having electron-withdrawing groups, such as COMe, CN, COOMe, and NO_2, underwent coupling reaction smoothly with the diboron reagent (entries 1, 2, 5, and 7, Table 1). Consistent with Miyaura's results, arylbromides having electron-donating groups, such as NMe_2 and OMe, coupled poorly with the diboron under the palladium acetate catalysis conditions. Prolonged heating resulted in an insignificant change in the reaction mixture (entries 8 and 10, Table 1). Electron-rich arylboronates can alternatively be made from the corresponding aryliodides under the conditions for electron-poor arylbromides (entry 9, Table 1).

Palladium removal appears to be facile with this new palladium acetate catalyzed arylboronate formation. The crude arylboronates (white to off-white solids) obtained after a simple workup showed low palladium contamination (entries 1, 2, 5, 7, and 9, Table 1). In contrast, an experiment, catalyzed with $PdCl_2$(dppf) and worked up identically, yielded a crude product (a dark brown solid) that contained 350 times more palladium (entry 7, Table 1).

In several instances, the arylboronate products were accompanied by small amounts (5−15%) of the symmetric

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(1) (a) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508. (b) Masuda and co-workers have reported the preparation of pinacol arylboronates by $PdCl_2$(dppf)-catalyzed coupling of aryl halides/triflates with pinacolborane. This method, however, produces arene by reduction of the aryl halides as a significant byproduct. Murata, M.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **1997**, *62*, 6458. Murata, M.; Oyama, T.; Watanabe, S.; Masuda, Y. *J. Org. Chem.* **2000**, *65*, 164.

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(3) (a) For boronic acids via organomagnesium reagents, see: Washburn, R. M.; Levens, E.; Albright, C. F.; Billig, F. A.; Cernak, E. S. *Adv. Chem. Ser.* **1959**, *23*, 102. Washburn, R. M.; Billig, F. A.; Bloom, M.; Albright, C. F.; Levens, E. *Adv. Chem. Ser.* **1961**, *32*, 208. Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316. (b) For boronic acids via organolithium reagents, see a review: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

(4) (a) $PdCl_2$(dppf) $9000/mol; $Pd(OAc)_2$ $2000/mol. Aldrich catalog 2001−2002. (b) Catalysts other than $PdCl_2$(dppf) which have been used for the Miyaura arylboronate reaction include $PdCl_2(PPh_3)_2$ (Takahashi, K.; Takagi, J.; Ishiyama, T.; Miyaura, N. *Chem. Lett.* **2000**, 126. Iovine, P. M.; Kellett, M. A.; Redmore, N. P.; Therien, M. J. *J. Am. Chem. Soc.* **2000**, *122*, 8717) and Pd_2dba_3 (Todd, M. H.; Abell, C. *J. Comb. Chem.* **2001**, *3*, 319). We thank a reviewer for bringing this information to our attention.

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TABLE 1. Arylboronate Formation Mediated by Ligandless Palladium Catalysts

entry	Pd catalyst[a]	aryl halide (ArX)	reaction time, h	yield, % (isolated)[b]	Pd content, ppm
1	A	4-BrC_6H_4COMe	3	(86)[c]	57
2	A	3-BrC_6H_4CN	2	(81)[d]	17
3	B	3-BrC_6H_4CN	2	29[d]	ND[f]
4	B	3-BrC_6H_4CN	22	15[d]	ND
5	A	4-Br-3-$MeC_6H_3CO_2Me$	3	(70)[d]	100
6	B	4-Br-3-$MeC_6H_3CO_2Me$	20	34[d]	ND
7	A	4-$BrC_6H_4NO_2$	3	(90)[c]	35 (12300)[e]
8	A	4-BrC_6H_4OMe	15	21[c]	ND
9	A	4-IC_6H_4OMe	2	80[c]	140
10	A	4-$BrC_6H_4NMe_2$	23	23[c]	ND

[a] Catalyst: (A) $Pd(OAc)_2$, 3 mol %; (B) Pd/C (Degussa, wet, 10 wt % on dry basis), 3 mol %. [b] Estimated by ^1H NMR spectroscopy in $CDCl_3$. Isolated yields are shown in parentheses. [c] Originally made by Miyaura et al., see ref 1a for details. Spectroscopic data (^1H NMR and MS) are consistent with the desired structure and match those reported by Miyaura et al. [d] New compound, fully characterized (see Experimental Section for details). [e] Pd content for an experiment, catalyzed with $PdCl_2$(dppf), and worked up identically, is shown in parentheses. [f] Not determined.

biaryls in the reaction mixture as shown by ^1H NMR. Two control experiments were then carried out to probe the origin of dimer formation (Scheme 2). In the first experiment, *p*-acetylbromobenzene was treated with 1 equiv of the diboron reagent under our standard conditions. ^1H NMR analysis of the resultant reaction mixture showed a 9:1 ratio of the boronate and the homo-dimer with no presence of the starting bromide. This reaction mixture was then kept at 80 °C for an extended period of time (18 h). ^1H NMR revealed no significant change in the product ratio. This result showed that the arylboronate was thermally stable in the reaction mixture, and essentially ruled out the possibility of homo-coupling of the boronate as the primary origin of the dimer formation. In the second experiment, *p*-acetylbromobenzene was treated with 0.5 equiv of the diboron reagent. Upon heating, under standard conditions, for the same amount of time (18 h), the boronate:dimer ratio was 1:4 as shown by ^1H NMR. This experiment clearly demonstrated that the dimer formation resulted from Suzuki coupling of the boronates and their halide precursors under the reaction conditions.

We also examined Pd/C as another ligandless palladium catalyst, but it proved to be much less effective than palladium acetate for the boronate formation. With Pd/C, poor yields were observed for the boronates due to significant homo-dimer formation (entries 3, 4, and 6, Table 1). It suggests that Pd/C is more effective in catalyzing the Suzuki coupling reaction than the boronate formation under these conditions (vide infra).

Our success in replacing $PdCl_2$(dppf) by a ligandless palladium catalyst for such arylboronate formation is unprecedented in the literature. We investigated the scope of this reaction and elaborated the results into a convenient one-pot Suzuki coupling reaction (Chart 1 and Table 2). The strategy of using organoboranes generated in situ for Suzuki coupling reactions was first documented by Keay,[5] and was recently demonstrated to be quite successful with arylboronates, especially in solid-phase applications.[6] Clearly, avoiding the often troublesome isolation of arylboronates via the Miyaura procedure can be very valuable to synthetic chemists. To carry out the two steps in one pot, the boronate formation needs to be reasonably clean. Furthermore, proper selection of solvent and base is also essential. In a typical experiment, the first arylhalide (ArX) was converted into its boronate via bis(pinacolato)diboron under standard conditions (Pd-$(OAc)_2$, KOAc, DMF, 80 °C). The Suzuki coupling partner Ar′X was then added to the reaction mixture together with 3 mol % of $Pd(PPh_3)_4$ and 1.5 equiv of cesium carbonate. The reaction mixture was then heated at 80 °C overnight to afford the biaryl product. The results are summarized in Table 2 and generally demonstrate satisfactory yields.

In our studies, DMF was the solvent of choice because it had proven suitable for both the arylboronate formation and the Suzuki coupling reaction.[7a] Potassium acetate was used in the arylboronate formation due to its mild basicity, a crucial factor for this reaction.[1a] A stronger base, cesium carbonate, was later introduced to promote the Suzuki coupling.[7] Although palladium acetate alone was sufficient to catalyze both the boronate formation and the Suzuki coupling in some cases, we found that, in general, the addition of 3 mol % of $Pd(PPh_3)_4$ *after* the boronate formation would accelerate the cross-coupling step.[7] Palladium catalysts were easily removed during workup by filtration through a pad of Celite. The biaryl products are usually obtained as crystalline solids in high purity after extraction and trituration.

As expected, the outcomes of the cross-coupling reactions were greatly influenced by the substituents on the arylhalides. In the cases where both ArX and Ar′X are electron deficient, high yields (>90%) of the biaryls were obtained regardless of the addition order of the halides (entries 1, 2, 7, and 8, Table 2). Significantly, nonsubstituted bromobenzene **i** coupled efficiently with the electron-poor *p*-acetylbromobenzene **f** under these conditions (entry 15, Table 2). With the same halide **f**, *p*-bromonitrobenzene **h** and *p*-methylbromobenzoate **g** underwent the cross-coupling reaction smoothly even without the addition of $Pd(PPh_3)_4$ (entries 9 and 12, Table 2). However, bromobenzene **i** did not react with **f** under the same conditions (entry 16, Table 2). In the absence of both Cs_2CO_3 and $Pd(PPh_3)_4$, the Suzuki coupling reactions proceeded very slowly (entries 10 and 13, Table 2). For electron-rich arylbromides, only a trace amount of the biaryl products was obtained due to their poor boronate formation (entries 3 and 4, Table 2), although an aryliodide afforded the biaryl in good yield (61%, entry 5, Table 2). Reversing the roles of the coupling partners can rectify this situation. For example, biaryls **9** and **10** were obtained in 60% and 20% yields, respectively, when electron-rich Ar′X's were coupled with the boronate

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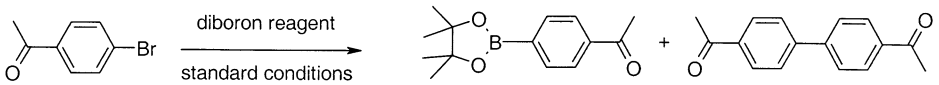
(6) (a) Piettre, S. R.; Baltzer, S. *Tetrahedron Lett.* **1997**, *38*, 1197. (b) Giroux, A.; Han, Y.; Prasit, P. *Tetrahedron Lett.* **1997**, *38*, 3841. (c) Brown, S. D.; Armstrong, R. W. *J. Am. Chem. Soc.* **1996**, *118*, 6331. (d) Ishiyama, T.; Itoh, Y.; Kitano, T.; Miyaura, N. *Tetrahedron Lett.* **1997**, *38*, 3447. (e) Carbonnelle, A.; Zhu, J. *Org. Lett.* **2000**, *2*, 3477.

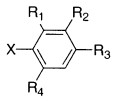
(7) The selection of base and catalyst for the Suzuki coupling step was not a focus of this study. For reviews regarding Cs_2CO_3 and Pd-$(PPh_3)_4$ in Suzuki coupling reactions, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Wallow, T. I.; Novak, B. M. *J. Org. Chem.* **1994**, *59*, 5034. (c) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207.

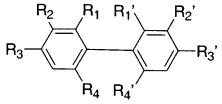
SCHEME 2



equivalents of diboron reagent	boronate:dimer ratio
1.0	9:1 (no change after 18 h at 80 °C)
0.5	1:4 (after 18 h at 80 °C)

CHART 1. Structures of Aryl Halides (ArX or Ar′X) and Biaryl Products (Ar−Ar′)





a, X = Br, R_2 = CN

b, X = Br, R_1 = Me, R_3 = CO_2Me

c, X = Br, R_3 = $N(Me)_2$

d, X = Br, R_3 = OMe

e, X = I, R_3 = OMe

f, X = Br, R_3 = COMe

g, X = Br, R_3 = CO_2Me

h, X = Br, R_3 = NO_2

i, X = Br

j, X = Cl

k, X = I, R_1 = R_3 = R_4 = Me

l, X = I , R_3 = Br

R = H, when not specified in the chart.

1, R_2 = CN, R_3' = CO_2Me

2, R_1 = Me, R_3 = R_3' = CO_2Me

3, R_3 = $N(Me)_2$, R_3'= CO_2Me

4, R_3 = OMe, R_3' = CO_2Me

5, R_3 = COMe, R_2'= CN

6, R_3 = COMe, R_3' = NO_2

7, R_3 = COMe, R_3' = CO2Me

8, R_3 = COMe

9, R_3 = COMe, R_3' = OMe

10, R_3 = COMe, R_3' = $N(Me)_2$

11, R_3 = COMe, R_1' = R_3' = R_4' = Me

12, R_3 = COMe, R_3' = Br

generated in situ from the electron-poor halide **f** (entries 22 and 23, Table 2). Sterically hindered halides, such as 3-iodomesitylene **k**, coupled satisfactorily with **f** under the "one-pot" conditions (entry 24, Table 2). Iodobromobenzene **l** underwent coupling chemoselectively with **f** to provide the bromobiaryl product **12** (entry 26, Table 2). The aryl chloride **j** failed to couple with **f** under these Suzuki conditions (entries 19, 20, and 21, Table 2). In the cases where ArX and Ar′X are both electron-rich, the yields of the biaryls are expected to be low because of the inability to generate the aryl boronates cleanly.

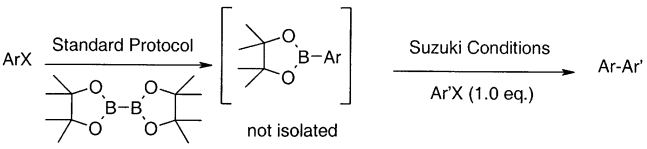
For active arylhalide Suzuki coupling partners, the cross-coupling step can also be facilitated by addition of Pd/C (Degussa, wet, 10 wt % on dry basis, typically 3 mol %) after the completion of the boronate formation catalyzed by palladium acetate (Table 2) (vide supra). Both catalysts can be easily removed together by a simple filtration through a pad of Celite after the Suzuki reaction. For many substrates, cesium carbonate was unnecessary for the Suzuki coupling with Pd/C. An exception was the unsubstituted bromobenzene **i** where only 30% biaryl yield was obtained in the absence of cesium carbonate (entry 17, Table 2). For unactivated arylhalide Suzuki coupling partners, $Pd(PPh_3)_4$ gave better yields for the cross-coupling step than Pd/C (entries 24/25 and 26/27, Table 2).

We also examined the residual palladium content in the biaryl products under various Suzuki conditions (Table 2). Just as expected, Pd/C resulted in the least palladium contamination in the biaryl products among the various Suzuki conditions examined (entries 6, 11, 14, and 18, Table 2). Removing traces of heavy metal from a drug substance can be a nontrivial exercise in many instances.[8] Thus, our one-pot Suzuki biaryl coupling process involving this unique combination of ligandless palladium catalysts will find applications in drug synthesis where very low heavy metal content is desired.

We have shown that palladium acetate, a better choice than $PdCl_2$(dppf) in terms of cost[4] and catalyst removal, effectively catalyzes the cross-coupling of a wide variety of arylhalides with bis(pinacolato)diboron to form the corresponding boronates. Boronates prepared in this procedure either can be conveniently isolated or used in situ for Suzuki cross-coupling reactions with arylhalides to provide biaryls.

(8) Rosso, V. W.; Lust, D. A.; Bernot, P. J.; Grosso, J. A.; Modi, S. P.; Rusowicz, A.; Sedergran, T. C.; Simpson, J. H.; Srivastava, S. K.; Humora, M. J.; Anderson, N. G. *Org. Process Res. Dev.* **1997**, *1*, 311.

TABLE 2. One-Pot Suzuki Coupling Reactions via Arylboronates Generated in Situ[a]



entry	halide pairs (ArX, Ar′X)	biaryls (Ar−Ar′)	yield, %	Suzuki conditions[h]	Pd content, ppm
1	**a**, **g**	**1**	88[b]	A	ND[g]
2	**b**, **g**	**2**	90[b]	A	ND
3	**c**, **g**	**3**	trace[c]	A	ND
4	**d**, **g**	**4**	trace[c]	A	ND
5	**e**, **g**	**4**	61[d]	A	ND
6	**a**, **f**	**5**	98[b]	D	60
7	**f**, **a**	**5**	95[b]	A	1000
8	**f**, **h**	**6**	95[b]	A	3300
9	**f**, **h**	**6**	90[b]	B	ND
10	**f**, **h**	**6**	trace	C	ND
11	**f**, **h**	**6**	98[b]	D	417
12	**f**, **g**	**7**	90[b]	B	208
13	**f**, **g**	**7**	trace	C	ND
14	**f**, **g**	**7**	91[b]	D	82
15	**f**, **i**	**8**	88[d]	A	2500
16	**f**, **i**	**8**	trace	B	ND
17	**f**, **i**	**8**	30[f]	D	ND
18	**f**, **i**	**8**	92[b]	E	149
19	**f**, **j**	**8**	trace	A	ND
20	**f**, **j**	**8**	trace	D	ND
21	**f**, **j**	**8**	trace	E	ND
22	**f**, **d**	**9**	60[d]	A	ND
23	**f**, **c**	**10**	20[e]	A	ND
24	**f**, **k**	**11**	69[d]	A	ND
25	**f**, **k**	**11**	10[f]	E	ND
26	**f**, **l**	**12**	75[d]	A	ND
27	**f**, **l**	**12**	50[f]	E	ND

[a] Refer to Chart 1 for structures. [b] Crude yield, 90−95% purity by ^{1}H NMR. [c] Low-yielding boronate formation. [d] Isolated yield. [e] GC yield. [f] ^{1}H NMR yield. [g] Not determined. [h] Suzuki conditions: (A) $Pd(PPh_3)_4$ (0.03 equiv); Cs_2CO_3 (1.5 equiv), 80 °C, 18 h. (B) Cs_2CO_3 (1.5 equiv), 80 °C. (C) No $Pd(PPh_3)_4$, no Cs_2CO_3. (D) Pd/C (Degussa, wet, 10 wt %, 0.03 equiv). (E) Pd/C (Degussa, wet, 10 wt %, 0.03 equiv), Cs_2CO_3 (1.5 equiv), 80 °C.

Experimental Section

All chemicals and reagents used in this study were purchased commercially and used without purification. NMR spectroscopic data were recorded on a Varian (300 MHz) NMR spectrometer. Elemental analyses were performed by Robertson Microlit Labs.

Typical Procedure for the Preparation of Arylboronates As Illustrated by the Synthesis of 3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzonitrile. To a 50-mL, three-necked, round-bottomed flask were charged 3-bromobenzonitrile (0.95 g, 5.20 mmol), bis(pinacolato)diboron (1.43 g, 5.62 mmol), potassium acetate (1.53 g, 15.6 mmol), palladium acetate (0.04 g, 0.16 mmol, 3 mol %), and DMF (20 mL). The mixture was degassed by gently bubbling nitrogen for 30 min. It was then heated in an oil bath at 85 °C until completion (ca. 5 h). The reaction mixture was then cooled to room temperature and diluted with water (75 mL) to induce precipitation. The gray solid was collected by filtration, rinsed with water, and dried. It was then dissolved in ethyl acetate (50 mL). The insoluble material was removed by filtration through a pad of Celite. The filtrate yielded the title compound as a white solid (0.37 g) after removal of solvent in vacuo. The mother liquor from the first filtration was extracted with ethyl acetate (75 mL). The organic layer was washed with water (50 mL × 2) and dried over anhydrous sodium sulfate. Removal of solvent yielded additional product as a colorless oil that solidified shortly (0.60 g). The combined yield was 81%. An analytically pure sample obtained by recrystallization in ethyl acetate exhibited the following spectroscopic data: ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 12H), 7.46 (t, J = 7.6, 1H), 7.71 (d, J = 7.7, 1H), 8.00 (d, J = 7.6, 1H), 8.08 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 25.72, 84.90, 112.23, 119.00, 128.47, 134.44, 138.41, 138.75. GCMS (EI), m/z 229. Anal. Calcd for $C_{13}H_{16}BNO_2$: C, 68.16; H, 7.04; N, 6.11. Found: C, 67.90; H, 7.23; N, 6.50.

Methyl 2-Methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate. This boronate was prepared in a similar manner as described above in 70% yield. An analytically pure sample obtained by silica gel column chromatography exhibited the following spectroscopic data: ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 12H), 2.58 (s, 3H), 3.91 (s, 3H), 7.79 (s, 2H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.99, 25.75, 52.76, 84.25, 125.65, 130.49, 131.78, 135.75, 144.85, 167.12;. GCMS (EI), m/z 276. Anal. Calcd for $C_{15}H_{21}BO_4$: C, 65.24; H, 7.67. Found: C, 65.44; H, 7.67.

Typical Procedure for the One-Pot Suzuki Reaction with $Pd(PPh_3)_4$ via the in Situ Generated Aryl Boronate As Illustrated by the Preparation of Biaryl 6. To a 50-mL, three-necked, round-bottomed flask were charged, in no specific order, 4′-bromoacetophenone (0.52 g, 2.6 mmol, 1.0 equiv), bis(pinacolato)diboron (0.70 g, 2.8 mmol, 1.05 equiv), palladium acetate (17 mg, 0.078 mmol, 3 mol %), potassium acetate (0.77 g, 7.9 mmol, 3.0 equiv), and 10 mL of DMF. The mixture was degassed by gently bubbling argon through for 30 min at room temperature. The mixture was then heated at 80 °C under argon protection until completion of the reaction (2−3 h). After the reaction mixture was cooled to room temperature, 1-bromo-4-nitrobenzene (0.52 g, 2.6 mmol, 1.0 equiv), cesium carbonate (1.3 g, 3.9 mmol, 1.5 equiv), and $Pd(PPh_3)_4$ (90 mg, 0.078 mmol, 3 mol %) were added. The reaction mixture was then heated at 80 °C overnight under argon, then cooled to room temperature and diluted with water (20 mL) and ethyl acetate (20 mL). Black particles were removed by passing through a pad of Celite. The organic layer was separated, and washed twice with 15 mL of brine solution. After drying over sodium sulfate, the solvent was removed at reduced pressure to afford 1-(4′-nitro-biphenyl-4-yl)-ethanone **6** as a yellow solid (0.7 g, >99% yield, >95% purity by ^{1}H NMR). An analytically pure sample was obtained by column chromatography (silica gel, ethyl acetate/hexanes): light yellow solid, mp 145.5−146.5 °C. ^{1}H NMR (DMSO-d_6) δ 8.32 (d, J = 8.8 Hz, 2H), 8.08 (d, J = 8.7 Hz, 2H), 8.03 (d, J = 9.1 Hz, 2H), 7.93 (d, J = 8.6 Hz, 2H), 2.63 (s, 3H); ^{13}C NMR (DMSO-d_6) δ 198.03, 147.79, 145.86, 142.61, 137.37, 129.59, 128.88, 128.10, 124.82, 27.78. GCMS (EI), m/z 241. Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.60; N, 5.81. Found: C, 69.85; H, 4.55; N, 5.59.

Typical Procedure for the One-Pot Suzuki Reaction with Pd/C As Illustrated by the Preparation of Biaryl 6. To a 50-mL, three-necked, round-bottomed flask were charged, in no specific order, 4′-bromoacetophenone (0.52 g, 2.6 mmol, 1.0 equiv), bis(pinacolato)diboron (0.70 g, 2.8 mmol, 1.05 equiv), palladium acetate (17 mg, 0.078 mmol, 3 mol %), potassium acetate (0.77 g, 7.9 mmol, 3.0 equiv), and 10 mL of DMF. The mixture was degassed by gently bubbling argon through for 30 min at room temperature. The mixture was then heated at 80 °C under argon until completion of the reaction (2−3 h). After the reaction mixture was cooled to room temperature, 1-bromo-4-nitrobenzene (0.52 g, 2.6 mmol, 1.0 equiv), cesium carbonate (1.3 g, 3.9 mmol, 1.5 equiv), and Pd/C (Degussa, 160 mg, 0.075 mmol, 0.03 equiv) were added. The reaction mixture was then heated at 80 °C overnight, then cooled to room temperature, diluted with cold water (30 mL), and stirred for 10 min. Solids were filtered through a pad of Celite, and rinsed with water (30 mL). The filter cake was stirred in 50 mL of ethyl acetate, and filtered through a pad of Celite. After drying over sodium sulfate, the solvent was removed at reduced pressure to afford 1-(4′-nitro-biphenyl-4-yl)-ethanone **6** as an off-white solid (0.61 g, 98%, >95% purity by ^{1}H NMR).

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Supporting Information Available: Complete characterization data for biaryls **1**, **2**, **4**, **5**, **7**, **8**, **9**, **11**, and **12**. This material is available free of charge via the Internet at http://pubs.acs.org.

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