Palladium on Activated Carbon – A Recyclable Catalyst for Suzuki–Miyaura Cross-Coupling of Aryl Chlorides in Water

Morten Lysén,*[a,b] Klaus Köhler[a]

[a] Department Chemie, Anorganische Chemie, TU München, Lichtenbergstr. 4, 85747 Garching, Germany

[b] The Danish University of Pharmaceutical Sciences, Universitetsparken 2, 2100 Copenhagen, Denmark
Fax +4535306040; E-mail: mly@dfuni.dk

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Abstract: Aryl chlorides are efficiently coupled with aryl boronic acids using ligandless Pd/C in water. The catalyst is easily recovered via filtration and reused up to four times with an overall yield of 73%. In addition the catalytic activity and selectivity of a variety of homogeneous and heterogeneous palladium sources have been compared.

Key words: aryl chlorides, water, palladium, cross-coupling, biaryls

The coupling of aryl boronic derivatives with aryl halides known as the Suzuki–Miyaura[1] reaction has become the most popular way of accessing biaryls. The literature is flooded with reports of different catalytic systems and conditions that transform the boronic nucleophiles to valuable fine chemicals and pharmaceutically interesting compounds.[2] Much effort has been invested in preparing catalytic systems that allow the activation of aryl chlorides as these are generally cheaper and more abundant than aryl iodides and bromides. A vast number of ligands have been developed that enhance the coupling of aryl chlorides, and likewise, a lot of palladium catalysts such as palladacycles[3] have evolved. Some major drawbacks are the handling and the availability of these catalysts and ligands, as not many are commercially accessible and some are air-sensitive.

Suzuki coupling in water has received much attention since water as a solvent is very attractive and many catalytic systems have been reported.[4] The use of ligandless palladium is also well documented in the coupling of aryl iodides and bromides.[5] However, only a few examples have appeared, proving that ligandless palladium can be efficiently applied to the coupling of aryl chlorides in water.[6]

In our preliminary study[7] we demonstrated that Pd/C in combination with TBAB in water is an excellent system for the coupling of aryl chlorides. Our reason for using a heterogeneous palladium source was the prospect of attaining much cleaner reactions as palladium can be removed by simple filtration,[8] thus opening the possibility of recycling the catalyst. We investigated a commercially available Pd/C source that possesses high palladium dispersion and a high degree of Pd(II), as it was shown to be the most effective in the Heck reaction of chlorobenzene with styrene.[9] We employed this catalyst and demonstrated that aryl chlorides with various sensitive functional groups like nitrile and ester couple readily under the environmentally friendly conditions developed (Table 1). We now wish to report our results on the comparison of this catalyst with other palladium sources as well as the attempts to recycle the catalyst.

As summarized in Table 1 various electron-deficient as well as electron-rich aryl chlorides were suitable substrates for the reaction, and the reactivity of the aryl chlorides is reflected in the reaction conditions. All reactions were performed under an ambient atmosphere as homocoupling was minimal. Activated aryl chlorides reacted smoothly at low palladium concentrations (0.2–0.5 mol%), and with only 1.1 equivalents of phenylboronic acid. The deactivated chloroarenes required higher catalyst concentrations (2.0 mol%) and longer reaction times (six hours). Addition of TBAB was essential to stabilize the catalyst[10] and 0.5 equivalent was found to be optimal as lower concentrations resulted in diminished yields. Screening of several bases proved NaOH to be superior and 2.5–5 equivalents were found to be the most favorable. For the reaction of chlorobenzonitriles and methyl esters (Table 1, entries 2–5) it was necessary to change the base due to substantial hydrolysis to the benzoic acid. K_2CO_3 and K_3PO_4 both led to benzoic acid formation but KF[11] proved efficient to activate the phenylboronic acid without causing hydrolysis. Chlorobenzene coupled with 4-tolylboronic acid at 140 °C after a reaction time of six hours, using only 0.5 mol% Pd (Table 1, entry 7). 2- and 4-Chlorotoluene gave high conversions using 2 mol% Pd (Table 1, entries 8–10). 4-Chloroanisole (Table 1, entry 11) gave a high yield (83%) and even 4-chlorophenol and 4-chloroaniline (Table 1, entries 12 and 13) could be converted, though in moderate yield. Attempts to couple 2-chloropyridine (Table 1, entry 14) under these conditions failed and changing the base to K_2CO_3 or KF did not induce the reaction. Tagata and Nishida[12] found it necessary to use PPh_3 as ligand, DME as solvent, and heating overnight in order to couple 2-chloropyridine with phenylboronic acid. Attempts to couple 2-chloropyridine by the addition of ligands was not pursued.

The use of aryl bromides and aryl iodides as coupling partners is well-documented but Badone[5a] reported prob-

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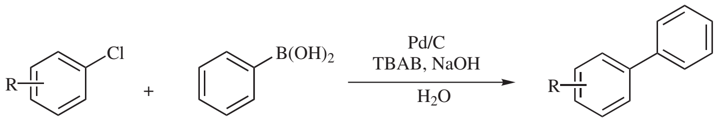
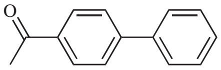
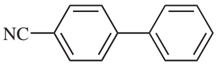
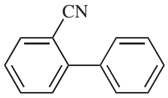
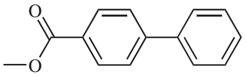
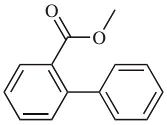
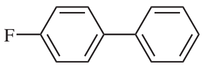
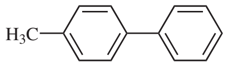
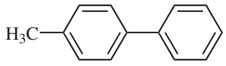
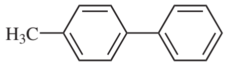
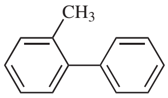
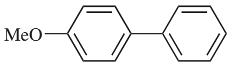
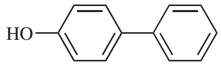
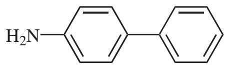
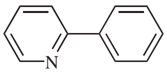
Table 1 Cross-Coupling of Aryl Chlorides in Water Using Pd/C as Catalyst



Entry	R	Pd (mol%)	Temp (°C)	Time	$PhB(OH)_2$ (equiv)	NaOH (equiv)	Product	Isolated yield (%)[b]
1[17]	4-$COCH_3$	0.2	100	2 h	1.1	2.5		99
2[18]	4-CN	0.5	100	3 h	1.1	2.5		98[c]
3[19]	2-CN	0.5	140	3 h	1.1	2.5		89[c]
4[20]	4-CO_2CH_3	0.5	140	3 h	1.1	2.5		87[c]
5[21]	2-CO_2CH_3	0.5	140	3 h	1.1	2.5		63[c,d]
6[19]	4-F	0.5	140	3 h	1.1	2.5		87
7[22]	H	0.5	140	6 h	1.1	2.5		73[e]
8[22]	4-CH_3	2.0	140	6 h	1.1	2.5		70
9[22]	4-CH_3	2.0	140	6 h	1.5	5		81
10[23]	2-CH_3	2.0	140	6 h	1.5	5		74[f]
11[22]	4-OCH_3	2.0	140	6 h	1.5	5		83
12[17]	4-OH	2.0	140	6 h	1.5	5		56
13[24]	4-NH_2	2.0	140	6 h	1.5	5		66[g]
14	2-Cl-pyridine	2.0	140	6 h	1.5	5		trace

[a] Reaction conditions: aryl halide (4 mmol), TBAB (2 mmol), H_2O (6 mL), pressure tube, air.
[b] Yield of chromatographically pure products.
[c] KF used as base.
[d] Product contaminated with 6% 2-chlorobenzoic acid methyl ester.
[e] 4-Tolylboronic acid was used as a nucleophile.
[f] Product contaminated with 5% biphenyl.
[g] Determined by ^1H NMR spectroscopy.

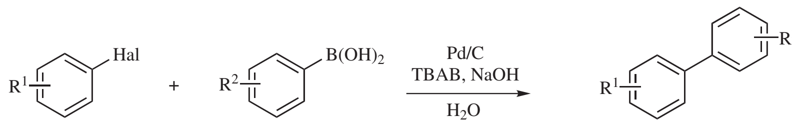
lems when coupling aryl iodides under aqueous conditions as the reaction stopped after one hour, resulting in incomplete conversion. Using our standard conditions with low palladium loading (0.2 mol%) we found that 4-iodobenzene and 4-iodophenol coupled readily and gave an excellent yield (ca. 90%) after two hours at 70 °C (Table 2, entries 1 and 2) whereas 4-iodoanisole only gave trace amounts of coupling product (Table 2, entry 3). However, all aryl iodides could be completely converted to the corresponding biaryls by raising the temperature to 100 °C for two hours.

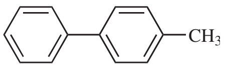
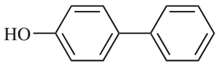
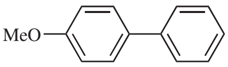
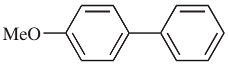
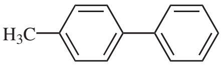
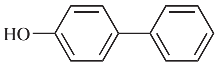
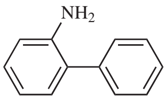
Under the same conditions aryl bromides coupled efficiently and gave full conversion within two hours with excellent isolated yield (95–99%; Table 2, entries 4–6). Even 2-bromoaniline gave a high yield (89%) requiring only 0.5 mol% Pd and a reaction time of three hours at 100 °C to reach completion (Table 2, entry 7).

Traditionally, boronic acids were the only organoboron compounds utilized in the cross-coupling but in the last ten years several other boron derivatives like esters[13] and trifluoropotassium salts[14] have found wide application. Conditions that allow coupling of these derivatives have been developed but only in organic solvents. Coupling of different arylboronic acids, esters, and potassium trifluoroborates under these aqueous conditions were tested. As seen in Table 3 they generally coupled efficiently producing a high yield of the biaryls. Attempts to couple 2-methoxyphenylboronic acid and 2-chloronitrobenzene (Table 3, entry 2) resulted in a lower yield (53%) probably due to steric interactions. Heating the reaction for six hours gave a similar conversion and higher palladium concentrations were not tested. The coupling of the 2-cyano boronic ester (Table 3, entry 6) led to no product formation probably due to hydrolysis of the nitrile. Changing the base to KF only produced trace amounts of product. All the potassium trifluoroborates tested were readily coupled resulting in high yields of the biaryls (Table 3, entries 7–9).

Using these aqueous conditions, alternative palladium sources were tested to see if this was a general reaction or due to the use of the optimized catalyst (Table 4). Heterogeneous palladium catalysts together with homogenous $PdCl_2$ and $Pd(OAc)_2$ all showed excellent activity. This indicates that the heterogeneous palladium sources simply leach palladium into solution during the reaction as previously reported.[8] When homogenous palladium was employed a low concentration (Table 4, entries 9 and 11) resulted in quantitative conversion, however, at higher concentrations (Table 4, entries 8 and 10) conversion decreases. This is probably due to the formation of palladi-

Table 2 Cross-Coupling of Aryl Iodides and Aryl Bromides



Entry[a]	R^1	Hal	R^2	Product	Temp (°C)	Conversion (%)[b]	Yield (%)[b]
1	H	I	CH_3		70 100	94 100	90 >99
2	4-OH	I	H		70 100	90 100	90 >99
3	4-OMe	I	H		70 100	5 100	5 >99
4[22]	4-OMe	Br	H		100	nd	99[c]
5[22]	$4-CH_3$	Br	H		100	nd	95[c]
6[17]	4-OH	Br	H		100	nd	97[c]
7[25]	$2-NH_2$	Br	H		100	nd	89[c,d]

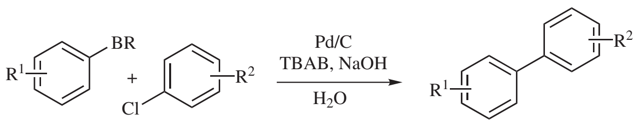
[a] Reaction conditions: aryl halide (2 mmol), arylboronic acid (2.2 mmol), Pd (0.2 mol%), TBAB (1 mmol), NaOH (5 mmol), H_2O (4 mL), 2 h, 100 °C.

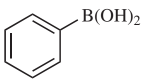
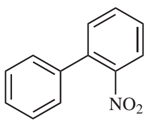
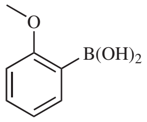
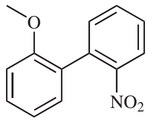
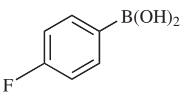
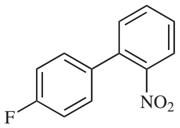
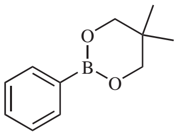
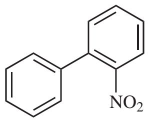
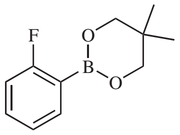
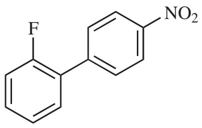
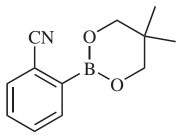
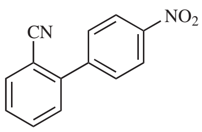
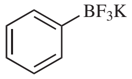
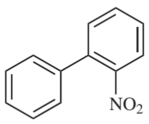
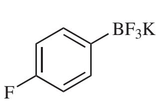
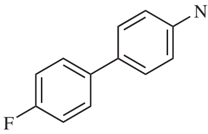
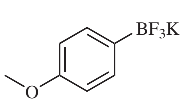
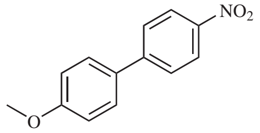
[b] Determined by GC with diethylene glycol dibutyl ether as internal standard; nd = not determined.

[c] Yield of chromatographically pure products.

[d] Experiment performed with Pd/C (0.5 mol%) at 100 °C for 3 h.

Table 3 Cross-Coupling of Various Aryl Boronic Derivatives



Entry	ArBR	R^2	Product	Yield (%)[a]
1[26]		2-NO_2		97
2[27]		2-NO_2		53
3[28]		2-NO_2		98
4[26]		2-NO_2		96
5[28]		4-NO_2		98
6		4-NO_2		trace[c]
7[26]		2-NO_2		89
8[29]		4-NO_2		98
9[30]		4-NO_2		97

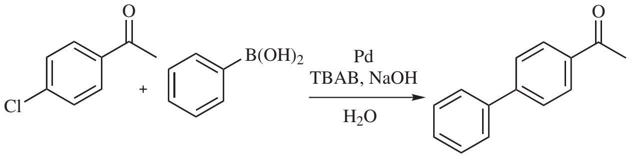
[a] Reaction conditions: aryl chloride (1 mmol), ArBR (1.2 mmol), TBAB (0.5 mmol), NaOH (2.5 mmol), H_2O (2 mL), 100 °C, 2 h.

[b] Yield of chromatographically pure product.

[c] KF used as base.

um clusters and precipitation of palladium black, thereby decelerating the reaction. Pd/C from different suppliers all showed the same reactivity and selectivity (Table 4, entries 1–4), whether reduced to Pd(0) or dried. It is also evident that at catalyst concentrations lower than 0.2 mol% the reaction fails to reach completion within two hours (Table 4, entries 5 and 6). As expected, palladium immobilized on Zeolite[15] (Table 4, entry 7) displayed similar activity as it is also able to release palladium under these reaction conditions.

Table 4 Screening of Various Palladium Sources



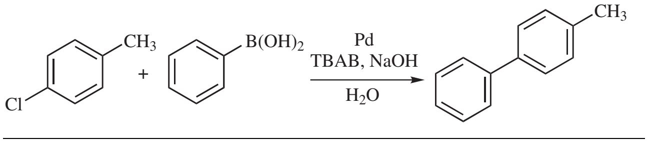
Entry[a]	Pd[b]	Amount (mol%)	Conversion (%)[c]	Yield (%)[c]
1	Pd/C (A)	0.22	98	95
2	Pd/C (B)	0.24	100	>99
3	Pd/C (C)	0.22	100	>99
4	Pd/C (D)	0.21	100	>99
5	Pd/C (D)	0.08	64	62
6	Pd/C (D)	0.04	68	67
7	Pd/NaY	0.22	100	>99
8	$PdCl_2$	3.45	86	59
9	$PdCl_2$	0.56	100	>99
10	$Pd(OAc)_2$	3.10	79	55
11	$Pd(OAc)_2$	0.28	100	>99

[a] Reaction conditions: 4-chloroacetophenone (2 mmol), phenylboronic acid (2.2 mmol), TBAB (1 mmol), H_2O (4 mL), 100 °C, 2 h.

[b] A: Johnson-Mattey 5% Pd/C (H_2O, 49.37%); B: Aldrich 5% Pd/C; C: Degussa 5% Pd/C dried and reduced to Pd(0); D: Degussa 5% Pd/C (H_2O, 51.90%).

[c] Determined by GC with diethylene glycol dibutyl ether as internal standard.

Table 5 Palladium Sources under More-Demanding Conditions



Entry[a]	Pd	Amount (mol%)	Conversion (%)[b]	Yield (%)[b]
1	Pd/C (A)	0.53	31	14
2	Pd/C (B)	0.58	23	10
3	Pd/C (C)	0.58	10	10
4	Pd/C (D)	0.54	34	25
5	Pd/NaY	0.46	19	19
6	$PdCl_2$	0.79	21	12
7	$Pd(OAc)_2$	0.75	10	8

[a] Reaction conditions: 4-chlorotoluene (2 mmol), phenylboronic acid (3 mmol), TBAB (1 mmol), NaOH (10 mmol), H_2O (4 mL), 140 °C, 6 h.

[b] Determined by GC with diethylene glycol dibutyl ether as internal standard.

In order to couple electron-rich aryl chlorides, extended reaction times and higher temperatures were needed and therefore the stability of the palladium could be questioned. The palladium sources listed in Table 4 were investigated to identify if the palladium source could have a major influence on the success of the reaction. As is evident from Table 5, all the palladium sources showed similar activity under these reaction conditions. Employing 0.5 mol% Pd in the reaction of 4-chlorotoluene with phenylboronic acid, using NaOH as base and heating to 140 °C for six hours all led to less than 30% yield. The heterogeneous palladium sources (Table 5, entries 1–7) showed slightly better activity than $PdCl_2$ and $Pd(OAc)_2$ (Table 5, entries 6 and 7) at this temperature. The unreduced and wet Pd/C-catalysts from Johnson-Mattey (Table 5, entry 1) and Degussa (Table 5, entry 4) both showed the best reactivity but the Degussa catalyst displayed superior selectivity. The Pd/C catalyst from Aldrich (Table 5, entry 2) proved less reactive and selective under these conditions and the reduced and dried Pd/C catalyst (Table 5, entry 3), though exhibiting excellent selectivity, showed poor activity. The palladium immobilized on Zeolite again shows good reactivity and excellent selectivity. The experiments demonstrate that, under more demanding conditions, the nature of the palladium (catalyst preparation, pre-treatment) becomes more relevant for its catalytic properties.

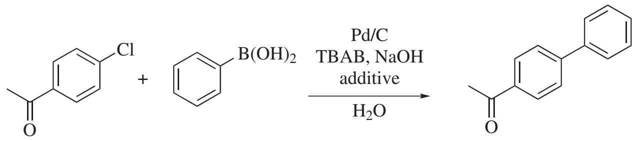
All the palladium sources tested under these conditions proved excellent in the cross-coupling of aryl chlorides and we chose to continue with catalyst C to investigate the scope and limitations of recycling the catalyst.

Although a low palladium loading is sufficient to achieve high conversions it is desirable to have a catalyst that can easily be separated from the reaction and reused.

Recovery of the catalyst was accomplished by simple filtration through celite or by centrifugation. As shown in Table 6, the procedure by which the palladium is recovered is of great importance. In the reaction where the catalyst was reused without any activator, whether it was recovered by centrifugation or filtration, it had lost most of its activity by the time it was reused for a third reaction. Although the selectivity is still very high when the catalyst is first reused, satisfactory yields of 80% and 67% are obtained, subsequent use only gives 38% and 32% yield (Table 6, entries 1 and 3).

De Vries et al.[16] have shown that palladium activity can be restored by addition of iodine which (partially) re-oxidizes palladium to Pd(II). Addition of 0.1 mmol iodine to the catalyst retrieved by centrifugation did not restore the reactivity as the yield after it is first reused is only 60% (Table 6, entry 2) and then only 20% after its second reuse. The low yield of the reaction could be due to incomplete recovery of the catalyst by centrifugation. The catalyst retrieved by filtration on the other hand exhibited full activity by addition of iodine in the first reuse. This activity was retained as the catalyst was further reused.

Table 6 Catalyst Recovery and Reuse



Entry[a]	Catalyst recycling[b]	Additive[c]	Original use	1st Reuse	2nd Reuse	3rd Reuse	4th Reuse	Overall yield (%)[d]
1	Centrifugation	–	99	80	38	–	–	72
2	Centrifugation	I_2	99	60	20	–	–	60
3	Filtration	–	99	65	32	–	–	65
4	Filtration	I_2	99	99	99	25	32	71
5	Filtration	I_2	99	99	80	47	41	73

[a] Reaction conditions: 4-chloroacetophenone (4 mmol), phenylboronic acid (4.4 mmol), Pd/C (0.2 mol%), NaOH (10 mmol), H_2O (6 mL), 2 h, 100 °C.

[b] See experimental section for details.

[c] Additive was added prior to the reaction only when the catalyst was reused; I_2 (0.1 mmol).

[d] Yield was determined by GC using diethylene glycol dibutyl ether as internal standard.

When reused for the third time, the activity dropped remarkably giving only 26% conversion but activity was maintained even after the fourth time, resulting in an overall yield of 71% over five reactions. A second sequence gave similar results, a quantitative yield was obtained when the catalyst was reused twice, then the yield starts to decrease resulting in an overall yield of 73%.

In conclusion, we have demonstrated that different commercially available ligandless palladium sources, in combination with TBAB, are efficient catalysts for the coupling of aryl chlorides in water. Furthermore we have proven that Pd/C can be recovered by simple filtration and reused several times with high overall yield.

Flash column chromatography was performed using silica gel (Merck, 40–63 mesh). TLC was performed using Merck silica gel 60 F254 aluminum sheets. GC analysis was performed on a HP6890 with diethylene glycol dibutyl ether as internal standard. NMR spectra were recorded in $CDCl_3$ on a 400 MHz Bruker spectrometer with TMS/$CDCl_3$ as internal standards.

All solvents and reagents were obtained from Fluka or Aldrich and used without further purification. Pd/C was purchased from Degussa AG (E105CA/W), Johnson-Mattey, and Aldrich and used as received. The palladium on NaY-zeolite was prepared as previously reported.[15] H_2O was passed through a standard universal ion-exchange and used without further purification.

Pd/C-Catalyzed Suzuki Cross-Coupling; General Procedure

A pressure tube was charged with Pd/C, E105CA/W (0.2–2 mol%), TBAB (2 mmol), NaOH (2.5–5 equiv), phenylboronic acid (1.2–1.5 equiv), and aryl halide (4 mmol). H_2O (6 mL) was added and the flask was sealed with a Teflon screw cap and stirred in a preheated oil bath for the time indicated. After cooling to r.t., CH_2Cl_2 (10 mL) was added, and the mixture was filtered through a plug of celite to remove the catalyst, washed with CH_2Cl_2 (2 × 10 mL), the combined organic phase was dried ($MgSO_4$), adsorbed onto celite, and purified by flash chromatography to yield the corresponding biaryl. The spectroscopic data of the biaryls were in agreement with those previously reported.

4-Fluoro-2′-nitrobiphenyl[28]

^1H NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, 1 H, J = 7.9, 1.3 Hz), 7.59 (dt, 1 H, J = 7.5, 1.3 Hz), 7.47 (dt, 1 H, J = 7.9, 1.5 Hz), 7.39 (dd, 1 H, J = 7.6, 1.5 Hz), 7.30–7.23 (m, 2 H), 7.13–7.05 (m, 2 H).

Recycling of the Pd/C Catalyst – Centrifugation

The reaction was carried out as above, after cooling to r.t. and addition of CH_2Cl_2 (5 mL) the reaction was transferred to a centrifuge flask, CH_2Cl_2 (4 mL) and H_2O (4 mL) were added and the resulting mixture was centrifuged at 8000 rpm for 20 min. The liquids were decanted and the Pd/C was washed with CH_2Cl_2 (4 mL) and centrifuged again. After decantation the Pd/C was transferred to a clean pressure tube and the experiment was repeated on the same scale. The reaction mixture was analyzed by GC; the yield and conversion were calculated with diethylenglycol dibutylether as the internal standard.

In the sequence where iodine was added as activator, I_2 (25 mg, 0.1 mmol) was added with the other reagents and the reaction and work-up was as above.

Recycling of the Pd/C Catalyst – Filtration

The reaction was carried out as above, after cooling to r.t. and addition of CH_2Cl_2 (5 mL), the reaction was vacuum-filtered through a 3 cm plug of celite in a glass filter funnel (pore 4, ∅ 210 mm). The celite was washed with CH_2Cl_2 (5 mL). The Pd/C was scraped off and transferred to a clean pressure tube and the experiment was repeated on the same scale. The remaining celite was washed with CH_2Cl_2 (10 mL) and the reaction mixture was analyzed by GC; the yield and conversion were calculated with diethylene glycol dibutyl ether as the internal standard.

In the sequence where iodine was added as activator, I_2 (25 mg, 0.1 mmol) was added with the other reagents and the reaction and work-up was as above.

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References

(1) (a) Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun.* **1981**, *11*, 513. (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (c) Suzuki, A. *J. Organomet. Chem.* **1999**, *576*, 147.

(2) (a) Stanford, S. P. *Tetrahedron* **1998**, *54*, 263. (b) Smith, G. B.; Dezeny, G. C.; Hughes, D. L.; King, A. O.; Verthoeven, T. R. *J. Org. Chem.* **1994**, *59*, 8151.

(3) (a) For a recent review, see: Bellina, F.; Carpita, A.; Rozzi, R. *Synthesis* **2004**, 2419. (b) See also: Littke, A. F.; Fu, G. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 4176.

(4) Shaughnessy, K. H.; DeVasher, R. B. *Curr. Org. Chem.* **2005**, *9*, 585.

(5) (a) Badone, D.; Baroni, R.; Cardamone, A.; Ielmini, A.; Guzzi, U. *J. Org. Chem.* **1997**, *62*, 7170. (b) Arcadi, A.; Cerichelli, G.; Chiarini, M.; Correa, M.; Zorzan, D. *Eur. J. Org. Chem.* **2003**, 4080. (c) Lu, G.; Franzén, R.; Zhang, Q.; Xu, Y. *Tetrahedron Lett.* **2005**, *46*, 4255. (d) Arvela, R. K.; Leadbeater, N. E.; Sangi, M. S.; Williams, V. A.; Granados, P.; Singer, R. *J. Org. Chem.* **2005**, *70*, 161.

(6) (a) Arvela, K. R.; Leadbeater, N. E. *Org. Lett.* **2005**, *7*, 2101. (b) Bumagin, N. A.; Bykov, V. V. *Tetrahedron* **1997**, *53*, 14437. (c) Bedford, R. B.; Blake, M. E.; Butts, C. P.; Holder, D. *Chem. Commun.* **2003**, 466.

(7) Lysén, M.; Köhler, K. *Synlett* **2005**, 1671.

(8) (a) Heidenreich, R. G.; Krauter, J. G. E.; Pietsch, J.; Köhler, K. *J. Mol. Catal. A: Chem.* **2002**, *182-183*, 499. (b) Biffis, A.; Zecca, M.; Basato, M. *J. Mol. Catal. A: Chem.* **2001**, *173*, 249.

(9) Heidenreich, R. G.; Köhler, K.; Krauter, J. G. E.; Pietsch, J. *Synlett* **2002**, 1118.

(10) Reetz, M. T.; de Vries, J. G. *Chem. Commun.* **2004**, 1559.

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

(12) Tagata, T.; Nishida, M. *J. Org. Chem.* **2003**, *68*, 9412.

(13) (a) Chaumeil, H.; Signorella, S.; Drian, C. L. *Tetrahedron* **2000**, *56*, 9655. (b) Kristensen, J. L.; Lysén, M.; Vedsø, P.; Begtrup, M. *Org. Lett.* **2001**, *3*, 1435. (c) Barder, T. E.; Walker, S. D.; Martinelli, J. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 4685.

(14) (a) Vedejs, J.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 3020.
(b) Molander, G. A.; Biolatto, B. *Org. Lett.* **2002**, *4*, 1867.
(c) Barder, T. E.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 2649.

(15) Pröckl, S. S.; Kleist, W.; Gruber, M. A.; Köhler, K. *Angew. Chem. Int. Ed.* **2004**, *43*, 1881.

(16) de Vries, A. H. M.; Parlevliet, F. J.; Vondervoort, L. S.; Mommers, J. H. M.; Henderickx, H. J. W.; Walet, M. A. M.; de Vries, J. G. *Adv. Synth. Catal.* **2002**, *344*, 996.

(17) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550.

(18) Leadbeater, N. *J. Org. Chem.* **2001**, *66*, 7539.

(19) Zapf, A.; Beller, M. *Chem. Eur. J.* **2000**, *6*, 1830.

(20) Riggleman, S.; DeShong, P. *J. Org. Chem.* **2003**, *68*, 8106.

(21) Glover, S. A.; Goosen, A.; McCleland, C. W.; Schoonraad, J. L. *J. Chem. Soc., Perkin Trans. 1* **1984**, *10*, 2255.

(22) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722.

(23) Kabalka, G. W.; Wang, L.; Pagni, R. M.; Hair, M. C.; Namboodiri, V. *Synthesis* **2003**, 217.

(24) Nájera, C.; Gil-Molto, J.; Karlström, S.; Falvello, L. R. *Org. Lett.* **2003**, *5*, 1451.

(25) Herndon, J. W.; McMullen, L. A. *J. Organomet. Chem.* **1989**, *368*, 83.

(26) Li, J.-L.; Liu, N.-J. *Org. Lett.* **2004**, *6*, 2809.

(27) Downie, I. M.; Hearey, H.; Kemp, G.; King, D.; Wosley, M. *Tetrahedron* **1992**, *48*, 4005.

(28) Hermann, E. C.; Hoyer, G.-A.; Kelm, J. *Spectrochim. Acta, Part A* **1982**, *38*, 1057.

(29) Enokido, T.; Fugami, K.; Endo, M.; Kameyama, M.; Kosugi, M. *Adv. Synth. Catal.* **2004**, *346*, 1685.

(30) Denmark, S. E.; Ober, M. H. *Org. Lett.* **2003**, *5*, 1357.