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Pd/C as a Reusable Catalyst for the Coupling Reaction of Halophenols and Arylboronic Acids in Aqueous Media

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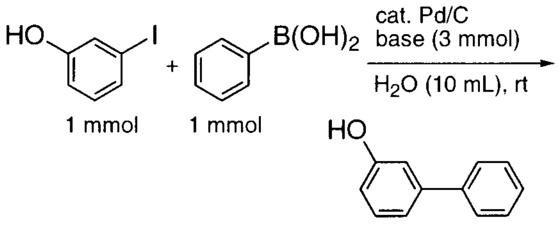
Abstract: Pd/C was found to catalyze the Suzuki−Miyaura coupling reaction of halophenols in aqueous media. When halophenols were treated with $ArB(OH)_2$ and a catalytic amount of 10% Pd/C (0.3 mol % Pd) in aqueous K_2CO_3 solution, the corresponding hydroxybiaryls were obtained in a high yield or quantitatively. The palladium catalyst was easily recovered and reused.

Palladium-catalyzed coupling reaction of haloarenes with arylboronic acids, the Suzuki−Miyaura reaction, is one of the most versatile methods for the preparation of biaryl compounds.[1] Its usefulness mainly lies in the use of less toxic substrates and aqueous organic solvent such as toluene−H_2O, as well as wide applicability. However, it usually requires toxic phosphine ligands and high-temperature conditions. From both scientific and environmental points of view, development of a new catalytic system without use of stabilizing phosphine ligands in aqueous media under mild conditions has attracted much attention. In this paper we report that Pd/C works as a reusable catalyst for the Suzuki−Miyaura coupling reaction of halophenols in aqueous media.

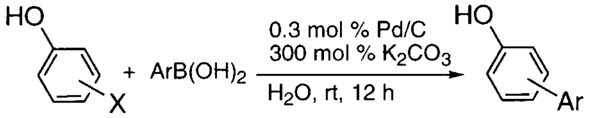
Pd/C is one of the most common heterogeneous palladium catalysts, and recent reports have demonstrated the application of Pd/C for the Suzuki−Miyaura coupling as a convenient and phosphine-free catalyst.[2,3] Iodophenols are readily soluble in basic aqueous media and are important starting materials for the synthesis of substituted biaryls. Therefore, they might be suitable substrates for the Suzuki−Miyaura coupling in aqueous media. However, since the early report from Beletskaya et al.,[4] no example for the Suzuki−Miyaura coupling of iodophenols in aqueous media has been reported.

Table 1. Pd/C-Catalyzed Coupling of 3-Iodophenol and Phenylboronic Acid



entry	Pd/C (mol %)	base	time (h)	yield (%)
1	0.3	K_2CO_3	3	30
2	0.3	K_2CO_3	6	64
3	0.3	K_2CO_3	9	88
4	0.3	K_2CO_3	12	97
5	0.3	K_2CO_3	24	97
6	0.2	K_2CO_3	12	89
7	0.1	K_2CO_3	12	88
8	0.3	K_3PO_4	12	81
9	0.3	KOH	12	65
10	0.3	NaOH	12	48

Table 2. Pd/C-Catalyzed Coupling of Halophenol and Arylboronic Acid in Aqueous Media[a]



entry	halophenol	arylboronic acid	yield (%)
1	2-iodophenol	$PhB(OH)_2$	70
2	3-iodophenol	$PhB(OH)_2$	97
3	4-iodophenol	$PhB(OH)_2$	>99
4	4-iodophenol	$4\text{-}FC_6H_4B(OH)_2$	>99
5	4-iodophenol	$4\text{-}MeOC_6H_4B(OH)_2$	>99
6	4-iodophenol	$4\text{-}MeC_6H_4B(OH)_2$	>99
7	4-iodophenol	$2\text{-}MeC_6H_4B(OH)_2$	>99
8	4-iodophenol	$2\text{-}MeOC_6H_4B(OH)_2$	98
9	4-bromophenol	$PhB(OH)_2$	35 (76[b])

[a] Reaction conditions: halophenol (1 mmol), $ArB(OH)_2$ (1 mmol), K_2CO_3 (3 mmol), Pd/C (3 mg, 0.3 mol %) in H_2O (10 mL) at room temperature for 12 h. [b] The reaction was performed at 50 °C for 12 h.

As expected, Pd/C was found to catalyze the coupling of 3-iodophenol and phenylboronic acid, giving 3-hydroxybiphenyl. The reaction conditions were optimized, and the representative results are listed in Table 1. When 0.3 mol % of Pd/C (purchased from Wako Chemicals), suspended in aqueous K_2CO_3 solution, was treated with stoichiometric amounts of 3-iodophenol and $PhB(OH)_2$, the yields of 3-hydroxybiphenyl were 30%, 64%, 88%, 97%, and 97% with quenching after 3, 6, 9, 12, and 24 h, respectively (entries 1−5). Next, the amount of Pd/C was examined (entries 4, 6, and 7). Although 0.1 mol % of Pd/C also worked sufficiently, the use of 0.3 mol % of Pd/C realized almost quantitative yield with good reproducibility. Finally, the effect of base was screened as shown in entries 8−10 to find that K_2CO_3 is suitable.

The above procedure could be applied to the coupling of a variety of iodophenols and arylboronic acids, giving the corresponding hydroxybiphenyls as demonstrated in Table 2. In many cases, the coupling product was obtained quantitatively. When the coupling of 4-bromophenol with $PhB(OH)_2$ was performed under the same

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Table 3. Reaction of 4-Iodophenol with Phenylboronic Acid Using Recovered Pd/C as Catalyst

Pd/C	yield (%)
	>99
first reuse	95
second reuse	94
third reuse	90
fourth reuse	89
fifth reuse	89

conditions as the reaction of 4-iodophenol, the yield of 4-hydroxybiphenyl was only 35%, but the yield could be increased up to 76% when the reaction was operated at 50 °C for 12 h (entry 10).

The experimental procedure is very simple. The reaction was quenched by acidification with diluted HCl solution to precipitate the coupling product. Filtration gave the mixture of the product and Pd/C, and the former was easily separated by extraction with common organic solvent such as ethyl acetate.

It is noteworthy that the recovered Pd/C possesses enough catalytic activity for the coupling reaction. The activity of the recovered Pd/C was monitored by the reaction of 4-iodophenol and $PhB(OH)_2$ as shown in Table 3. Although the catalytic activity was gradually diminished, the yield was still 89% even in the fifth reuse. As reported previously, the reaction may proceed via a usual oxidative addition, transmetalation, and reductive elimination cycle.[1] The regenerated Pd(0) species might be trapped by charcoal effectively, giving the reusable catalyst.

As described above, Pd/C is found to catalyze the Suzuki−Miyaura coupling reaction of halophenols in aqueous media. The present method is promising as a result of the simple operation and reusability of Pd/C.

Experimental Section

General Methods. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were measured on a Varian Mercury 300 spectrometer. $CDCl_3$ was used as a solvent, and residual chloroform ($\delta = 7.24$ ppm; ^{13}C, 77.0 ppm) or Me_4Si was used as an internal standard. All reagents are of commercial quality. Pd/C (10%) and halophenols were purchased from Wako Pure Chemical Industries, Ltd. Arylboronic acids were purchased from Aldrich. H_2O was of Milli-Q grade with specific resistance above 18 Ω cm.

General Procedure. A 30 mL Erlenmeyer flask equipped with a magnetic stirring bar was charged with 10% Pd/C (3 mg), K_2CO_3 (415 mg, 3 mmol), arylboronic acid (1 mmol), halophenol (1 mmol), and H_2O (10 mL). The mixture was vigorously stirred for 12 h at room temperature. The reaction was quenched with 1.5 M HCl solution (10 mL) to precipitate a white solid. Suction filtration gave the mixture of the Pd/C and the product, which could be separated by the extraction with ethyl acetate. Further purification by recrystalization or chromatography gave the pure hydroxylbiaryl. Pd/C was also recovered almost quantitatively and reusable.

The products were identified by comparison of ^1H NMR spectral data with those of the authentic samples. **Biphenyl-4-ol** [92-69-3];[5] **biphenyl-3-ol** [580-51-8];[6] **biphenyl-2-ol** [90-43-7];[6] **4′-methyl-biphenyl-4-ol** [26191-64-0];[7] **4′-fluoro-biphenyl-4-ol** [324-94-7];[8] **4′-methoxy-biphenyl-4-ol** [16881-71-3];[9] **2′-methyl-biphenyl-4-ol** [38262-85-0];[9] **2′-methoxy-biphenyl-4-ol** [65109-82-2].[10]

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