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Ligandless palladium chloride-catalyzed homo-coupling of arylboronic acids in aqueous media

George W. Kabalka* and Lei Wang

Departments of Chemistry and Radiology, The University of Tennessee, Knoxville, TN 37996-1600, USA

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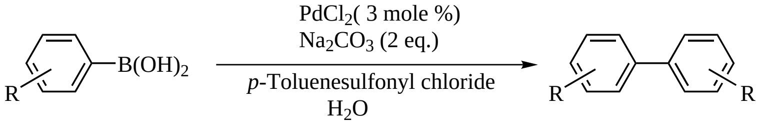
Abstract—In the presence of *p*-toluenesulfonyl chloride, ligandless palladium chloride catalyzes the homo-coupling of arylboronic acids to afford symmetrical biaryls in excellent yields. © 2002 Published by Elsevier Science Ltd.

The palladium-catalyzed coupling of arylboronic acids and esters with organic halides (Suzuki reaction) is an excellent method for preparing unsymmetrical biaryls, which are important building blocks in natural products and in the material sciences.[1] The synthesis of symmetrical biaryls via homo-coupling of arylboronic acids is also of interest to synthetic organic chemists. Suzuki reported a self-coupling reaction of arylboronic acids, carried out under anhydrous conditions using $Pd(OAc)_2$ along with PPh_3 and a $Cu(OAc)_2$ catalyst.[2] Wong reported self-coupling of organoboroxines catalyzed by $Pd(PPh_3)_4$ in a methanol/toluene solvent system.[3] Tamao then found that palladium(II) complexes catalyzed the oxidative homo-coupling of areneboronic acids in the presence of acrylate dibromides to afford biaryls,[4] but the phenyl groups in PPh_3 can also couple with arylboronic acids to give an unsymmetrical biaryl.[5] Jackson reported the homo-coupling of arylboronic acids catalyzed by $Pd(OAc)_2$ in the presence of oxygen, but the reaction proceeds rather slowly and affords only moderate yields.[6] Most recently, Wong found that phosphine and phosphite are efficient ligands for palladium-catalyzed homo-coupling of arylboronic acids in DMF.[7]

We report a ligandless palladium chloride catalyzed homo-coupling of arylboronic acids in water, or a water/ethanol mixture (v/v, 1/1), at room temperature in the presence of *p*-toluenesulfonyl chloride in the absence of oxygen. Excellent yields of the desired biaryl products are obtained (Scheme 1).

A variety of sulfonyl chlorides were investigated and our results are summarized in Table 1. In the absence of an additive, homo-coupling occurs but the yield is poor. Addition of an arylsulfonyl chloride improves the yield dramatically (95%, entry 4, Table 1). Among the sulfonyl chlorides we tested, *p*-toluenesulfonyl chloride and phenylsulfonyl chloride were the most effective. *p*-Toluenesulfonyl chloride was chosen for the study since it is readily available. The optimum quantity of *p*-toluenesulfonyl chloride was found to be 0.5 equiv. *p*-Toluenesulfonamide, *p*-toluenesulfonic acid and thionyl chloride were not effective.

The results of the arylboronic acid homo-coupling study are summarized in Table 2. For arylboronic acids, containing groups such as Cl, F or CH_3, the reaction affords excellent yields of biaryl products. The addition of ethanol increases the solubility of the arylboronic acid and has little, if any, effect on reaction yields. (Compare entries 2 and 6 in Table 2.)



Scheme 1.

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* Corresponding author. Tel.: 865-974-3260; fax: 865-974-2997; e-mail: kabalka@utk.edu

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Table 1. Homocoupling of *p*-tolueneboronic acid[a]

Entry	Additive	Yield (%)[b]
1	None	35
2	*p*-Toluenesulfonamide	17
3	*p*-Toluenesulfonic acid	46
4	*p*-Toluenesulfonyl chloride	95
5	Phenylsulfonyl chloride	95
6	*p*-Bromophenylsulfonyl chloride	84
7	*m*-Nitrophenylsulfonyl chloride	92
8	2-Mesitylenesulfonyl chloride	83
9	2,4-Dinitrophenylsulfonyl chloride	66
10	*p*-Toluenesulfonyl chloride	77
11	*n*-Butylsulfonyl chloride	70
12	Thionyl chloride	11

[a] Reaction conditions: *p*-tolueneboronic acid (1.0 mmol), $PdCl_2$ (0.03 mmol), Na_2CO_3 (2.0 mmol), additive (0.5 mmol), H_2O (20 mL) room temperature under nitrogen atmosphere for 12 h with stirring.

[b] Isolated yield.

Table 2. Ligandless palladium-catalyzed homo-coupling of arylboronic acids[a]

Entry	Boronic acid	Reaction media	Yield (%)[b]
1	$C_6H_5B(OH)_2$	H_2O	95
2	p-$CH_3C_6H_4B(OH)_2$	H_2O	95
3	p-$FC_6H_4B(OH)_2$	H_2O	96
4	p-$ClC_6H_4B(OH)_2$	H_2O	97
5	p-$BrC_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	96
6	p-$CH_3C_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	92
7	$C_6H_5CH{=}CHB(OH)_2$	H_2O–C_2H_5OH (1/1)	95
8	p-$CH_3COC_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	96
9	p-$CH_3SC_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	94
10	m-$CHOC_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	90
11	Naphthalene-1-boronic acid	H_2O–C_2H_5OH (1/1)	93
12	o-$CH_3C_6H_4B(OH)_2$	H_2O–C_2H_5OH (1/1)	56

[a] Reaction conditions: arylboronic acid (1.0 mmol), $PdCl_2$ (0.03 mmol), Na_2CO_3 (2.0 mmol), *p*-toluenesulfonyl chloride (0.5 mmol), solvent (20 mL) room temperature for 12 h.

[b] Isolated yield.

Very good yields are observed for arylboronic acids containing both electron donating and electron withdrawing groups. It is noteworthy that substituents at the *ortho*-position lead to decreased yields (entry 12, Table 2). Functional groups such as halide, methoxy, and acetyl are not affected. Vinyl boronic acids also homo-couple under the reaction conditions (81% yield, Scheme 2). However, heteroaromatic boronic acids and aliphatic boronic acids are not reactive.

The mechanism of the reaction has not been investigated but a sulfonyl chloride is required. We have carried out the reaction in the presence of sodium *p*-toluenesulfonate and sodium chloride and the results were not satisfactory. Furthermore, the addition of either *p*-toluenesulfonic acid or hydrochloric acid does not induce homo-coupling.

General procedure: The synthesis of 4,4′-dimethylbiphenyl is representative. To a stirred solution of *p*-tolueneboronic acid (1.0 mmol), palladium(II) chloride (3 mol%), sodium carbonate (2 mmol in 20 mL of H_2O), was added *p*-toluenesulfonyl chloride in one portion (0.5 mmol). The solution was stirred at room temperature overnight. Hexane (2×20 mL) was added to extract the product. The combined organic phase was dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure to yield 4,4′-dimethylbiphenyl (87 mg, 95%).

In conclusion, a simple, environmentally friendly, procedure for the synthesis of symmetrical biaryls from corresponding arylboronic acids has been developed. The procedure does not require anhydrous conditions and utilizes ligandless palladium chloride.

Acknowledgements

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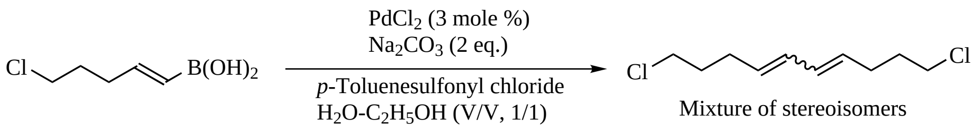

Scheme 2.