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Electrooxidative homo-coupling of arylboronic acids catalyzed by electrogenerated cationic palladium catalysts

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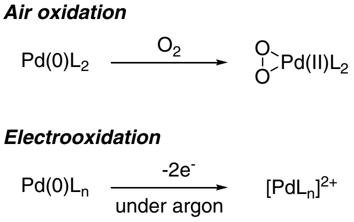
ABSTRACT

An electrochemical method for generating cationic palladium complexes was integrated into an electrooxidative homo-coupling of arylboronic acids. In the presence of a catalytic amount of TEMPO, the homo-coupling reaction proceeded efficiently under argon to afford symmetric biaryls.

Biaryl compounds are significant building blocks for the materials and pharmaceutical sciences. One of the most commonly used methods to construct biaryls is the palladium-catalyzed coupling of arylboronic acids or esters with aryl halides (Suzuki–Miyaura coupling).[1] Pd-catalyzed oxidative homo-coupling of arylboronic acids has also received attention as a method for constructing biaryls. While there have been several reports on efficient Pd-catalyzed oxidative homo-coupling of arylboronic acids, these methods have usually required stoichiometric amounts of oxidants or an oxygen atmosphere.[2–4] Recently, Yamamoto and co-workers reported an excellent air-oxidative Pd-catalyzed homo-coupling of arylboronic acids.[5] They found that several arylboronic acids can be transformed to biaryls at room temperature without base or ligand in MeOH. Mao and Zhang also reported an air-oxidative coupling reaction using $Pd(OAc)_2$ as a catalyst and K_2CO_3 as a base in acetone/H_2O.[6] In 2006, a mechanistic study of the palladium-catalyzed homo-coupling of arylboronic acids was reported by Amatore and Jutand.[7] They documented that the peroxo complex $(\eta^2\text{-}O_2)PdL_2$ (L = ligand), generated in situ by the reaction of Pd(0) and O_2, plays a key role in the reaction.

We have been interested in the electrochemical reactions,[8] in particular, in electrochemical generation of transition-metal complexes, and reported the electrooxidative synthesis of cationic Pd catalysts ($[Pd(CH_3CN)_4][Y]_2$, Y = BF_4^-, PF_6^-, and ClO_4^-) and the integration of this system into electrooxidative Wacker-type reactions.[9] The advantages of these reactions are (i) high reactivity of the active cationic Pd species generated in situ, and (ii) electrochemical regeneration of the cationic Pd complexes in situ. We extended our interest to the homo-coupling reaction of arylboronic acids catalyzed by the electrogenerated cationic Pd(II) catalysts (EG Pd), which would be different species than peroxo Pd complexes (Scheme 1). We thought that an electrogenerated cationic oxygen-free Pd catalyst would be so electrophilic as to exhibit a similar catalytic activity to that of $(\eta^2\text{-}O_2)PdL_2$. According to this hypothesis, we studied the electrooxidative homo-coupling of arylboronic acids and found that electrochemically generated cationic Pd(II) catalysts are efficient for the homo-coupling of arylboronic acids. We report here, the electrogenerated cationic Pd-catalyzed electrooxidative homo-coupling of arylboronic acids.



Scheme 1. Key catalysts of Pd-catalyzed homo-coupling of arylboronic acids.

First, we chose phenylboronic acid as a representative arylboronic acid, and attempted Pd-catalyzed electrooxidative homo-coupling (Table 1). Electrooxidation was carried out in a divided-type cell under argon. Passage of 3 F/mol of electricity through CH_3CN/H_2O (7/1) solution of phenylboronic acid (0.2 mmol), $Pd(OAc)_2$ (10 mol %), and TEMPO (30 mol %) in the presence of 0.05 M of sodium perchlorate ($NaClO_4$) afforded biphenyl (**2a**) in 65% yield (entry 1). While the reaction proceeded without base, the yield of biphenyl **2a** was unsatisfactory. To improve the reaction efficiency, we next tried the reaction in the presence of bases (entries 2–8). No appreciable change was observed with the addition of Et_3N or Cy_2NMe (entries 2 and 3). Interestingly, the addition of *i*-Pr_2NEt, an electron-donating and sterically hindered base (Hunig's base), enhanced the reaction efficiency, and biphenyl **2a** was obtained in 78% yield (entry 4). In contrast, the addition of *N*-methylpiperidine or *N*-methylmorpholine (NMM) was ineffective for the reaction, and the yield of **2a** was

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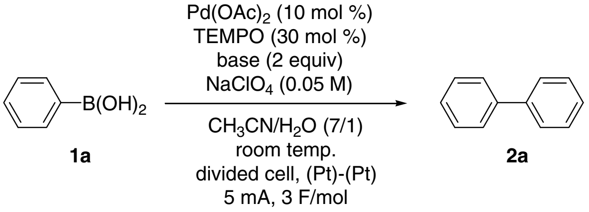
Table 1
Electrogenerated Pd-catalyzed electrooxidative homo-coupling of phenylboronic acid (**1a**) with several bases[a]



1a **2a**

Entry	Base	Yield[b] (%)
1	None	65
2	Et_3N	66
3	Cy_2NMe	66
4	*i*-Pr_2NEt	78
5	*N*-methylpiperidine	14
6	*N*-methylmorpholine	13
7	Na_2CO_3	61
8	K_2CO_3	73

[a] The reactions were performed using **1a** (0.20 mmol), $Pd(OAc)_2$ (10 mol %), TEMPO (30 mol %), base (2 equiv), and $NaClO_4$ (0.05 M) in CH_3CN/H_2O (10 mL, 7/1).
[b] Isolated yield.

dramatically reduced, probably because these amines underwent oxidation faster than TEMPO (entries 5 and 6). Inorganic bases can also be used for the reaction (entries 7 and 8). In particular, with potassium carbonate (K_2CO_3), the yield of **2a** increased to 73% (entry 8).

The addition of TEMPO as a mediator was indispensable for the reaction. The effect of the mediator on the electrooxidative coupling of **1a** is summarized in Table 2. With hydroquinone, a typical mediator, the yield of **2a** decreased to 49% (entry 2). Ph_3N was also ineffective for the reaction (36% yield, entry 3). Without any mediator, the reaction did not proceed, and **2a** could not be detected (entry 4). These results suggest that Pd(0) species generated in situ could not be oxidized to Pd(II) species directly on the anode. A mediator would be oxidized on the anode, and the generated cationic species (*N*-oxoammonium) would oxidize Pd(0) complexes.

We next examined the electrolyte (Table 3).[10] Since the anionic part of the electrolyte would become the counter-anion of EG cationic Pd(II) catalyst, was optimized first (entries 1–3). Using Et_4NBF_4 or Et_4NPF_6, **2a** was obtained in respective yields of 64% and 76% (entries 1 and 2). In contrast, when Et_4NClO_4 was used as an electrolyte, the yield of **2a** increased drastically to 88% (entry 3). Therefore, with the anionic part fixed at ClO_4^-, the effect of the cationic part of the electrolytes was investigated (entries 4–6). With Bu_4NClO_4, the efficiency of the reaction decreased, probably due to the low solubility of the electrolyte in highly polar solvents. $LiClO_4$ was also an efficient electrolyte for the reaction. In the presence of $LiClO_4$, biphenyl **2a** was obtained in 86% yield (entry 5). These results indicated that K_2CO_3 and *i*-Pr_2NEt were suitable bases for the reaction and Et_4NClO_4 and $LiClO_4$ were appropriate electrolytes for electrolysis.

Table 2
Electrooxidative homo-coupling of **1a** using several mediators[a]

Entry	Mediator	Yield[b] (%)
1	TEMPO	73
2	Hydroquinone	49
3	Ph_3N	36
4	None	N.D.

[a] The reactions were performed using **1a** (0.20 mmol), $Pd(OAc)_2$ (10 mol %), mediator (30 mol %), K_2CO_3 (2 equiv), and $NaClO_4$ (0.05 M) in CH_3CN/H_2O (10 mL, 7/1).
[b] Isolated yield.

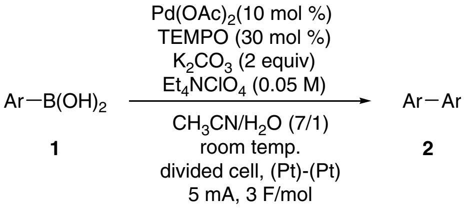
Table 3
Electrooxidative homo-coupling of **1a** in the presence of several electrolytes[a]

Entry	Electrolyte	Yield[b] (%)
1	Et_4NBF_4	64
2	Et_4NPF_6	76
3	Et_4NClO_4	88
4	Bu_4NClO_4	56
5	$LiClO_4$	86
6	$NaClO_4$	73

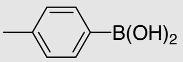
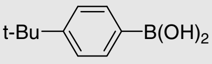
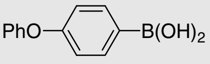
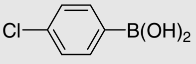
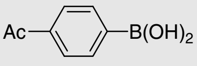
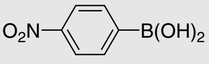
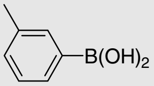
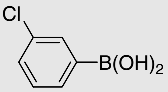
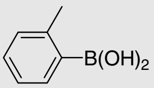
[a] The reactions were performed using **1a** (0.20 mmol), $Pd(OAc)_2$ (10 mol %), TEMPO (30 mol %), K_2CO_3 (2 equiv), and electrolyte (0.05 M) in CH_3CN/H_2O (10 mL, 7/1).
[b] Isolated yield.

To clarify the scope and limitations of the reaction, we performed the electrooxidative homo-coupling of several kinds of arylboronic acids under the optimized conditions (Table 4). First, electron-donating arylboronic acids were examined. A solution of *p*-tolylboronic acid (**1b**), $Pd(OAc)_2$ (10 mol %), TEMPO (30 mol %), and K_2CO_3 (2 equiv) in CH_3CN/H_2O was electrooxidized under a constant current (5 mA, 3 F/mol) in the presence of Et_4NClO_4. The reaction proceeded smoothly to afford bi(*p*-tolyl) (**2b**) in 91% yield (entry 1). The reaction of *p*-*tert*-butylphenylboronic acid (**1c**) and

Table 4
Electrooxidative homo-coupling of several arylboronic acids[a]



1 **2**

Entry	1		Product	Yield[b] (%)
1		**1b**	**2b**	91
2		**1c**	**2c**	89
3		**1d**	**2d**	95
4		**1e**	**2e**	93
5		**1f**	**2f**	95
6		**1g**	**2g**	98
7[c]		**1h**	**2h**	85
8		**1i**	**2i**	87
9		**1j**	**2j**	74

[a] The reactions were performed using **1** (0.20 mmol), $Pd(OAc)_2$ (10 mol %), TEMPO (30 mol %), K_2CO_3 (2 equiv), and Et_4NClO_4 (0.05 M) in CH_3CN/H_2O (10 mL, 7/1).
[b] Isolated yield.
[c] 4 F/mol of electricity was passed.

p-phenoxyphenylboronic acid (**1d**) smoothly afforded **2c** and **2d** in 89% and 95% yields, respectively (entries 2 and 3). We next examined the electrooxidative homo-coupling reaction of several boronic acids bearing electron-withdrawing groups (entries 4–6). The reaction of *p*-chlorophenylboronic acid (**1e**), *p*-acetylphenylboronic acid (**1f**), and *p*-nitrophenylboronic acid (**1g**) proceeded smoothly to give the corresponding biaryls in respective yields of 93%, 95%, and 98%. The results showed that both electron-rich and electron-deficient arylboronic acids could be used for the electrooxidative homo-coupling reaction. *m*-Substituted arylboronic acids could also be applied to the reaction. The reaction of *m*-tolylboronic acid (**1h**) and *m*-chlorophenylboronic acid (**1i**) gave the corresponding biaryls (**2h** and **2i**) in 85% and 87% yields, respectively (entries 7 and 8). Similarly, the homo-coupling of *o*-tolylboronic acid proceeded to afford **2j** in 74% yield (entry 9).

In summary, we have developed an electrooxidative coupling reaction of arylboronic acids catalyzed by cationic Pd(II) catalysts electrogenerated in situ. The scope of the use of EG transition metal catalysts are being investigated further in our laboratory.

Acknowledgments

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10. *Typical procedure for the electrooxidative homo-coupling of boronic acids* (Table 3, entry 3): The electrooxidation was carried out in an H-type divided cell (glass filter) equipped with two platinum electrodes ($1.0 \times 1.5\ \text{cm}^2$). In the anodic chamber was placed a solution of phenylboronic acid (**1a**, 25 mg, 0.21 mmol), $Pd(OAc)_2$ (4.3 mg, 0.02 mmol), TEMPO (9.4 mg, 0.06 mmol), and K_2CO_3 (55 mg, 0.40 mmol) in a 0.05 M Et_4NClO_4 solution of CH_3CN/H_2O (7/1, 5 mL). In the cathodic chamber was placed a 0.05 M Et_4NClO_4 solution of CH_3CN/H_2O (7/1, 5 mL). Under argon, a constant current (5 mA, 3 F/mol) was supplied at room temperature with vigorous stirring. To the resulting mixture was added aq satd NaCl (10 mL) and extracted with Et_2O (3×10 mL). The combined organic extracts were washed with aq satd NaCl (15 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane) to afford biphenyl (**2a**, 14 mg, 88%).