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Base-free oxidative homocoupling of arylboronic esters

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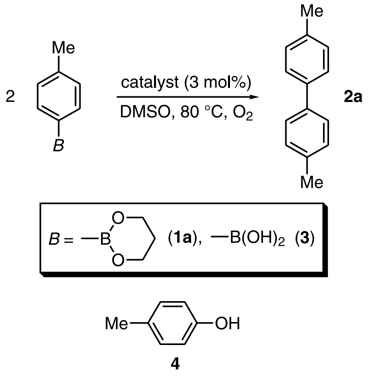
Abstract—Base-free oxidative homocoupling reaction of arylboronic esters has been found to proceed using a catalytic amount of a palladium–1,3-bis(diphenylphosphino)propane (DPPP) complex under an oxygen atmosphere, affording a variety of biaryls in modest to excellent yields. Even arylboronic esters bearing a base-sensitive functional group are applicable to the reaction. © 2003 Elsevier Science Ltd. All rights reserved.

Palladium-catalyzed cross-coupling of organic halides (pseudohalides) with organoboron compounds, i.e. Suzuki–Miyaura coupling, has proven to be one of the most powerful and popular carbon–carbon bond forming reactions, widely used for the synthesis of valuable organic compounds such as pharmaceuticals and functionality materials.[1] Similarly, palladium-catalyzed homocoupling of organoboron compounds, although less familiar, is also a potential method for carbon–carbon bond formation, where symmetrical organic compounds are produced straightforwardly.[2] In these reactions, however, addition of a stoichiometric or excess amount of bases is indispensable for smooth transformation, which precludes the application of base-sensitive compounds to the coupling process, and the production of an equivalent amount of waste salts is unavoidable besides. Consequently, development of palladium-catalyzed coupling reactions of organoboron compounds without added bases has been a challenging and urgent issue.[3,4] We report herein the base-free oxidative homocoupling of arylboronic esters, which is efficiently catalyzed by a palladium–1,3-bis(diphenylphosphino)propane (DPPP) complex under an oxygen atmosphere.[5]

We first carried out the reaction of *p*-tolylboronic acid (**3**) in dimethylsulfoxide (DMSO) at 80°C without any added bases using a palladium–DPPP complex as the catalyst under an oxygen atmosphere and found that the homocoupling product, 4,4′-dimethylbiphenyl (**2a**), was produced in 75% yield along with an 11% yield of *p*-cresol (**4**) (Scheme 1, Entry 1 of Table 1). This side product should result from the oxidation of the C–B bond of **3** with hydrogen peroxide[6] arising from boron peroxide (vide infra) and water, which would be generated in situ from **3** via tri(*p*-tolyl)boroxine production.[7] Therefore, we expected that the employment of an organoboronic ester in lieu of an organoboronic acid would eliminate the in situ-generation of water to lead to the exclusive formation of the desired homocoupling product. Thus, when the cyclic ester of **3**, 2-(*p*-tolyl)-1,3,2-dioxaborinane (**1a**), was treated under the above reaction conditions, **2a** was actually formed in 99% yield (Entry 2). The use of tetrakis(triphenylphosphine)palladium or a ligandless palladium salt was less effective than a palladium–DPPP complex and gave an 81% or 90% yield of **2a**, respectively (Entries 3 and 4). The reaction did not proceed at all under a strictly prepared argon atmosphere, implying that molecular oxygen was indispensable for the homocoupling (Entry 5).



Scheme 1.

Keywords: biaryls; boron; homocoupling; oxygen; palladium.

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Table 1. Palladium-catalyzed homocoupling of *p*-tolylboranes[a]

Entry	*p*-Tolylborane	Catalyst	Time (h)	Yield (%)[b]	Product(s)
1[c]	**3**	DPPP/Pd(OAc)$_2$	15	75(11)[d]	**2a**, **4**
2[c]	**1a**	DPPP/Pd(OAc)$_2$	26	99	**2a**
3	**1a**	Pd(PPh$_3$)$_4$	23	81	**2a**
4	**1a**	Pd(OAc)$_2$	26	90	**2a**
5[c,e]	**1a**	DPPP/Pd(OAc)$_2$	38	<1	**2a**

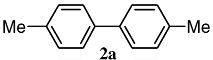
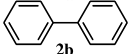
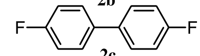
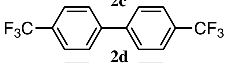
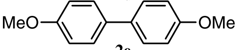
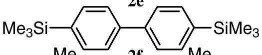
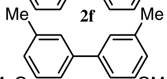
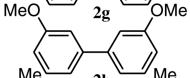
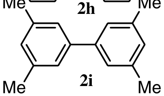
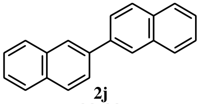
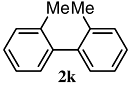
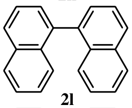
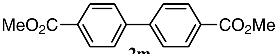
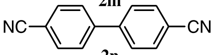
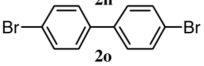
[a] The reaction was carried out in DMSO (1.0 mL) at 80°C using *p*-tolylborane (0.30 mmol) in the presence of a palladium (8.9 μmol) under an oxygen atmosphere.
[b] Isolated yield based on *p*-tolylborane.
[c] DPPP/Pd = 1.5.
[d] GC yield of **4**.
[e] Under an argon atmosphere.

Other results of the base-free oxidative homocoupling of various arylboronic esters **1** are summarized in Table 2. Similarly to the case of **1a**, phenylboronic ester (**1b**) and arylboronic esters bearing an electron-withdrawing group (**1c** and **1d**) or an electron-donating group (**1e** and **1f**) at the *para*-position afforded the corresponding homocoupling products in excellent yields (Scheme 2, Entries 1–6). Furthermore, the reaction of *meta*-substituted arylboronic esters (**1g–i**) took place successfully, providing a 73%, 90% or 86% yield of biaryls (**2g–i**), respectively (Entries 7–9). Naphthylboronic ester **1j** also reacted efficiently to give 2,2′-binaphthyl (**2j**) in 78% yield (Entry 10), whereas the reaction of sterically more congested arylboronic esters **1k** and **1l** resulted in moderate yields (Entries 11 and 12). It should be stressed that the present base-free conditions allow the employment of arylboronic esters with a relatively base-sensitive group (**1m** and **1n**) to the reaction, leading to the formation of the corresponding homocoupling products (**2m** and **2n**) in reasonable yields (Entries 13 and 14). Moreover, the homocoupling was also applicable to a cross-coupling-active substrate, 4-bromophenylboronic ester (**1o**), whose C–Br bond remained intact (Entry 15).

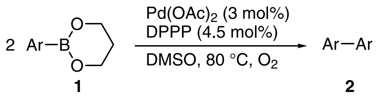
Although details of the reaction pathway remain unclear at present, the fact that oxygen readily reacts with palladium(0) to afford palladium(II) peroxide may enable us to propose the following catalytic cycle (Scheme 3).[8] Initially, three-membered palladium(II) peroxide complex **7** is formed by oxidative cyclization of molecular oxygen with palladium(0) complex **6**. Subsequent double transmetalation of an organic moiety in **1** from boron to palladium(II) would occur without an aid of a base to give diorganopalladium **9** and boron peroxide **10**[9] through intermediary complex **8**, and then reductive elimination of homocoupling product **2** from **9** follows with regeneration of palladium(0)–DPPP complex **6**.[10] Since transmetalation of a neutral organoboron compound with an oxygen-bound palladium(II) complex[11] has been reported to be facile process, this catalytic cycle rationally explains the overall results.[12,13]

In conclusion, we have developed the palladium–DPPP complex-catalyzed base-free oxidative homocoupling reaction of arylboronic esters. In view of the disuse of not only bases but also special oxidants, the present reaction offers a general and environmentally-benign method for the synthesis of diverse biaryls. Further studies on details of the mechanism as well as other

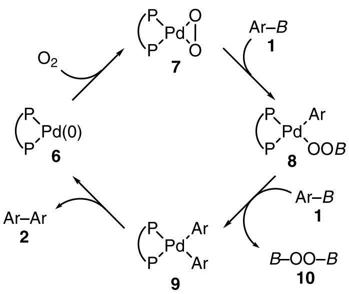
Table 2. Pd–DPPP-catalyzed oxidative homocoupling of arylboronic esters

Entry	R	Time (h)	Yield (%)[a]	Product
1	4-MeC$_6$H$_4$ (**1a**)	26	99	 **2a**
2	Ph (**1b**)	18	91	 **2b**
3	4-FC$_6$H$_4$ (**1c**)	14	93	 **2c**
4	4-CF$_3$C$_6$H$_4$ (**1d**)	24	87	 **2d**
5	4-MeOC$_6$H$_4$ (**1e**)	26	87	 **2e**
6	4-Me$_3$SiC$_6$H$_4$ (**1f**)	48	74	 **2f**
7	3-MeC$_6$H$_4$ (**1g**)	24	73	 **2g**
8	3-MeOC$_6$H$_4$ (**1h**)	36	90	 **2h**
9	3,5-Me$_2$C$_6$H$_3$ (**1i**)	24	86	 **2i**
10	2-Naphthyl (**1j**)	24	78	 **2j**
11	2-MeC$_6$H$_4$ (**1k**)	20	56	 **2k**
12	1-Naphthyl (**1l**)	17	50	 **2l**
13[b]	4-MeO$_2$CC$_6$H$_4$ (**1m**)	72	51	 **2m**
14[b]	4-NCC$_6$H$_4$ (**1n**)	90	64	 **2n**
15[b]	4-BrC$_6$H$_4$ (**1o**)	96	73	 **2o**

[a] Isolated yield based on the organoboronic ester.
[b] 60 °C.



Scheme 2.



Scheme 3.

palladium-catalyzed base-free carbon–carbon bond forming reactions of organoboron compounds are in progress.

General procedure: A DMSO solution (1.0 mL) of 1,3-bis(diphenylphosphino)propane (5.5 mg, 0.013 mmol) and $Pd(OAc)_2$ (2.0 mg, 8.9 μmol) was degassed through two freeze-thaw cycles, and the reaction flask was charged with oxygen. To this solution was added an arylboronic ester (0.30 mmol) and the resulting mixture was stirred at 80°C. After the time specified in Table 2, the mixture was diluted with ether, washed with water and dried over magnesium sulfate. Evaporation of the solvent followed by silica-gel column chromatography (hexane or hexane–ethyl acetate as an eluent) gave the corresponding product.

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12. Since addition of 10 mol% of galvinoxyl (a radical scavenger) to the homocoupling of **1b** did not affect both the reaction rate and the yield of **2b**, we can eliminate the possibility that the present homocoupling proceeds through oxygen-mediated radical pathways. For the radical-chain process observed in the reaction of trialkylboranes with oxygen, see Ref. 6.
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