

## Novel Palladium(0)-Catalyzed Coupling Reaction of Dialkoxyborane with Aryl Halides: Convenient Synthetic Route to Arylboronates

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Received June 2, 1997

Arylboronic acids and their esters are valuable reagents in organic synthesis,<sup>1,2</sup> and much attention has been paid to them in the study of molecular recognition.<sup>3</sup> Arylboron compounds can be prepared by the transmetalation between arylmagnesium or -lithium reagents and boron compounds having good leaving groups, such as halogen and alkoxy groups,<sup>4</sup> and then in a few cases this synthesis has been accomplished using boranes that contain a boron–hydrogen bond.<sup>5</sup>

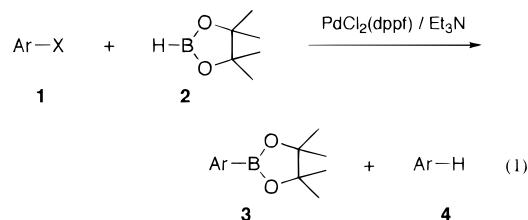
Recently, Miyaura and co-workers reported on a palladium-catalyzed coupling reaction of tetraalkoxydiboron, which provided a one-step procedure for deriving arylboronates from aryl halides.<sup>6</sup> Kunai and his colleague have found that the PdCl<sub>2</sub>-catalyzed reaction of alkyl iodides with Et<sub>2</sub>SiH<sub>2</sub> afforded Et<sub>2</sub>Si–R to some extent,<sup>7</sup> indicating the potential use of metal hydrides as a metalating reagent in the presence of palladium catalyst. To our knowledge, however, there has been no report of a catalytic reaction using hydroboranes as a boron source other than for hydroboration.<sup>8</sup> We here describe a novel palladium-catalyzed coupling reaction of dialkoxyhydroborane **2** with aryl halides **1** in the presence of a base and affording the corresponding arylboronates **3** (eq 1). Since pinacolborane **2** tolerates various functional groups

**Table 1.** Reaction of 1-Iodonaphthalene under Various Conditions<sup>a</sup>

entry	catalyst	base	solvent	yield (%) <sup>b</sup>	
				<b>3</b>	<b>4</b>
1	PdCl <sub>2</sub> (dppf) <sup>c</sup>	none	dioxane	0	3
2	PdCl <sub>2</sub> (dppf)	Et <sub>3</sub> N	dioxane	89	6
3	PdCl <sub>2</sub> (dppf)	<i>i</i> -Pr <sub>2</sub> NEt	dioxane	64	29
4	PdCl <sub>2</sub> (dppf)	pyridine	dioxane	12	47
5	PdCl <sub>2</sub> (dppf)	DBU	dioxane	3	36
6	PdCl <sub>2</sub> (dppf)	KOAc	dioxane	6	82
7	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub>	Et <sub>3</sub> N	dioxane	75	13
8	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> /PPh <sub>3</sub>	Et <sub>3</sub> N	dioxane	0	0
9	Pd(PPh <sub>3</sub> ) <sub>4</sub>	Et <sub>3</sub> N	dioxane	10	1
10	PdCl <sub>2</sub> (dppf)	Et <sub>3</sub> N	toluene	79	7
11	PdCl <sub>2</sub> (dppf)	Et <sub>3</sub> N	CH <sub>2</sub> ClCH <sub>2</sub> Cl	81	7
12	PdCl <sub>2</sub> (dppf)	Et <sub>3</sub> N	CH <sub>3</sub> CN	83	8
13	PdCl <sub>2</sub> (dppf)	Et <sub>3</sub> N	DMF	27	23

<sup>a</sup> Reactions of 1-iodonaphthalene **1** (1.0 mmol) with **2** (1.5 mmol) were carried out at 80 °C for 2 h in 4 mL of solvent by using 3 mol % of catalyst and base (3 mmol). <sup>b</sup> GLC yields are based on **1** used. <sup>c</sup> dppf is 1,1'-bis(diphenylphosphino)ferrocene.

and the expecting pinacolboronates **3** are insensitive to air and moisture,<sup>9</sup> the coupling reaction should allow for a wide range of **3**.



The results of the reaction using 1-iodonaphthalene as **1** with 1.5 equiv of **2** under various conditions are summarized in Table 1. This coupling was achieved with the aid of palladium catalysts and bases in analogy with the Suzuki–Miyaura cross-coupling reaction (entry 1 and 2).<sup>1c</sup> The products were contaminated with naphthalene **4**, the normal cross-coupling product, in each case as a result of the behavior of pinacolborane as a hydride. However, this situation was prevented by the choice of a suitable base. Thus, the tertiary amine, especially Et<sub>3</sub>N, was recognized to be most effective for the selective formation of **3** (entry 2 and 3).<sup>10</sup> In the presence of other weak bases, which were generally known not to contribute to the transmetalation of boron compounds, the formation of undesirable **4** unexpectedly predominated (entries 4–6). The reaction was efficiently catalyzed by the palladium(II) complexes having 2 equiv of phosphine ligands (entry 2 and 7). An additional phosphine ligand tended to retard the reaction (entry 8 and 9). In testing the four solvents, dioxane, toluene, MeCN, and CH<sub>2</sub>ClCH<sub>2</sub>Cl, it was found that these did not play an important role in the present reaction (entries 2 and 10–12). However, the use of polar solvent, DMF, caused low yield and low selectivity due to decomposition of dialkoxyborane to diborane (entry 13).<sup>11</sup>

The results obtained with representative aryl iodides or bromides **1**, giving the corresponding products **3** similarly as above, are listed in Table 2.<sup>12</sup> The differences in the yields and the selectivity among aryl iodides having electron-donating or -withdrawing groups were not particularly large (entries 1–9). Above all, the presence of functional groups, such as CO<sub>2</sub>Et (entry 6), COMe (entry 7), and CN (entry 8), in the starting **1** did not interfere with the outcome of the present reaction at

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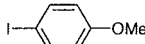
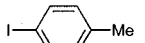
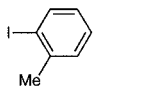
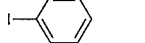
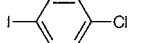
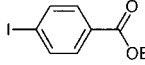
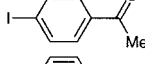
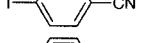
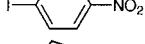
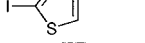
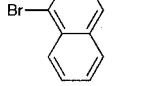


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(12) A representative procedure is as follows. A flask was charged with PdCl<sub>2</sub>(dppf) (0.03 mmol), dioxane (4 mL), aryl iodide **1** (1.0 mmol), Et<sub>3</sub>N (3.0 mmol), and pinacolborane **2** (1.5 mmol) under an argon flow, and the mixture was stirred at 80 °C. GLC analysis showed the completion of the reaction. The reaction mixture was diluted with benzene, washed with water, and dried over MgSO<sub>4</sub>. The solvent was evaporated, and product **3** was isolated by Kugelrohr distillation.

**Table 2. Reaction of Representative 1 with 2<sup>a</sup>**

entry	aryl halide <sup>1</sup>	time (h)	yield (%) <sup>b</sup>
1		1	77
2		1	(79)
3		5	(78)
4		2	84
5		3	(83)
6		2	79
7		4	(74)
8		4	(73)
9		5	(84)
10		3	(80)
11		6	75 <sup>c</sup>
12		2	(79) <sup>c, d</sup>
13		4	(49) <sup>c, d</sup>

<sup>a</sup> Reactions of **1** (1.0 mmol) with **2** (1.5 mmol) were carried out at 80 °C by using PdCl<sub>2</sub>(dppf) (3 mol %), Et<sub>3</sub>N (3 mmol), and dioxane (4 mL). <sup>b</sup> GLC yields of **3** are based on **1**. Yields in parentheses are isolated yields. <sup>c</sup> Reactions were carried out at 100 °C. <sup>d</sup> PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> was used as catalyst.

80 °C because **2** is unusually inert to many functional groups.<sup>9</sup> This procedure appears to better tolerate various functional groups than the previous methods using magnesium or lithium reagents. Also, the yield and selectivity are not as likely to depend on the steric requirement (entry 3). A heteroaromatic iodide was also coupled with **2** without any difficulty (entry 10). On the one hand, the reaction of 1-bromonaphthalene was sluggish at 80 °C (33%, 18 h), requiring 6 h at 100 °C to give a 75 % yield of the corresponding **3** together with an 18% yield of **4** (entry 11). On the other hand, when the aryl bromide having an electron-donating group such as NMe<sub>2</sub> was used, the reaction proceeded smoothly at 100 °C (entry 12), although the presence of electron-withdrawing substituents remarkably decreased the yield of **3** due to the reductive dehalogenation of **1** (entry 13).

The above results differ widely from those of the well-known palladium-catalyzed coupling reaction between

organometallic reagents and halides. Generally, in the presence of palladium catalyst, such metal hydrides as Bu<sub>3</sub>SnH,<sup>13</sup> Et<sub>3</sub>SiH,<sup>14</sup> and NaBH<sub>4</sub><sup>15</sup> greatly facilitate the hydrogenolysis of organic electrophiles. It is recognized that this common process involves sequential oxidative addition of the electrophiles giving an R–Pd<sup>II</sup>–X species, transmetalation with the hydride forming an R–Pd<sup>II</sup>–H, and reductive elimination of the R–H. It now can be seen that, under the present conditions, the slow transmetalation with **2** due to the low nucleophilicity of the hydride suppresses the hydrogenolysis.

Bearing in mind the previously described result,<sup>16</sup> a hydroborane as well as an aryl halide can add oxidatively to palladium(0) complexes. However, the treatment of the authentically isolated Ar–Pd<sup>II</sup>–X with **2** in the presence of Et<sub>3</sub>N gave almost no **4** or corresponding arylboronate **3**.<sup>17</sup> Accordingly, the mechanism involving the oxidative addition of **1** can be ruled out. On the other hand, Kunai and Ishikawa proposed a mechanism of the PdCl<sub>2</sub>-catalyzed silylation of alkyl iodides, in which the hydrosilane first added oxidatively to Pd catalyst, followed by  $\sigma$ -bond metathesis between an Si–Pd bond and a C–I bond.<sup>7</sup> In analogy with this mechanism, the oxidative addition of dialkoxyborane **2** to palladium(0) complexes may be a key step in the present reaction, although our evidence for the reaction mechanism is still inconclusive.

In conclusion, we found that dialkoxyhydroborane **2** acted as a boron source for the coupling with **1** in the presence of the palladium catalyst and the tertiary amine. The present coupling reaction provides a new and available synthetic route to a wide range of **3**. Investigations for the mechanistic studies and the coupling with other halides are currently underway.

**Acknowledgment.** We are grateful to Dr. Tatsuo Ishiyama and Professor Norio Miyaura of Hokkaido University for their useful discussions and suggestions.

**Supporting Information Available:** Experimental details and <sup>1</sup>H- and <sup>13</sup>C-NMR, IR, HRMS spectral data for the products (3 pages).

JO970963P

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