

Silver(I) Oxide-promoted Chemoselective Cross-coupling Reaction of (Diborylmethyl)trimethylsilane

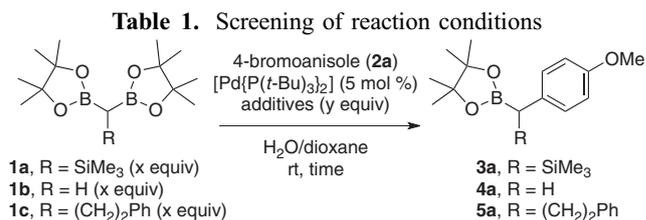
Kohei Endo,^{*1,2} Fumiya Kurosawa,¹ and Yutaka Ukaji¹¹Division of Material Sciences, Graduate School of Natural Science and Technology, Kanazawa University, Kakuma, Kanazawa 920-1192²PRESTO, Japan Science and Technology Agency (JST), 4-1-8 Honcho, Kawaguchi, Saitama 332-0012

(Received July 10, 2013; CL-130643; E-mail: kendo@se.kanazawa-u.ac.jp)

The present paper describes a synergistic effect in the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction. The chemoselective cross-coupling reaction of (diborylmethyl)trimethylsilane and aryl halides proceeded at room temperature when a silver salt and KOH were added. The reaction gave benzylboronate derivatives bearing a trimethylsilyl group at the benzylic position.

The Suzuki–Miyaura cross-coupling reaction achieves reliable C–C bond formation in organic chemistry.¹ The use of alkylboron compounds requires further manipulations, since the low reactivities of alkylboron compounds and the isomerization of Pd intermediates often give low chemo- and regioselectivity.² During our studies of the Suzuki–Miyaura cross-coupling reaction of diborylmethane derivatives,³ we found that (diborylmethyl)trimethylsilane required Ag₂O to give the desired product. We tentatively examined the coupling reaction of (diborylmethyl)trimethylsilane **1a** and 4-bromoanisole (**2a**) under the optimum reaction conditions, using [Pd{P(*t*-Bu)₃}₂] as a catalyst for the reaction of diborylmethane **1b** (Table 1, Entries 1 and 2). However, the reaction did not give any of the cross-coupling product **3a**.⁴ The neighboring bulky SiMe₃ group seems to prevent the coupling reaction at the α-carbon atom. When the reaction using **1a** or **1b** was carried out in the presence of Ag₂O as a base, the desired product **3a** or **4a**, respectively, was obtained in low yield (Entries 3 and 4). The Suzuki–Miyaura cross-coupling reaction took place chemoselectively to give benzylboronate derivatives exclusively. The present results encouraged us to examine the effect of additives. The use of KOH and Ag₂O significantly promoted the coupling reaction of **1a** to give the desired product **3a** (Entries 5–7). The reaction in the presence of a catalytic amount of Ag₂O or the absence of [Pd{P(*t*-Bu)₃}₂] did not give the product **3a** (Entries 8 and 9).⁵ Acidic workup seems to be detrimental to the yield of product **3a**; simple extraction of the reaction mixture using ether improved the yield of product **3a** (Entries 10 and 11). Although we confirmed that Ag₂O affected the coupling reaction of diborylmethane **1b** in Entry 4, the reaction rate was similar to that in the absence of Ag₂O (Entries 2 and 12). The coupling reaction of diborylalkane **1c** and **2a** gave a similar reaction rate, regardless of the presence or absence of Ag₂O (Entries 13 and 14). An unexpected cooperative effect of Si and Ag might play an important role in the present Pd-catalyzed cross-coupling reaction. Other silver salts or bases hardly promoted the reaction (Entries 15–22). This is a rare example of the synthesis of *gem*-borylsilyltoluene derivatives under ambient conditions.^{6–8}

The scope of aryl bromides is shown in Table 2. The use of 4-substituted aryl bromides **2a–2f** gave the products **3a–3f** in

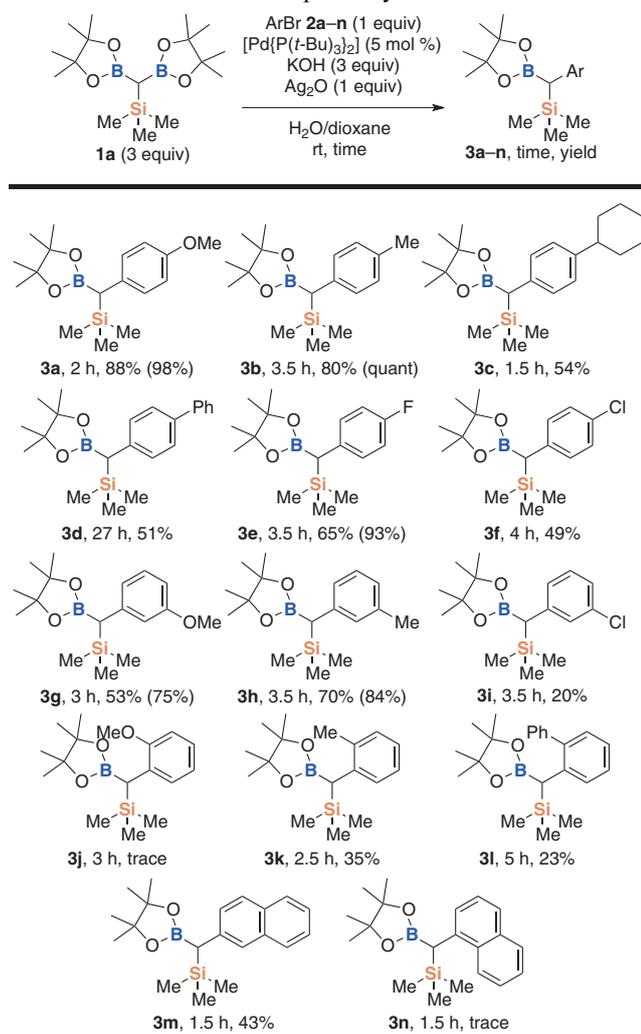


Entry ^a	Substrate (x)	Additives (y)	Time/h	Yield/% ^b
1	1a (2)	KOH (2)	24	not obtained
2	1b (2)	KOH (2)	1.5	4a , >98
3	1a (2)	Ag ₂ O (2)	24	3a , 7
4	1b (1.5)	Ag ₂ O (1.5)	24	4a , 16
5	1a (2)	KOH (2), Ag₂O (2)	3	3a , 53
6	1a (3)	KOH (3), Ag ₂ O (3)	3	3a , 78
7	1a (3)	KOH (3), Ag ₂ O (1)	3	3a , 79
8	1a (3)	KOH (3), Ag ₂ O (0.1)	2	not detected
9 ^c	1a (3)	KOH (3), Ag ₂ O (1)	24	not obtained
10	1a (3)	KOH (3), Ag ₂ O (1)	2	3a , 49
11	1a (3)	KOH (3), Ag₂O (1)	2	3a , 98
12	1b (3)	KOH (3), Ag ₂ O (1)	2	4a , 94
13	1c (3)	KOH (3), Ag ₂ O (1)	4.5	5a , 31
14	1c (3)	KOH (3)	4.5	5a , 57
15	1a (3)	KOH (3), Ag ₂ CO ₃ (1)	2	not obtained
16	1a (3)	KOH (3), AgOAc (1)	2.5	3a , 16
17	1a (3)	KOH (3), AgNO ₃ (1)	2.5	not obtained
18	1a (3)	KOH (3), AgOTf (1)	2.5	not obtained
19	1a (3)	NaOH (3), Ag ₂ O (1)	2.5	3a , 12
20	1a (3)	K ₂ CO ₃ (3), Ag ₂ O (1)	2.5	not obtained
21	1a (3)	KOAc (3), Ag ₂ O (1)	2.5	not obtained
22	1a (3)	CsF (3), Ag ₂ O (1)	2.5	not obtained

^aThe reaction was stopped with silica gel (Entries 1–9). The reaction was stopped with 6M HCl aq. (Entry 10). The reaction was stopped with H₂O (Entries 11–22). ^bNMR yields.

^cThe reaction was carried out in the absence of [Pd{P(*t*-Bu)₃}₂].

moderate to high yields. However, strong electron-withdrawing groups such as NO₂, CN, and acetyl groups gave unidentified products. The use of 3-substituted aryl bromides **2g–2i** gave the products **3g–3i** in moderate yields, but electron-withdrawing groups diminished the product yield. Relatively bulky aryl bromides **2j–2n** gave the products **3j–3n** in low to moderate yields. The use of heteroaromatic bromides gave unidentified products. The subsequent coupling reaction to give diaryl-methane derivatives was not observed at all.^{3d} In every case,

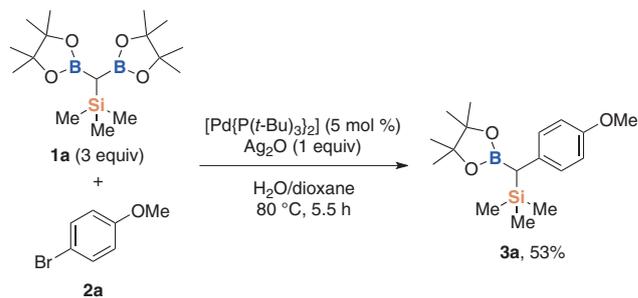
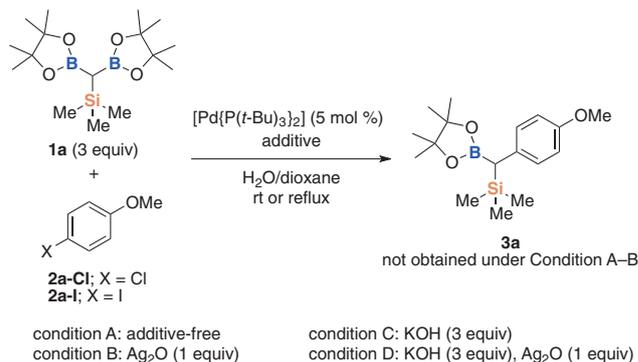
Table 2. Scope of arylhalides^{a,b}

^aIsolated yields. NMR yields were described in parentheses.

^bThe unidentified by-products generated in all cases. The careful purification by silica gel column decreased the product yields.⁹

careful purification to remove unidentified by-products and/or decomposition of the desired products by silica gel column chromatography decreased the product yield.^{9,10}

To clarify the effects of Si and Ag, ¹¹B NMR spectroscopic analyses of the borate intermediates derived from (diborylmethyl)trimethylsilane **1a** were performed.¹¹ A solution of **1a** in dioxane-*d*₈ was treated with 8 M KOH (aq) (1 or 3 equiv); the NMR spectrum revealed only a trace amount, if any, of borate intermediate. Our previous studies using diborylmethane or diboryllalkanes showed that we could obtain borate intermediates using KOH at room temperature.^{3a,3b} Furthermore, the addition of Ag₂O to the mixture of **1a** and KOH in dioxane-*d*₈ did not change the chemical shift. These results clearly indicated that Ag₂O did not affect the generation of borate intermediates derived from **1a**. The present reaction using **1a** should, therefore, proceed via a different pathway from the reaction pathways of **1b** and **1c**, which easily generated borate intermediates at room

**Scheme 1.** KOH-free coupling under thermal conditions.**Scheme 2.** Use of ArCl or ArI with or without KOH and/or Ag₂O.

temperature. DFT calculations (B3LYP/6-31G^{*}) provided LUMO maps of (diborylmethyl)trimethylsilane **1a** and diborylmethane **1b**.¹¹ The LUMO was observed around the B–C–B moieties in **1a** and **1b**, which seem to have similar distributions, although the boronate moieties B–C–B in **1a** are distorted.

Previous reports have indicated that Ag₂O activates ArPdX after oxidative addition of Pd(0) to ArX. The reaction of ArPdX in the presence or absence of Ag₂O could generate ArPd(OH) with a base or H₂O.¹² Accordingly, the generation of ArPd(OH) would promote the transmetalation step without any base such as KOH.^{13,14} We confirmed that the present reaction of **1a** and **2a** proceeded to give the product **3a** in 53% yield and unidentified by-products in the absence of KOH at 80 °C after 5.5 h; the generation of ArPd(OH) might be possible at high reaction temperatures (Scheme 1). The present results indicated that KOH accelerated the reaction at room temperature. However, reports in the literature showed that the conversion of ArPdBr to ArPd(OH) hardly proceeded without any base; the use of additional base could promote the reaction. In contrast, the conversion of ArPdI to ArPd(OH) typically proceeded in the presence of a trace amount of H₂O without any base.^{2a,2c,2f,2g} We, therefore, examined the reaction using 4-iodoanisole or 4-chloroanisole under the same reaction conditions without KOH; unexpectedly, the reaction did not proceed at all (Scheme 2). Moreover, the addition of Ag₂O and/or KOH to promote the reaction did not give any of the desired product. Reflux conditions gave a small amount of unidentified by-products. We previously reported that the reaction of simple diborylmethane **1b** or diboryllalkanes and iodoarene occurred.^{3a,3b} The previous results suggested that there is a mecha-

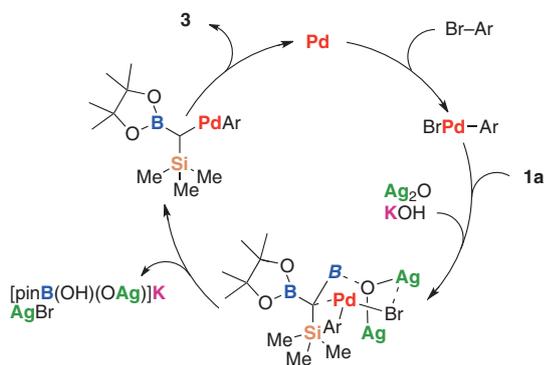


Figure 1. Proposed mechanism.

nistic change when **1a** is used. The generation of ArPd(OH) does not seem to be necessary in the present reaction, since ArPdI, which was more reactive for the generation of ArPd(OH), did not give any of the desired product.^{2c,15} A different active intermediate may be generated via ArPdBr.

In the Hiyama coupling reaction using organosilanes as a coupling partner, it has been reported that Ag₂O promotes the transmetalation step, with activation of the ArPd–X bond.¹⁶ Such activation of ArPdX and organoboron compounds using Ag₂O has also been deduced and reported in the Suzuki–Miyaura cross-coupling reaction, although the exact role is unclear.^{2a,2c,2f,2g} We assumed that similar activation would be possible in the transmetalation step. The Ag₂O-assisted transmetalation step with a silyl group in the diborylmethane derivative **1a** seems to be reasonable, since acceleration of the reaction was not observed using **1b** or **1c** and Ag₂O. The use of iodoarene, which did not give any of the desired product, would generate ArPd(OH) in the presence of Ag₂O; thus, the generation of ArPd(OH) might not be preferable in the present reaction using (diborylmethyl)trimethylsilane.¹³ It is unclear how KOH participates in the transmetalation step, although the use of KOH and Ag₂O promoted the present reaction at room temperature.

The proposed mechanism according to the literature is shown in Figure 1. The oxidative addition of a Pd(0) intermediate to an aryl halide proceeds to give an ArPd(II) intermediate. Transmetalation between an ArPd(II) intermediate and (diborylmethyl)trimethylsilane **1a** proceeds in the presence of a silver salt. Finally, reductive elimination gives the desired coupling product and regenerates the Pd(0) intermediate. The cooperative activation of the boronate moiety with Ag₂O and/or KOH could not be confirmed at present. The detailed behavior of a silver salt and Si group was unclear; further studies are therefore required to elucidate the mechanism.

In conclusion, we found that Ag₂O significantly affected the chemoselective cross-coupling reaction of (diborylmethyl)trimethylsilane at room temperature. The results of a ¹¹B NMR spectroscopic experiment showed that there are apparently no borate intermediates derived from KOH and/or Ag₂O. The reaction in the absence of silver oxide did not proceed. We, therefore deduced that silver oxide promotes the transmetalation step between (diborylmethyl)trimethylsilane and an arylpalladium intermediate. The present cooperative effect may contribute to the discovery of reaction conditions for various types of metal-catalyzed reactions.

This work was supported by JST PRESTO program, Grants-in-Aid for Young Scientists (B) (Nos. 21750108 and 23750049) from the Japan Society for the Promotion of Science.

This paper is dedicated to Professor Teruaki Mukaiyama in celebration of the 40th anniversary of the Mukaiyama aldol reaction.

References and Notes

- For reviews of the Suzuki–Miyaura cross-coupling reaction, see: a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457. b) S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angew. Chem., Int. Ed.* **2001**, *40*, 4544. c) A. Suzuki, H. C. Brown, *Organic Syntheses Via Boranes*, Aldrich Chemical Co., Inc., Milwaukee, WI, **2002**, Vol. 3. d) S. Kotha, K. Lahiri, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633. e) F. Bellina, A. Carpita, R. Rossi, *Synthesis* **2004**, 2419.
- a) H. Chen, M.-Z. Deng, *J. Org. Chem.* **2000**, *65*, 4444. b) A. F. Litke, C. Dai, G. C. Fu, *J. Am. Chem. Soc.* **2000**, *122*, 4020. c) T. Korenaga, T. Kosaki, R. Fukumura, T. Ema, T. Sakai, *Org. Lett.* **2005**, *7*, 4915. d) S. D. Dreher, P. G. Dormer, D. L. Sandrock, G. A. Molander, *J. Am. Chem. Soc.* **2008**, *130*, 9257. e) T. Ohmura, T. Awano, M. Sugimoto, *Chem. Lett.* **2009**, *38*, 664. f) D. Imao, B. W. Glasspoole, V. S. Laberge, C. M. Crudden, *J. Am. Chem. Soc.* **2009**, *131*, 5024. g) E. M. Woerly, A. H. Cherney, E. K. Davis, M. D. Burke, *J. Am. Chem. Soc.* **2010**, *132*, 6941. h) T. Ohmura, T. Awano, M. Sugimoto, *J. Am. Chem. Soc.* **2010**, *132*, 13191. i) D. L. Sandrock, L. Jean-Gérard, C.-y. Chen, S. D. Dreher, G. A. Molander, *J. Am. Chem. Soc.* **2010**, *132*, 17108. j) T. Awano, T. Ohmura, M. Sugimoto, *J. Am. Chem. Soc.* **2011**, *133*, 20738. k) G. A. Molander, S. R. Wisniewski, *J. Am. Chem. Soc.* **2012**, *134*, 16856.
- a) K. Endo, T. Ohkubo, M. Hirokami, T. Shibata, *J. Am. Chem. Soc.* **2010**, *132*, 11033. b) K. Endo, T. Ohkubo, T. Shibata, *Org. Lett.* **2011**, *13*, 3368. c) K. Endo, T. Ohkubo, T. Ishioka, T. Shibata, *J. Org. Chem.* **2012**, *77*, 4826. d) K. Endo, T. Ishioka, T. Ohkubo, T. Shibata, *J. Org. Chem.* **2012**, *77*, 7223.
- The Suzuki–Miyaura cross-coupling reaction of (borylmethyl)trimethylsilane was reported: a) J. A. Soderquist, B. Santiago, I. Rivera, *Tetrahedron Lett.* **1990**, *31*, 4981. b) G. A. Molander, C.-S. Yun, M. Ribagorda, B. Biolatto, *J. Org. Chem.* **2003**, *68*, 5534. c) S. D. Dreher, S.-E. Lim, D. L. Sandrock, G. A. Molander, *J. Org. Chem.* **2009**, *74*, 3626.
- Silver-catalyzed Suzuki–Miyaura cross-coupling reaction: R. Das, D. Chakraborty, *Tetrahedron Lett.* **2012**, *53*, 7023.
- Other silyl groups, such as dimethylphenylsilyl, *tert*-butyldimethylsilyl, drastically decreased the yield of products.
- Other ligand, such as PCy₃, dppf, and NHC, gave the desired product in low yield.
- J. Kondo, H. Shinokubo, K. Oshima, *Org. Lett.* **2006**, *8*, 1185.
- S. Hitosugi, D. Tanimoto, W. Nakanishi, H. Isobe, *Chem. Lett.* **2012**, *41*, 972.
- The reaction of **1a** and cinnamyl bromide and benzyl bromide did not proceed; the further examination should be required.
- Supporting Information is available electronically on the CSJ-Journal Web site, <http://www.csj.jp/journals/chem-lett/index.html>.
- CsOH-promoted generation of ArPdOH: a) Y. Hayashi, S. Wada, M. Yamashita, K. Nozaki, *Organometallics* **2012**, *31*, 1073. KOH-promoted generation of ArPdOH: b) V. V. Grushin, H. Alper, *Organometallics* **1993**, *12*, 1890.
- Since we could not find the procedure for the preparation of ArPd(OH) bearing P(*t*-Bu)₃ as a ligand in literatures, the exact activity of ArPd(OH) bearing P(*t*-Bu)₃ could not be confirmed. Literature-known [(PPh₃)₂PhPd(OH)] and **1a** was tentatively used, but the product was not obtained at all (ref 12).
- C. Adamo, C. Amatore, I. Ciofini, A. Jutand, H. Lakmini, *J. Am. Chem. Soc.* **2006**, *128*, 6829.
- J. P. Flemming, M. C. Pilon, O. Y. Borbulevitch, M. Y. Antipin, V. V. Grushin, *Inorg. Chim. Acta* **1998**, *280*, 87.
- a) K. Hirabayashi, J. Kawashima, Y. Nishihara, A. Mori, T. Hiyama, *Org. Lett.* **1999**, *1*, 299. b) H. Zhou, C. Moberg, *J. Am. Chem. Soc.* **2012**, *134*, 15992.