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Tris(trimethylsilyl)silylboronate Esters: Novel Bulky, Air- and Moisture-Stable Silylboronate Ester Reagents for Boryl Substitution and Silaboration Reactions

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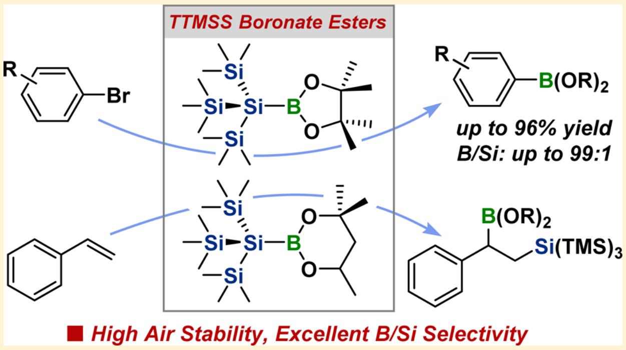
Supporting Information

ABSTRACT: New, bulky tris(trimethylsilyl)silylboronate pinacol and hexylene glycol esters ((TMS)$_3$Si−B(pin) and (TMS)$_3$Si−B(hg)) were prepared in 46 and 61% yields, respectively, by the reaction of tris(trimethylsilyl)silylpotassium with the corresponding boron electrophiles. Notably, these silylboronate esters exhibited high stability to air and silica gel and were applied to the transition-metal-free boryl substitution of aryl halides, providing the desired borylated products in high yields with excellent B:Si ratios (up to 96% yield, B/Si = 99/1). These new silylboronate esters were also applied to a sequential borylation/cross-coupling process with various aryl halides, as well as the base-mediated silaboration of styrene.



Silylboronate esters such as PhMe$_2$Si−B(pin) (**1a**) have been widely used as versatile reagents for preparing organoboron and -silicon compounds,[1] both of which are important building blocks in organic chemistry, because the C−B or C−Si bonds can be transformed to various functional groups.[2,3] We have reported the transition-metal-free boryl substitution of aryl halides with silylboronate ester **1a** and alkoxy base (Base-mediated Borylation with Silylboronate esters, denoted as BBS, Figure 1a).[4,5] This reaction provides facile access to various aryl-, heteroaryl-, and alkenylboronate esters because it can be operated under mild conditions with high reactivity in the absence of a transition-metal catalyst. This BBS strategy can also be used to directly prepare triarylborons, which have numerous potential applications in materials science, from various organic halides.[4d] However, the application of this strategy has been limited by an unwanted silylation reaction (typical borylation/silylation ratio (90/10)−(96/4)). Furthermore, the silylboronate ester reagents typically used in this strategy (e.g., PhMe$_2$Si−B(pin)) are unstable to air and moisture. Although there exist several reactions using the silylboronate ester reagent in the presence of air or water, significant decomposition of silylboronate esters after storage of the reagents in air is usually observed.[6]

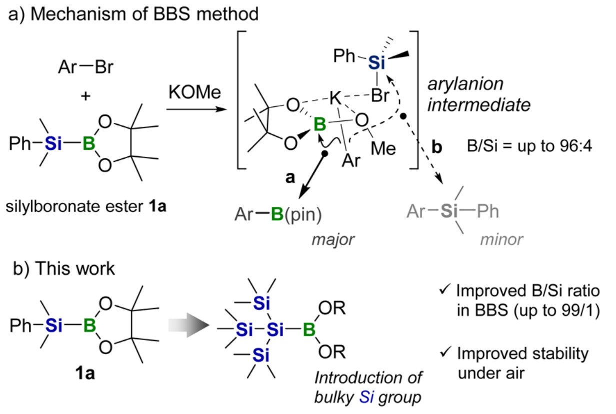


Figure 1. (a) Base-mediated borylation with silylboronate ester. (b) Concept of this work.

Mechanistic studies have suggested that this reaction proceeds via the halogenophilic attack of a silicon nucleophile on the halogen atom of an aryl halide, forming the corresponding aryl anion intermediate. The subsequent nucleophilic attack of the aryl anion determines the borylation/silylation (B/Si) ratio of the products (Figure 1a, path a or b). On the basis of this mechanism, we envisioned that the use of silylboronate esters bearing a bulky silyl group would improve the B/Si selectivity of the BBS by suppressing the undesired pathway (path b). As for the usability issue of silylboronate ester compounds, PhMe$_2$Si−B(pin) (**1a**) is sensitive to air and moisture. Although several analogous silylboronate esters[1,7,8] have been reported, very little is known about the stability of these compounds. Hartwig and co-workers reported the Ir-catalyzed borylation of hydrosilanes and synthesized several trialkylsilylboronate esters, including Et$_3$Si−B(pin) (**1b**), which they purified by column chromatography over silica gel.[8] These compounds are fairly stable, but

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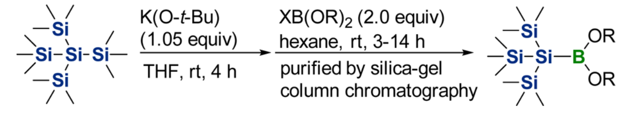
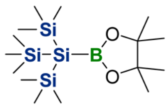
their reactivity in base-catalyzed reactions was not studied. It is necessary to develop a new silylboronate ester reagent that shows good bench stability as well as excellent reactivity and selectivity in reactions with alkoxy bases. We envision that silylboronate esters bearing considerable steric bulk would be sufficiently stabilized kinetically to tolerate air and moisture (Figure 1b). With this in mind, we focused on the use of a tris(trimethylsilyl)silyl ((TMS)$_3$Si) group,[9,10] which is comparable in size to a *tert*-butyl group.[9b]

Herein, we report the first synthesis of silylboronate esters ((TMS)$_3$Si−B(OR)$_2$) bearing a tris(trimethylsilyl)silyl ((TMS)$_3$Si) group,[9,10] which show high selectivity in the BBS and silaboration reactions with excellent air/moisture stability. Notably, these silyl boronates were readily purified by column chromatography over silica gel, highlighting their stability. Furthermore, these silylboronate ester reagents were successfully applied to transition-metal-free boryl substitution of aryl halides,[4] affording the corresponding arylboronates in high yields with high B/Si ratios (up to 99/1). We also conducted the KOMe-mediated silaboration of styrene[11,12] using silylboronate esters.

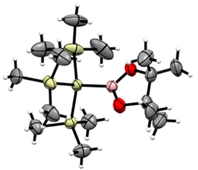
We initially explored the synthesis of tris(trimethylsilyl)silylboronate esters which have different alkoxy substituents on their boron atom (Table 1). Tris(trimethylsilyl)silylpinacolborane ((TMS)$_3$Si−B(pin) (**2a**)) was obtained in 46% yield as a colorless solid using in situ generated tris(trimethylsilyl)silylpotassium and *i*-PrOB(pin). This compound was successfully purified by column chromatography over silica gel. Tris(trimethylsilyl)silylboronic acid hexylene glycol ester ((TMS)$_3$Si−B(hg), (**2b**)) was also synthesized in the same manner (**2b**, 61% yield, colorless solid). Disappointingly, however, tris(trimethylsilyl)silylboronate esters bearing a diisopropoxy (**2c**), catecholato (**2d**), or neopentylglycolato (**2e**) moiety decomposed during column chromatography over silica gel, although the corresponding silylboronate esters seemed to be formed in the reaction mixtures on the basis of the GC analyses.

Table 1. Synthesis of (TMS)$_3$Si−B(OR)$_2$[a]

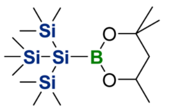




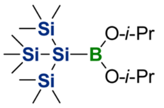
2a, 46% yield
(X = O-*i*-Pr)



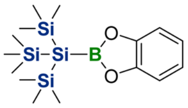
X-ray structure of **2a**



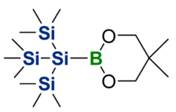
2b, 61% yield
(X =OEt)



2c, decomposed
(X = O-*i*-Pr)



2d, decomposed
(X = Cl)



2e, decomposed
(X = O-*i*-Pr)

[a]Reaction conditions: a mixture of (TMS)$_4$Si (1.0 equiv) and K(O-*t*-Bu) (1.05 equiv) in THF (0.50 M to (TMS)$_4$Si) was stirred for 4 h at room temperature. The reaction mixture was concentrated in vacuo, diluted with hexane (0.50 M to (TMS)$_4$Si), and treated with X−B(OR)$_2$ (2.0 equiv), before being stirred for 3−14 h. Compounds **2c**−**e** decomposed during column chromatography over silica gel.

The molecular structure of **2a** was confirmed by single-crystal X-ray analysis (Supporting Information). The Si−B bond length of **2a** (2.015(5) Å) was found to be shorter than that of a *B*-silylborazine bearing a (TMS)$_3$Si group ((TMS)$_3$Si-(Me)$_2$B$_3$N$_3$(Me); B−Si length, 2.097(5) Å)[10a] and even shorter than the sum of the covalent radii of B and Si (2.05 Å). Although (TMS)$_3$Si is well-known as a bulky group, these comparisons suggest that steric congestion around the Si−B bond is not significant because the substituents around B and Si atoms ((TMS)$_3$Si and pinacol) are far from each other.

Encouraged by the successful preparation of the (TMS)$_3$Si boronate esters, we proceeded to evaluate their stability to air (Figure 2). Pleasingly, (TMS)$_3$Si−B(pin) (**2a**) remained unchanged after 48 h at room temperature in toluene under air. In contrast, only less than 20% of PhMe$_2$Si−B(pin) (**1a**) was left after 5 h under the same conditions. (TMS)$_3$Si−B(hg) (**2b**) also showed greater stability to air than PhMe$_2$Si−B(pin) (**1a**), although the recovery of **2b** was 83% under the same conditions after 48 h. The stability of Et$_3$Si−B(pin) (**1b**) was similar to that of **2a**. The stability of silylboronate esters **1a** and **2a,b** to silica gel was also investigated on the basis of their recovery from silica gel swelled with hexane at room temperature under air for 1 h. The results revealed that the stabilities were in the order **2a** > **2b** > **1a** (recovery yields 95%, 85%, and 64%, respectively; for details, see the Supporting Information), which was in good agreement with the stability of these compounds to air.

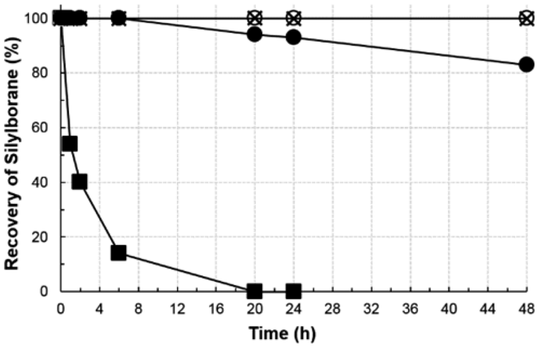
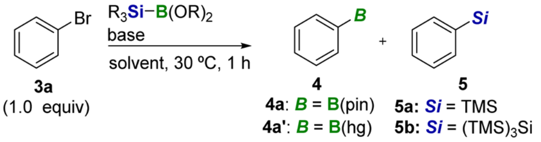


Figure 2. Stability of silylboronate esters under air: (■) PhMe$_2$Si−B(pin) (**1a**); (×) Et$_3$Si−B(pin) (**1b**); (○) (TMS)$_3$Si−B(pin) (**2a**); (●) (TMS)$_3$Si−B(hg) (**2b**). Conditions: a solution of silylboronate ester **1a**, **1b**, **2a**, or **2b** (0.2 mmol) in toluene (1.0 mL) was stirred at room temperature. After a set time, the recovery of the silylboronate ester was determined by GC.

To investigate the applicability of these silylboronate ester reagents to organic synthesis, we investigated the boryl substitution of phenyl bromide with (TMS)$_3$Si−B(pin) (**2a**) and (TMS)$_3$Si−B(hg) (**2b**) (Table 2).[4] We initially examined the reaction of **2a** with **3a** in the presence of KOMe using DME as a solvent, which afforded the desired product in 63% yield with a B/Si ratio (**4a**:(**5a** + **5b**)) of 89/11 (Table 2, entry 1). The use of silylboronate ester **2b** instead of **2a** led to an improvement in the yield and B/Si ratio (80%, B/Si = 93/7; Table 2, entry 2); thus, all of the subsequent optimization reactions were conducted using **2b**. The use of NaOMe provided results similar to those obtained with KOMe, whereas LiOMe failed to afford the desired products (Table 2, entries 3 and 4). The best results were obtained using the bulky base

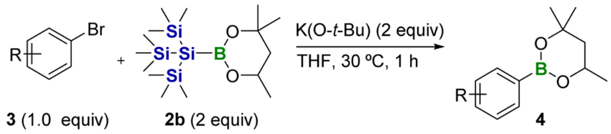
Table 2. Optimization of the Reaction Conditions for the Borylation of 3a with $(TMS)_3Si{-}B(OR)_2$/Alkoxy Base[a]

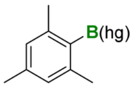


entry	Si−B	base (equiv)	solvent	yield (%)[b]	4/(5a + 5b)[c]
1[d]	**2a**	KOMe (2.0)	DME	63	89/11
2	**2b**	KOMe (2.0)	DME	80	93/7
3	**2b**	NaOMe (2.0)	DME	80	90/10
4	**2b**	LiOMe (2.0)	DME	0	
5	**2b**	K(O-*t*-Bu) (2.0)	DME	94	98/2
6	**2b**	Na(O-*t*-Bu) (2.0)	DME	91	96/4
7	**2b**	Li(O-*t*-Bu) (2.0)	DME	75	94/6
8	**2b**	K(O-*t*-Bu) (2.0)	THF	95 (76)[e]	96/4
9[f]	**2b**	K(O-*t*-Bu) (1.2)	DME	64	95/5
10[g]	**2b**	K(O-*t*-Bu) (2.0)	DME	62	97/3
11[h]	**2b**	K(O-*t*-Bu) (2.0)	DME	96	99/1
12	**1b**	K(O-*t*-Bu) (2.0)	THF	0	

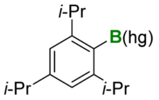
[a] Reaction conditions unless specified otherwise: silylboronate ester (2 equiv) and a base in a solvent was stirred for 10 min at 650 rpm at 30 °C, after which **3a** (0.3 mmol) was added. The resultant mixture was stirred for 1 h at 30 °C. [b] GC yield of **4a** or **4a′**. [c] Ratio of **4a** or **4a′** to **5a** + **5b**. [d] Reaction time: 3 h. [e] Isolated yield after sequential boryl substitution/Suzuki−Miyaura coupling. [f] 1.5 equiv of **2b** was used. [g] PhCl was used as a substrate. [h] PhI was used as a substrate.

Table 3. Substrate Scope for the Boryl Substitution of Aryl Halides using $(TMS)_3Si{-}B(hg)$/K(O-*t*-Bu)[a]

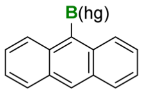




4b, 81%



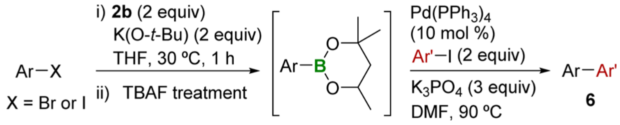
4c, 70%

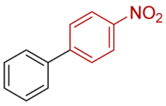


4d, 71%

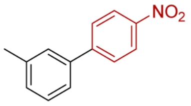
[a] Reaction conditions: a mixture of silylboronate ester **2b** (2 equiv) and K(O-*t*-Bu) (2.0 equiv) in THF was stirred for 10 min at 650 rpm and 30 °C. Aryl bromide **3** (0.3 mmol) was added, and the resulting mixture was stirred for 1 h at 30 °C.

Table 4. Substrate Scope for the Boryl Substitution of Aryl Halides with $(TMS)_3Si{-}B(hg)$/K(O-*t*-Bu)[a]

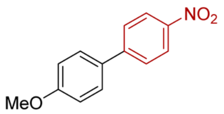




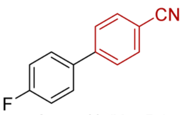
6a, 76% (X = Br)



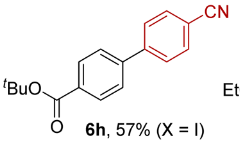
6e, 85% (X = Br)



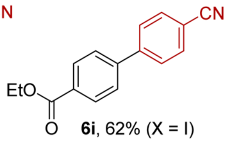
6f, 75% (X = Br)



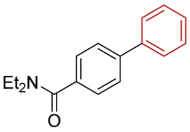
6g, 74% (X = Br)



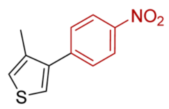
6h, 57% (X = I)



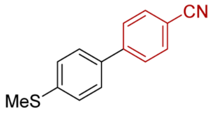
6i, 62% (X = I)



6j, 61% (X = Br)



6k, 75% (X = Br)



6l, 79% (X = Br)

[a] Isolated yield.

K(O-*t*-Bu) (Table 2, entry 5). Na(O-*t*-Bu) and Li(O-*t*-Bu) also showed better yields and B/Si selectivities than their methoxide counterparts (Table 2, entries 6 and 7). The replacement of DME with THF had very little effect on the yield or selectivity (Table 2, entry 8). We also examined the reaction with 1.5 equiv of **2b**, which resulted in a lower yield (64%, B/Si = 95/5; Table 2, entry 9). The effect of the leaving group of the aryl halide was also investigated. Chlorobenzene gave the corresponding borylated product in good yield and high selectivity (62%, B/Si = 97/3; Table 2, entry 10), whereas iodobenzene gave an excellent yield and higher selectivity (96%, B/Si = 99/1; Table 2, entry 11). In contrast, the reaction of bromobenzene with $Et_3Si{-}B(pin)$ (**1b**), which shows stability similar to that of **2b**, resulted in no reaction (Table 2, entry 12).

With the optimized reaction conditions in hand, we investigated the borylation of hindered aryl bromides with **2b** (Table 3). Pleasingly, sterically hindered aryl bromides **3b**−**d** also reacted to give the corresponding products in high yields (**4b**, 81%; **4c**, 70%; **4d**, 71%).

We also investigated the possibility of a one-pot borylation/Suzuki cross-coupling sequence to further explore the functional group compatibility of **2b** and the overall utility of this reaction (Table 4). Electron-neutral and electron-rich aryl bromides readily underwent the borylation, followed by a cross-coupling with 4-nitroiodobenzene, to provide the corresponding products in high yield (**6a**, 76%; **6e**, 85%; **6f**, 75%). Reactions with aryl bromides or iodides bearing an electron-withdrawing group (i.e., fluoro, *tert*-butyl or ethyl ester or amide group) also proceeded smoothly to afford the desired products in good yields (**6g**, 74%; **6h**, 57%; **6i**, 62%; **6j**, 61%). Notably, two sulfur-containing aryl bromides also underwent the one-pot borylation/cross-coupling to afford the desired products in good yields (**6k**, 75%; **6l**, 79%). **2a**,**b** could also be used as reagents for the base-mediated silaboration of alkenes,[11] which can provide access to synthetically useful 1,2-bis-metalated products.

The silaboration of styrene with **2b** in the presence of a catalytic amount of KOMe gave the desired silaborated product **7** in high yield (93% NMR yield). Furthermore, the one-pot, base-mediated silaboration of styrene with **2a**/$NaBO_3$ oxidation gave the corresponding alcohol **8** in 73% yield (Scheme 1). In contrast, the reaction of styrene with $Et_3Si{-}B(pin)$ (**1b**) in the presence of a catalytic amount of KOMe resulted in no reaction.

In conclusion, we have developed novel air- and moisture-stable TTMSS boronate esters. These reagents were stable for extended periods at room temperature in solution and also exhibited good stability to silica gel. Furthermore, these reagents were successfully used in the boryl substitution of aryl halides with K(O-*t*-Bu), as well as the silaboration of styrene in the presence of catalytic KOMe.

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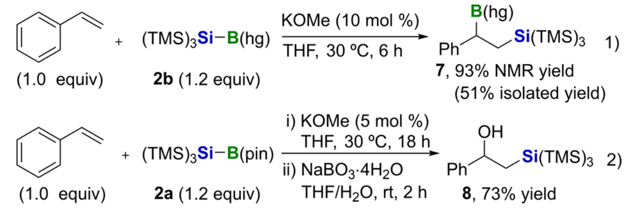
Scheme 1. Silaboration of Styrene with Silyl Boronate Ester 2a or 2b in the Presence of KOMe



■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.7b00476.

Synthetic details, characterization data, and crystallographic data (PDF)

Accession Codes

CCDC 1540097 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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