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Palladium-Catalyzed Benzylic Silylation of Diarylmethyl Carbonates with Silylboranes under Base-Free Conditions

Kento Asai, Koji Hirano,* and Masahiro Miura*

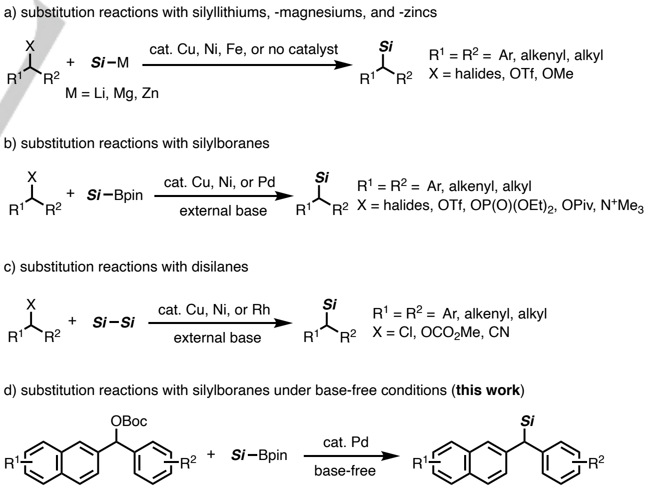
Dedication ((optional))

Abstract: A palladium-catalyzed benzylic silylation of diarylmethyl carbonates with silylboranes has been developed. The reaction proceeds smoothly even under external base-free conditions, and the corresponding benzylic silanes are formed in good to high yields. The obtained benzyl silane derivatives can work as the benzylic nucleophiles by the action of a suitable fluoride source and react with some carbon electrophiles to deliver the corresponding benzylic C–C cross-coupled products. Additionally, while still preliminary, the allylic silylation of the isoelectronic allylic carbonates is also achieved.

Introduction

Organosilicon compounds are now indispensable synthetic reagents in synthetic organic chemistry[1] as well as key substructures in the design of new organic functional materials and pharmaceuticals.[2] Accordingly, the development of carbon–silicon bond forming reactions for the synthesis of organosilicon compounds has been one of the long-standing research subjects in organic chemistry. The most classical but reliable approaches include the hydrosilylation of alkenes with hydrosilanes[3] and substitution reaction of nucleophilic organometallic reagents such as organolithium and -magnesium reagents with electrophilic halosilanes.[4] However, the former often suffers from the low regioselectivity and sensitivity to steric factors. In the latter case, the low-functional-group compatibility associated with the highly reactive organometallic reagents is observed. A good alternative is the umpolung-type coupling, that is, the reaction of carbon electrophiles and silyl nucleophiles. The silyllithiums,[5] -magnesiums,[6] and -zincs[7] are effectively coupled with the carbon electrophiles under transition-metal-catalyzed or noncatalyzed conditions to form the corresponding organosilicon compounds (Scheme 1a). However, these highly reactive silyl metal reagents are generally difficult to handle, and their instability is also sometimes problematic.[8] In this context, more stable and easy-to-handle silylboranes (Scheme 1b)[9] and disilanes (Scheme 1c)[10] have recently received significant attention as the potent silyl nucleophiles. Actually, the coupling reaction of the aforementioned reagents with organic (pseudo)halides is mediated by suitable transition metal catalysts to form the corresponding carbon–silicon bond with good efficiency. However, expect for specific examples using the nitrile substrates,[10b] the external bases such as strongly basic metal alkoxides are generally inevitable, which is the disadvantage to be addressed.

Meanwhile, our research group recently focused on the unique reactivity of diarylmethyl carbonates and successfully developed the palladium-catalyzed benzylic substitution reactions with several nucleophiles.[11,12] In our continuing interest in this chemistry, the catalytic benzylic silylation reaction with silylboranes was anticipated. Herein, we report a palladium-catalyzed benzylic carbon–silicon bond forming reaction of the readily available diarylmethyl carbonates with silylboranes (Scheme 1d). The reaction proceeds smoothly even under external base-free conditions, and the corresponding benzyl silanes are obtained in good to high yields. Moreover, the benzyl silane moiety can undergo fluoride-promoted post functionalizations. The related palladium-catalyzed benzylic silylation reaction was reported by Wang and Xu,[9e] but toxic and less stable benzyl halides were necessary as the starting substrates. Additionally, the stoichiometric Ag_2O was still required for the effective catalyst turnover.


a) substitution reactions with silyllithiums, -magnesiums, and -zincs

b) substitution reactions with silylboranes

c) substitution reactions with disilanes

d) substitution reactions with silylboranes under base-free conditions (**this work**)

Scheme 1. Carbon–silicon bond-forming reactions by umpolung-type cross-couplings with carbon electrophiles and silicon nucleophiles. Boc = *tert*-butoxycarbonyl, Bpin = pinacolatoboryl.

Results and Discussion

Our optimization studies commenced with the *tert*-butyl diarylmethyl carbonate **1a** and $PhMe_2Si$–Bpin (**2a**) for identification of the suitable metal catalyst. After the extensive screening,[13] we were pleased to find that $Pd(PPh_3)_4$ (5 mol%) catalyzed the benzylic substitution of **1a** (0.25 mmol) with **2a** (0.30 mmol) even in the absence of any external bases, and the corresponding benzyl silane **3aa** was isolated in 76% yield

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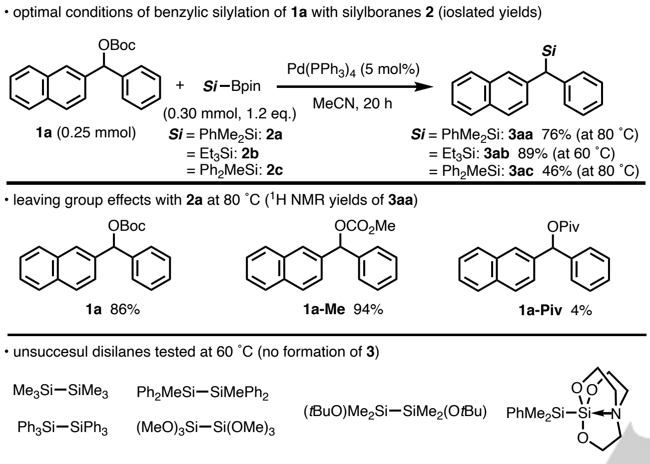
(Scheme 2). The trialkyl-substituted Et_3Si–Bpin (**2b**) and bulkier Ph_2MeSi–Bpin (**2c**) were also applicable as the silyl nucleophiles to form the targeted **3ab** and **3ac**, respectively. Some observations are to be noted: the choice of the leaving group was critical, and the corresponding methyl carbonate **1a-Me** also provided **3ab** in a high yield whereas the pivalate **1a-Piv** showed sluggish reactivity. Under identical base-free conditions, several disilanes instead of the silylboranes were also tested, but no silylated product was detected, thus suggesting that the higher Lewis acidity of Bpin plays an important role in the metathesis step with the Pd alkoxide intermediate (vide infra).



Scheme 2. Optimization of reaction conditions for Pd-catalyzed benzylic silylation of *tert*-butyl diarylmethyl carbonate **1a** with silylboranes **2**. Piv = *tert*-butylcarbonyl.

We next examined the scope and limitation of the carbonate substrates using *tert*-butyl carbonates **1**, because in Scheme 2 the methyl carbonate **1a-Me** showed slightly higher reactivity than the *tert*-butyl carbonate **1a** but concurrently formed a reduced byproduct (2-benzylnaphthalene), which hampered the purification of the desired silylated product.[14] The structures of products are illustrated in Figure 1. In addition to the model substrate **1a**, the electron-rich **1b** and -deficient **1c** were successfully converted to the corresponding benzylic silylation products **3bb** and **3cb** in 90 and 61% yields, respectively. Apparently, the electron-donating substituent showed better performance. The reaction was sensitive to steric factors, and the *ortho*-substituted **3da** was thus obtained in a moderate yield. The 2-naphthyl moiety in **1a** could be replaced with the methoxy-substituted 2-naphthyl (**3ea** and **3eb**) and regioisomeric 1-naphthyl groups (**3fb**). The higher fused phenanthryl substrate could also be employed (**3gb**). Particularly notable is the successful conversion of heteroaromatic substrates, including benzothiophene (**3hb**) and benzofuran (**3ib**). The primary naphthylmethyl carbonate also underwent the benzylic silylation, but in this case $PhMe_2Si$–Bpin resulted in higher reactivity than Et_3Si–Bpin (**3ja** vs **3jb**). Unfortunately, the Ar-Cl (**3kb**) and Ar-CN (**3la**) functionalities were incompatible; the former substrate suffered from low reproducibility probably because of competitive Ar-Cl oxidative addition to Pd(0), whereas the homocoupling byproduct was mainly observed in the latter case. The current limitation of the palladium catalysis is no conversion of the monocyclic substrate (**3mb**), which apparently means "naphthalene problem".[15] On the other hand, attempts to apply alkyl-substituted substrates such as *tert*-butyl (1-(naphthalen-2-yl)ethyl) carbonate (**3nb**) also remained unsuccessful; the major product was 2-vinylnaphthalene, which can arise from the benzylpalladium intermediates (**8** and/or **9** in Scheme 4; vide infra) via β-H elimination.

The benzyl silane moiety in the product can be a useful synthetic handle for further manipulations under suitable fluoride-mediated conditions (Scheme 3). The CsF/18-crown-6-promoted allylation and benzylation with allyl bromide and benzyl bromide were possible to afford the allylated **4** and benzylated **5** in 85 and 77% yields, respectively.[16a,b] The same conditions were applicable to the arylation reaction with phthalonitrile to deliver the corresponding triarylmethane **6** in a good yield.[16c]

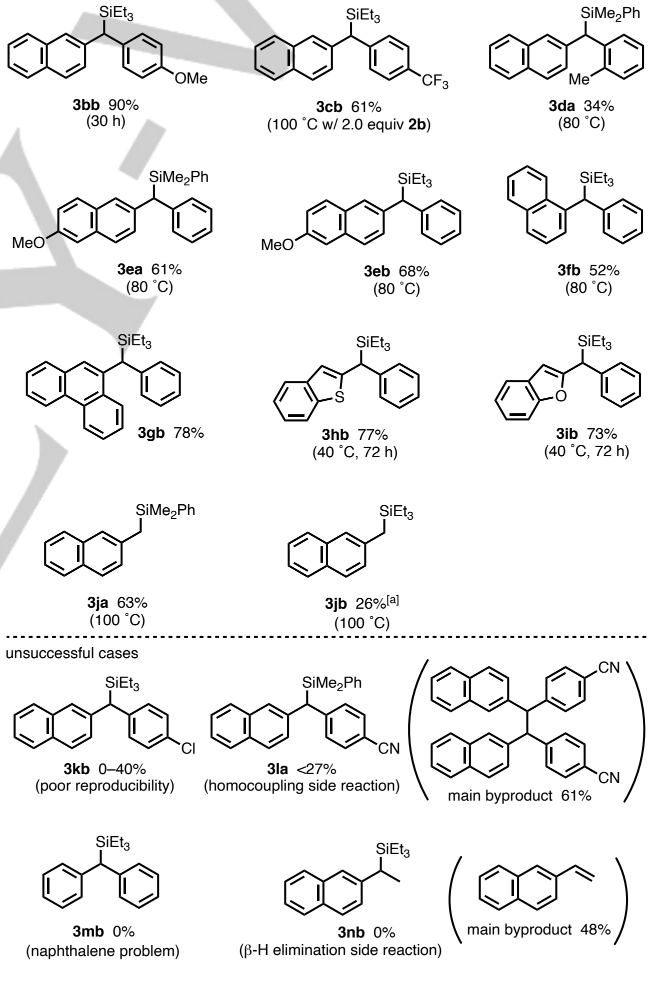
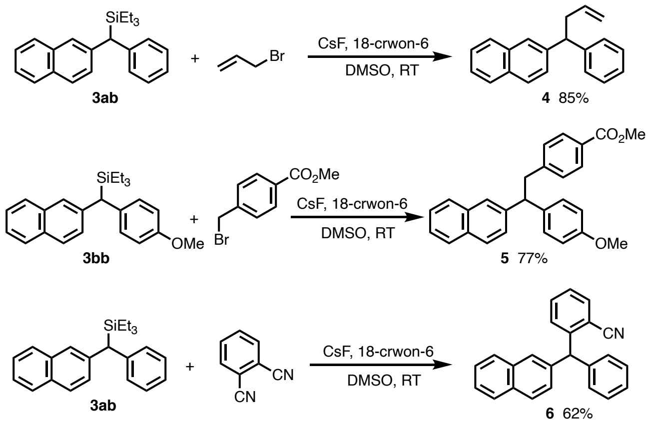
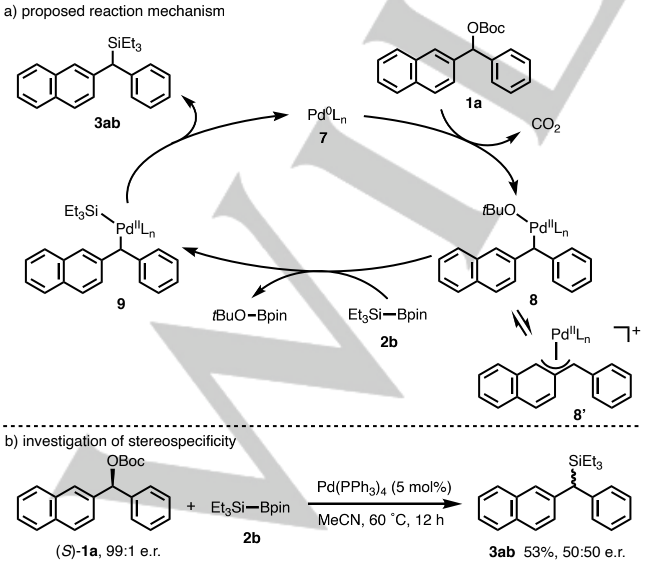


Figure 1. Structures of products in Pd-catalyzed benzylic silylation of *tert*-butyl diarylmethyl carbonates **1** with silylboranes **2**. Isolated yields are shown. Standard conditions: **1** (0.25 mmol), **2** (0.30 mmol), $Pd(PPh_3)_4$ (0.013 mmol), MeCN (1.5 mL), 60 °C, 20 h, N_2. The minor modifications from the standard conditions are in parentheses. [a] ^1H NMR yields.



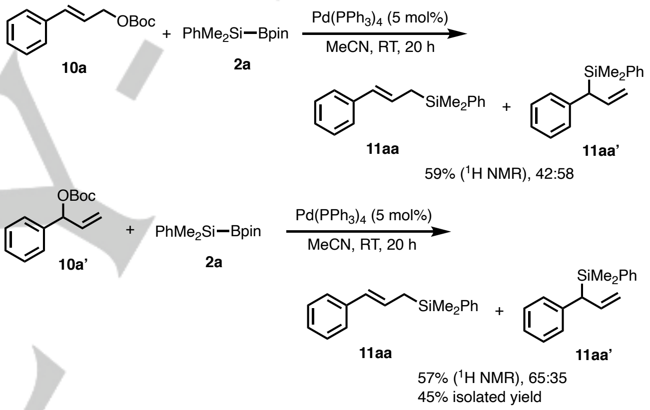
Scheme 3. Transformations of benzylic silylation products. See the Supporting Information for detailed conditions.

We are tempted to propose that the mechanism of reaction of **1a** with **2b** is as follows (Scheme 4a). The initial oxidative addition of **1a** to the starting palladium(0) species **7** with concomitant decarboxylation generates the σ-benzylpalladium intermediate **8**, which is in equilibrium with the corresponding π-benzyl isomer **8'**.[12g,h] Subsequently, σ-bond metathesis with the silylborane **2b** occurs to form the benzyl(silyl)palladium **9** and *t*BuO–Bpin. Actually, in the monitoring study with MeCN-*d*$_3$, the formation of *t*BuO–Bpin was observed by ^{11}B NMR (see the Supporting Information for details). This process can be uniquely accelerated by the interaction between the Lewis acidic Bpin in Et$_3$Si–Bpin and Lewis basic *t*BuO ligand on the palladium, which is consistent with the reactivity trends observed in the optimization studies (Scheme 2). Final productive reductive elimination delivers the benzylic silylation product **3ab** with regeneration of **7** to complete the catalytic cycle. In the investigation of stereospecificity with the enantiomerically pure (*S*)-**1a** (99:1 e.r.), the stereochemical information of the starting material completely lost, and **3ab** was obtained in a totally racemic form (Scheme 4b), thus suggesting the facile racemization process through an S_N2-type back side attack of additional Pd^0 species to the π-benzylpalladium species **8'**.[17]



Scheme 4. a) Proposed reaction mechanism and b) investigation of stereospecificity. L = PPh$_3$.

Given the much better reactivity of naphthalene-type substrates than the monocyclic substrate (e.g., **3ab** vs **3mb**), the isoelectronic allylic carbonate can also be a good candidate as the substrate. Pleasingly, the reaction of *tert*-butyl cinnamyl carbonate (**10a**) with **2a** proceeded even at room temperature to provide a 42:58 regiomixture of the linear and branched allylic silanes **11aa** and **11aa'** in 59% combined ^{1}H NMR yield (Scheme 5). The regioisomeric **10a'** was also converted to **11aa** and **11aa'** with a similar ratio (65:35), thus indicating the intermediacy of the common π-allyl palladium intermediate. While there are many reports of the copper-catalyzed allylic substitution reactions with the silylboranes,[9j,k,l] this is the first successful example of the external-base-free, palladium-catalyzed allylic silylation with the silylborane, to the best of our knowledge.[18] Detailed substrate scope investigation and development of regio- and enantioselective catalysts are ongoing.



Scheme 5. Preliminary results of Pd-catalyzed allylic silylation of allylic carbonates with silylborane.

Conclusion

In conclusion, we have developed a palladium-catalyzed benzylic silylation reaction of diarylmethyl carbonates with silylboranes. By using the internal Lewis basic alkoxide ligand arising from the carbonate, the benzylic silylation products are obtained even under external base-free conditions. The obtained benzyl silanes can work as the potent benzylic nucleophiles in the presence of a suitable fluoride. Additionally, while still preliminary, the allylic silylation of the isoelectronic allylic carbonates is also found to proceed under identical palladium catalysis.

Experimental Section

Experimental Procedure for Palladium-Catalyzed Benzylic Silylation of Diarylmethyl Carbonates with Silylboranes: Synthesis of **3aa** (Scheme 2) is representative. *tert*-Butyl (naphthalen-2-yl(phenyl)methyl) carbonate (**1a**, 83.4 mg, 0.25 mmol) was placed in a 20 mL Schlenk tube in a glovebox filled with nitrogen. A solution of dimethyl(phenyl)(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)silane (**2a**, 78.8 mg, 0.30 mmol) in

MeCN (1.0 mL), Pd(PPh$_3$)$_4$ (14.5 mg, 0.012 mmol), and MeCN (0.5 mL) were added to the reaction tube. The reaction tube was sealed with a cap and taken out of the glovebox. The suspension was stirred for 20 h at 80 °C (oil bath). The resulting mixture was filtered through a short pad of activated alumina and sodium sulfate, and the filtrate was concentrated in vacuo. 1-Methylnaphthalene (14.8 mg) was added as an internal standard, and the resulting mixture was analyzed by ^{1}H NMR in CDCl$_3$ solution. Concentration in vacuo and subsequent purification by column chromatography on neutral silica gel with hexane/ethyl acetate (20/1) and then by GPC (chloroform) as an eluent gave dimethyl(naphthalen-2-yl(phenyl)methyl)(phenyl)silane (**3aa**, 67.0 mg, 0.19 mmol) in 76% yield.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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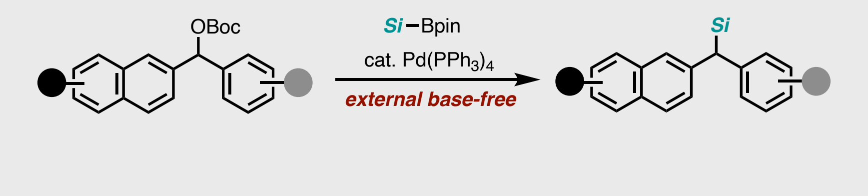

A palladium-catalyzed benzylic silylation reaction of diarylmethyl carbonates with silylboranes has been developed. By taking advantage of in-situ generated alkoxide ligand arising from the carbonate substrate, the reaction proceeds smoothly even under external base-free conditions. The resulting benzyl silane moiety can undergo the post functionalizations to deliver the more complex diarylmethane derivatives. Additionally, the related base-free allylic silylation reaction is also demonstrated.

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