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A NaOtBu-catalyzed regio- and diastereoselective cyclosilylborylation of styryl(vinyl)silanes with silylboronates has been developed for the synthesis of multi-substituted silacyclopentanes. 2-Silyl-5-boryl-1-silacyclopentanes obtained in the present catalysis can be further functionalized by taking advantage of the reactivity of the silyl and boryl groups.

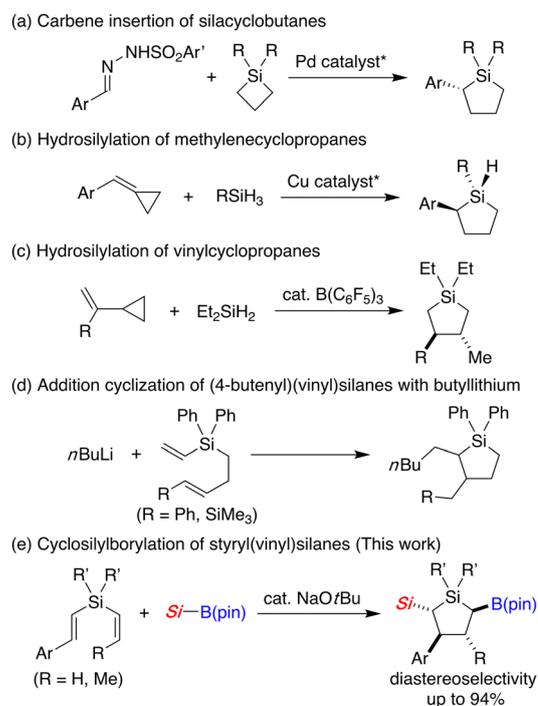
Substituting a carbon atom of organic molecules by silicon is a useful strategy to modify or improve their original properties particularly in the field of pharmaceutical science.¹ Since alicycles are ubiquitously found in various natural products and biologically active compounds, development of efficient synthetic methods of corresponding silacyclic compounds is of high importance.² In particular, silacyclopentanes, silicon-switched analogues of widely found cyclopentanes, are expected to display promising biological activity,³ but synthesis of highly functionalized silacyclopentanes is currently still underexplored. One way to achieve this goal is to introduce functional groups to preformed silacyclopentenes by utilizing the reaction toward a carbon–carbon double bond,^{3a,3d,4} but direct synthesis of such silacyclopentanes is rather difficult presumably due to the limited available methods to construct the silacyclopentane framework from readily available precursors. Other than the classical reaction of 1,4-dimetalloalkanes with dichlorosilanes toward the synthesis of silacyclopentanes,^{3b,3c,5} ring expansion reactions of silacyclobutanes with carbenoids have been relatively well investigated,⁶ including a recent enantioselective carbene insertion under palladium catalysis⁷ (Scheme 1a). In addition, metal-catalyzed hydrosilylation of methylenecyclopropanes⁸ (Scheme 1b) as well as Lewis acid-catalyzed hydrosilylation of vinylcyclopropanes⁹ (Scheme 1c) have also been reported.

Regio- and diastereoselective synthesis of multi-substituted silacyclopentanes by catalytic cyclosilylborylation of styryl(vinyl)silanes

 Kanta Ueji^a and Ryo Shintani^{id} *^{ab}

However, highly substituted silacyclopentanes could not be prepared in these approaches.

To overcome this synthetic problem, we imagined that introduction of multiple substituents during the five-membered ring formation would be realized in a straightforward manner by cyclo-difunctionalization of linear dialkenylsilanes. In this regard, although a somewhat related example has been reported in the reaction of (4-butenyl)(vinyl)silanes with *n*-butyllithium (Scheme 1d), applicable substrate combinations are quite limited and only 2,3-dialkyl-1-silacyclopentanes can be accessed with moderate diastereoselectivity.¹⁰ Considering the ease of



Scheme 1 (a)–(d) Reported synthetic methods of silacyclopentanes through the formation of 5-membered rings and (e) cyclosilylborylation of styryl(vinyl)silanes (this work).

^a Division of Chemistry, Department of Materials Engineering Science, Graduate School of Engineering Science, The University of Osaka, Toyonaka, Osaka 560-8531, Japan. E-mail: shintani.ryo.es@osaka-u.ac.jp

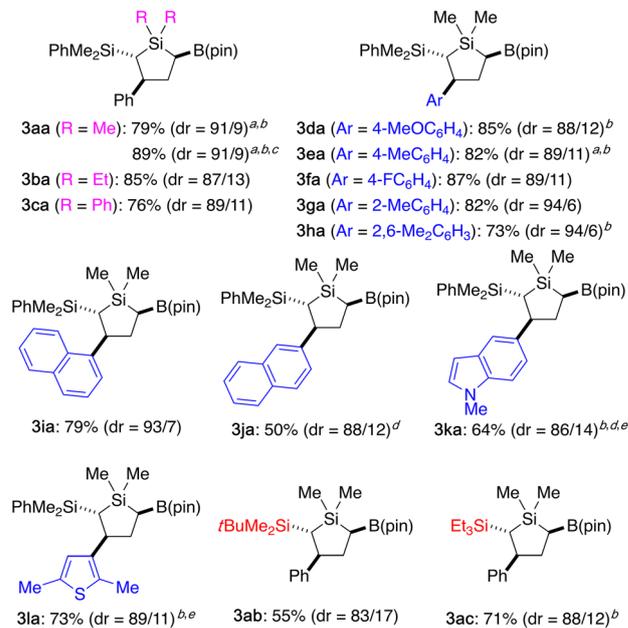
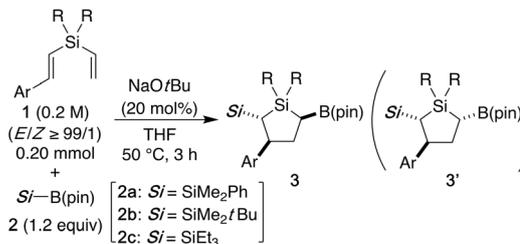
^b Innovative Catalysis Science Division, Institute for Open and Transdisciplinary Research Initiatives (ICS-OTRI), The University of Osaka, Suita, Osaka 565-0871, Japan



further derivatization reactions, we designed a reaction of silylboronates¹¹ with dialkenylsilanes to give 2-silyl-5-boryl-1-silacyclopentanes¹² and found that the both regioselectivity and diastereoselectivity can be effectively controlled by using styryl-(vinyl)silanes as the substrate in the presence of a catalytic amount of NaOtBu under mild conditions (Scheme 1e), and herein we describe the details of this process.

Because styrene derivatives are known to undergo regioselective silylborylation by using a combination of silylboronates and alkali metal alkoxide catalysts,¹³ we initially employed (*E*)-styryl(vinyl)silane **1a** as the model substrate and conducted a reaction with dimethylphenylsilylboronate **2a** in the presence of KOtBu (20 mol%) in THF at 50 °C (Table 1, entry 1). Under these conditions, the desired silylation–cyclization–borylation effectively took place to give the silacyclopentane product having three stereocenters as a mixture of two diastereomers **3aa/3aa'** out of four possible diastereomers in 88% combined yield in the ratio of 80/20. The diastereoselectivity was found to be improved by using LiOtBu (84/16; entry 2) or NaOtBu (89/11; entry 3). The use of NaN(SiMe₃)₂ showed the same level of selectivity as NaOtBu (entry 4), but other sodium alkoxides such as NaOEt and NaOMe were found to be less effective or unreactive (entries 5 and 6). In the present reaction, the diastereomeric ratio (dr) between **3aa** and **3aa'** was independent of the *E/Z* ratio of starting compound **1a** (entry 7). Finally, by lowering the reaction temperature to 10 °C, somewhat higher diastereoselectivity of 91/9 was realized while keeping the good reactivity (entry 8).

Under the conditions using NaOtBu (20 mol%), various other styryl(vinyl)silanes can be employed in the reaction with silylboronate **2a** to give 2-silyl-3-aryl-5-boryl-1-silacyclopentanes **3** diastereoselectively (Scheme 2). For example, in addition to **1a** having methyl groups on silicon, ethyl (**1b**) or phenyl (**1c**) substituted compounds gave the corresponding silacyclopentanes



^a The reaction was conducted at 10 °C.

^b The reaction was conducted for 16 h.

^c The reaction was conducted on 2.5 mmol scale.

^d The reaction was conducted at 0.07 M.

^e The reaction was conducted at 70 °C with 40 mol% of NaOtBu.

Scheme 2 Diastereoselective synthesis of 2,3,5-trisubstituted silacyclopentanes: scope.

Table 1 Cyclosilylborylation of **1a** with **2a** to give 2,3,5-trisubstituted 1,1-dimethyl-1-silacyclopentane **3aa**: effect of catalysts

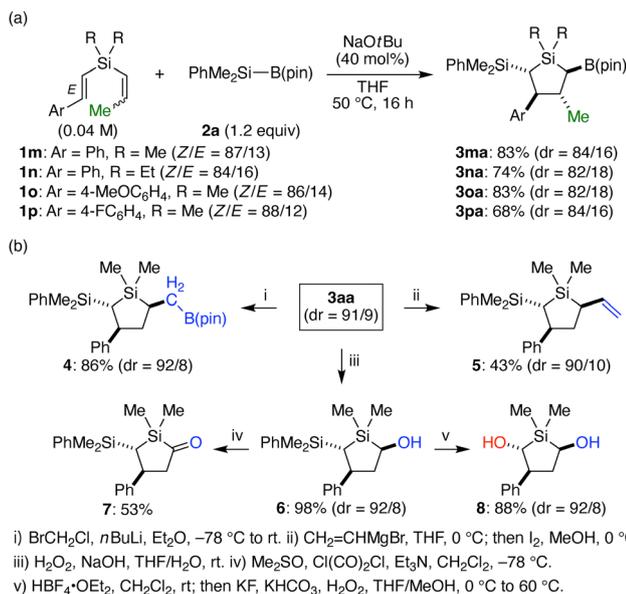
Entry	Catalyst	Yield of 3aa + 3aa' ^a (%)	Ratio of 3aa/3aa' ^a
1	KOtBu	88	80/20
2	LiOtBu	78	84/16
3	NaOtBu	90	89/11
4	NaN(SiMe ₃) ₂	79	89/11
5	NaOEt	71	84/16
6	NaOMe	0	—
7 ^b	NaOtBu	88	89/11
8 ^c	NaOtBu	80	91/9

^a Determined by ¹H NMR. ^b The reaction was conducted using **1a** with *E/Z* = 72/28. ^c The reaction was conducted at 10 °C for 16 h.

3ba–ca as well, and the relative configuration of **3ba** was firmly established by X-ray crystallographic analysis. With regard to the variation of the styryl group, several substituted aryl groups can be accommodated to give products **3da–ha** with similar efficiency, and higher diastereoselectivity of up to 94/6 was observed for substrates having a bulky aryl group such as **1g** and **1h**. The reaction could also be applied to substrates having naphthyl (**1i** and **1j**) or heteroaryl (**1k** and **1l**) groups to give **3ia–la**. In addition, other silylboronates such as **2b** and **2c** were compatible with the present reaction, leading to the formation of 2-trialkylsilylated products **3ab–ac**. It is worth noting that the present reaction could also be conducted on a preparative scale using 2.5 mmol of **1a** to give 1.0 g of **3aa** (89% yield, dr = 91/9).

To further expand the scope of accessible multi-substituted silacyclopentanes, we examined the reaction of styryl(1-propenyl)silane **1m** with silylboronate **2a** for the synthesis of 2,3,4,5-tetrasubstituted 1,1-dimethyl-1-silacyclopentane **3ma** (Scheme 3a). As a result, by conducting the reaction using 40 mol% of NaOtBu under a diluted condition, the desired product was successfully obtained in 83% yield as a mixture of



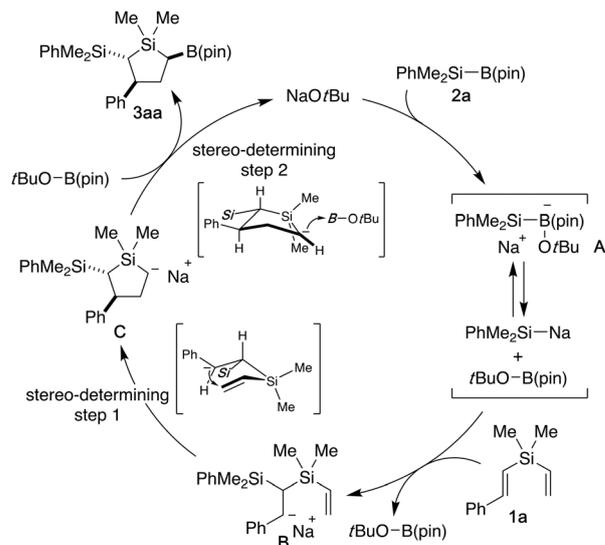


Scheme 3 (a) Diastereoselective synthesis of 2,3,4,5-tetrasubstituted silacyclopentanes. (b) Stereo-retentive transformations of **3aa**.

two diastereomers in the ratio of 84/16 out of eight possible diastereomers. Similarly, **1n** having ethyl groups on silicon as well as **1o** and **1p** having substituted styryl groups were converted to silacyclopentanes **3na–pa** in 68–83% yield with dr = 82/18–84/16, and X-ray crystal structure of the major diastereomer of **3na** revealed that the four substituents on the ring carbons were in all-*trans* relationship.

Silyl- and boryl-substituted silacyclopentane **3aa** obtained in the present reaction can be further derivatized with retaining the stereochemical integrity. For example, Matteson homologation by treatment with *n*-butyllithium in the presence of bromochloromethane gave compound **4** having a borylmethyl substituent in 86% yield.¹⁴ In addition, the boryl group could be converted to a vinyl group in 43% yield by Zweifel olefination of **3aa** with vinylmagnesium bromide followed by treating it with iodine in methanol.¹⁵ The boryl group of **3aa** could also be oxidized to a hydroxy group by hydrogen peroxide under basic conditions to give silacyclopentanol **6** in a nearly quantitative yield.¹⁶ Swern oxidation of the hydroxy group of **6** led to silacyclopentanone **7**,¹⁷ a type of underexplored cyclic acylsilane,¹⁸ in 53% yield as a single diastereomer, which confirms that **3aa** and **3aa'** have a common relative configuration between dimethylphenylsilyl group and phenyl group with the opposite configuration at the boryl group. On the other hand, oxidation of the carbon–silicon bond of **6** selectively took place under Tamao–Fleming conditions to give *trans*-silacyclopentanediol **8** in 88% yield.¹⁹

A proposed catalytic cycle for the reaction of styryl(vinyl)silane **1a** with silylboronate **2a** is illustrated in Scheme 4. Initially, coordination of NaOtBu to **2a** gives borate intermediate **A**, which would be in equilibrium with dissociated dimethylphenylsilyloxy-sodium and *t*BuOB(pin).^{13,20} The silicon nucleophile then attacks the β-position of styryl group of **1a** to give benzyl anion intermediate **B**. Subsequent ring-closure of this intermediate takes



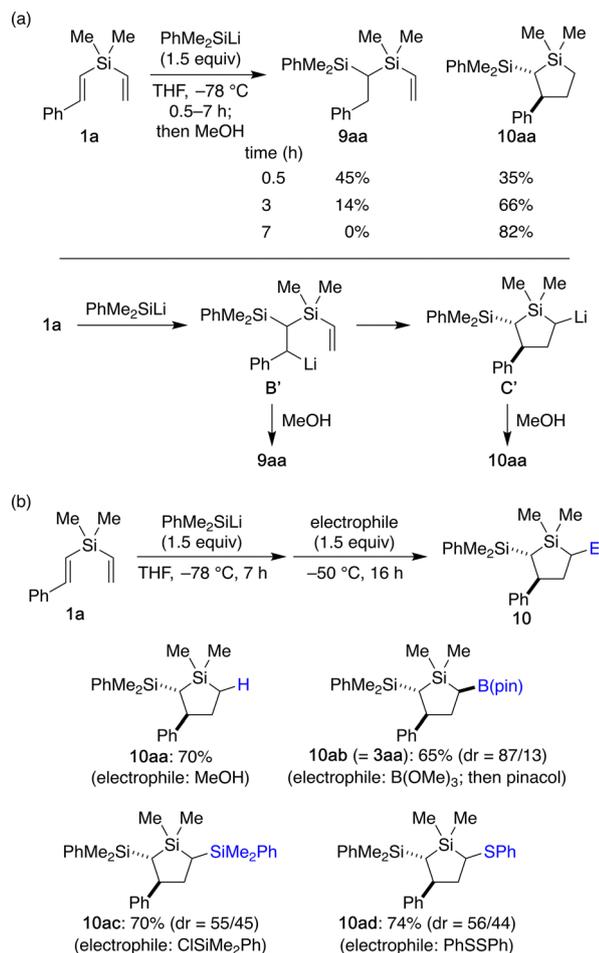
Scheme 4 Proposed catalytic cycle for the reaction of **1a** with **2a** to give **3aa**.

place through intramolecular nucleophilic attack at the β-position of vinylsilane to give silacyclopentyl anion **C**, which undergoes borylation with *t*BuOB(pin) to give cyclosilylborylation product **3aa** along with regeneration of NaOtBu. The relative configuration between the silyl group at 2-position and the phenyl group at 3-position would be controlled in *trans* relationship at the C–C bond-forming cyclization step, and the stereochemistry of the boryl group at 5-position is finally set to give major diastereomer **3aa** possessing three substituents on the ring carbons all in pseudo-equatorial positions of the chair-like silacyclopentane structure.

To gain some insights into the above-proposed mechanism, we prepared dimethylphenylsilyllithium as a discrete nucleophile and conducted stoichiometric reactions with styryl(vinyl)silane **1a** (Scheme 5a). The reactions were conducted at -78 °C and quenched by protonation using MeOH after different reaction times. When the reaction was stopped after 0.5 h, uncyclized (1-silyl-2-phenylethyl)(vinyl)silane **9aa** and cyclized 2-silyl-3-phenyl-1-silacyclopentane **10aa** were obtained in 45% yield and 35% yield, respectively. By extending the reaction time prior to the MeOH quench, the yield of **9aa** became lower and that of **10aa** became higher accordingly. These results suggest that the silacyclopentane formation takes place in a stepwise fashion consisting of addition of a silicon nucleophile to the β-position of the styrene moiety and subsequent intramolecular addition of the resulting benzyl nucleophile to the pendant vinyl group, supporting the proposed catalytic cycle in Scheme 4.

By taking advantage of the formation of a silacyclopentyl-lithium (**C'** in Scheme 5a) in a stoichiometric fashion, we also examined the use of some other electrophiles to introduce different substituents at 5-position (Scheme 5b). When the reaction was quenched with trimethyl borate followed by transesterification with pinacol, cyclosilylborylation product **10ab** (= **3aa**) was obtained in 65% yield with dr = 87/13. In addition, the use of chlorodimethylphenylsilane gave 2,5-disilyl-1-silacyclopentane





Scheme 5 Reactions of **1a** with dimethylphenylsilyllithium followed by electrophilic quench: (a) effect of reaction time and (b) scope of electrophiles.

10ac in a good yield of 70%, although the diastereoselectivity was low (dr = 55/45). Similarly, introduction of phenylthio group was also achieved by using diphenyl disulfide as the electrophile to give **10ad** in 74% yield.

In summary, we developed a regio- and diastereoselective cyclosilylborylation of styryl(vinyl)silanes with silylboronates in the presence of a catalytic amount of NaOtBu to give multi-substituted silacyclopentanes. The reaction can be performed for various substrates including styryl(1-propenyl)silanes, giving 2,3,4,5-tetrasubstituted compounds with all-*trans* configuration. The obtained 2-silyl-5-boryl-1-silacyclopentanes could be further functionalized by utilizing the reactivity of the silyl and boryl groups, and the reaction mechanism was also probed by conducting model stoichiometric reactions.

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Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: experimental procedures, characterization data, and NMR spectra. See DOI: <https://doi.org/10.1039/d6cc00416d>.

CCDC 2524632 (**3ba**) and 2524633 (**3na**) contain the supplementary crystallographic data for this paper.^{21a,b}

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