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2-Vinylindoles As the Four-Atom Component in a Catalytic [4+1] Cycloaddition with a Silylene-Palladium Species Generated from (Aminosilyl)boronic Ester

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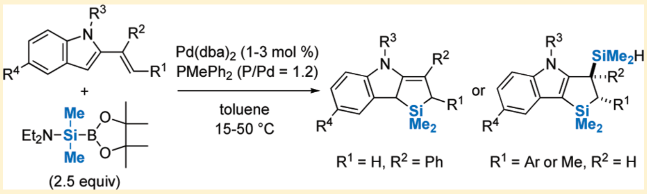
S Supporting Information

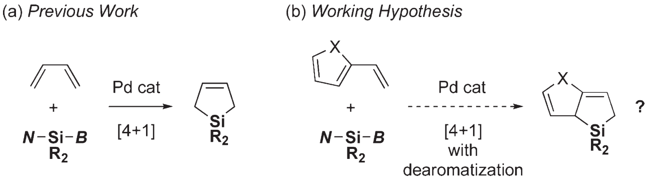
ABSTRACT: The palladium-catalyzed silylene transfer to 2-alkenylindoles from a silylboronic ester bearing a diethylamino group on the silicon atom takes place efficiently, resulting in the formation of a 1-sila-3-cyclopentene ring fused with the indole ring. Further silylene transfer proceeds in the reaction of 2-(1-alkenyl)indoles, giving bissilylated tricyclic indoles in high yields.



Silylene is a highly reactive divalent chemical species and is utilized in the synthesis of organosilicon compounds. Therefore, much effort has been devoted to the efficient generation and utilization of silylene.[1] Successful silylene-based transformations have been achieved using the kinetic stabilization technique, in which a specially designed sterically bulky group is introduced onto the silicon atom.[2] An alternative strategy to utilize silylene in synthesis is to use transition metal catalysts, which may be more versatile and practical for application to the synthesis of organosilicon compounds. Catalytic silylene transfer from relatively stable precursors, such as silacyclopropane and hydrodisilane, to organic substrates has been achieved in the presence of group 10 and 11 transition metal catalysts.[3−7] There is much more room to develop catalytic reactions involving silylene, not only for exploring new silylene-based transformation but also for establishing new routes to organosilicon compounds that are difficult to obtain using conventional methods.

On the basis of our recent findings on catalytic silylene transfer from (aminosilyl)boronic esters to 1-alkynes and 1,3-dienes,[8] we were interested in the reaction of the silylene species with alkenes. Our particular attention has been focused on vinylated heteroaromatic compounds because of their structural analogy to 1,3-dienes, which is expected to lead to unique bicyclic products via silylene-1,3-diene [4+1] cycloaddition (Scheme 1).[8b,9] Herein, we describe the palladium-catalyzed reaction of (aminosilyl)boronic ester with 2-alkenylindoles. The C2−C3 double bond conjugated to the alkenyl group was found to participate in the [4+1] cycloaddition with dearomatization of the indole.

Scheme 1. Catalytic Silylene Transfer to 1,3-Diene-Type Substrate



The reaction of 2-(β-styryl)-*N*-methylindole (**1a**) with silylboronic ester **2**[10] (2.0 equiv), which has a diethylamino group on the silicon atom, was carried out in C_6D_6 at 50 °C in the presence of $Pd(dba)_2$ (1.0 mol %) and PPh_3 (1.2 mol %) (entry 1, Table 1). The reaction gave aminoborane **4** in 55% yield after 12 h, indicating that a silylene equivalent was formed from **2** under the reaction conditions used. However, the expected silylene-1,3-diene [4+1] cycloaddition product **5a** was not observed in the products. We found that the reaction afforded bissilylated indole **3a** in 43% yield as a single diastereomer. The formation of **3a** took place more favorably using the palladium catalyst bearing $PMePh_2$ as a ligand (entry 2), whereas an inefficient formation of both **3a** and **4a** was observed in the reaction with other phosphines, such as PMe_2Ph and PMe_3 (entries 3 and 4). The palladium catalyst bearing a single $PMePh_2$ ligand demonstrated a high catalyst capability (entry 2), although **3a** was formed in lower yields when other P/Pd ratios (0, 2, or 4) were applied (entries 5−7). Finally, **3a** was obtained in the highest yield when the reaction was carried out using 2.5 equiv of **2** in the presence of the Pd/$PMePh_2$ (P/Pd = 1.2) catalyst (entry 8).[11]

Various 2-alkenylindoles **1** were then reacted with **2** (2.5 equiv) under the optimized catalyst conditions (Table 2). The bissilylative cyclization took place efficiently with *N*-methyl-2-alkenylindoles **1b−d** bearing both electron-donating and electron-withdrawing aryl groups, giving the corresponding bissilylatied indoles **3b−d** in 85−89% yields (entries 1−3). Indoles **1e** and **1f**, having *ortho*-substituted aryls, also reacted with **2** under the above conditions to give **3e** and **3f**, respectively, in high yields (entries 4 and 5). In addition to β-styryl-substituted indoles, 1-propenyl-substituted **1g** underwent the bissilylation (entry 6). However, the reaction of vinyl-substituted **1h** was sluggish, and **3h** was formed in low yield when the reaction was carried out at room temperature (entry 7). The methyl and chloro groups at the 5-position did not affect the

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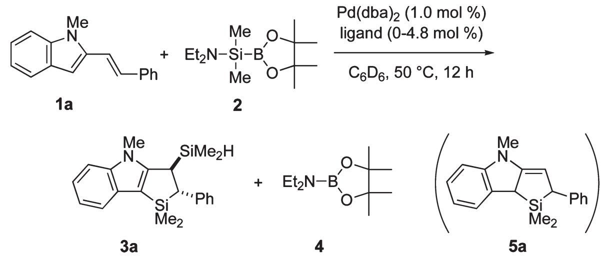
Table 1. Screening of Reaction Conditions in Bissilylative Cyclization of 1a[a]



entry	ligand	ligand/Pd	equiv of **2**	yield of **3a** (%)[b]	yield of **4** (%)[c]
1	PPh_3	1.2	2.0	43	55
2	$PMePh_2$	1.2	2.0	70	83
3	PMe_2Ph	1.2	2.0	35	47
4	PMe_3	1.2	2.0	13	26
5	none	0	2.0	3	11
6	$PMePh_2$	2.4	2.0	65	71
7	$PMePh_2$	4.8	2.0	33	42
8	$PMePh_2$	1.2	2.5	94 (91)[d]	89

[a] **1a** (0.20 mmol), **2** (0.40−0.50 mmol), $Pd(dba)_2$ (2.0 μmol), and ligand (0−9.6 μmol) were stirred in C_6D_6 (0.2 mL) at 50 °C for 12 h. [b] ^1H NMR yield based on **1a**. [c] ^1H NMR yield based on **2**. [d] Isolated yield on a 0.4 mmol scale reaction in toluene.

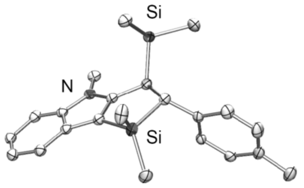


Figure 1. ORTEP drawing of **3b** at the 50% probability level. Hydrogen atoms were omitted for the clarity.

Scheme 2. Reaction of α-Styryl Group-Substituted 1l

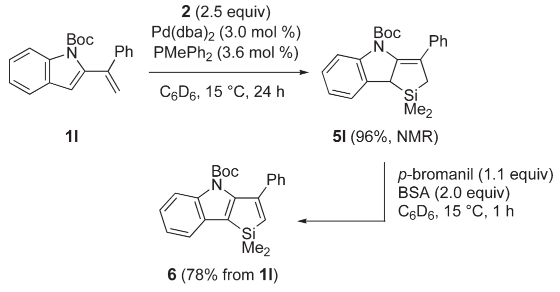
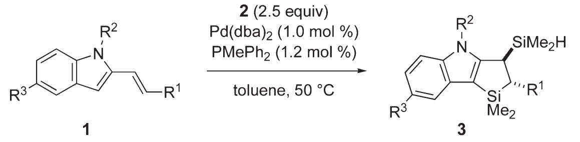


Table 2. Bissilylative Cyclization of 2-(1-Alkenyl)indoles 1[a]



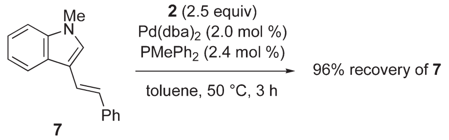
entry	R^1	R^2	R^3		time (h)	yield (%)[b]
1	4-MeC_6H_4	Me	H	**1b**	15	85 (**3b**)
2	4-$MeOC_6H_4$	Me	H	**1c**	5	87 (**3c**)
3	4-$CF_3C_6H_4$	Me	H	**1d**	5	89 (**3d**)
4[c]	2-MeC_6H_4	Me	H	**1e**	8	85 (**3e**)
5	2-ClC_6H_4	Me	H	**1f**	15	91 (**3f**)
6	Me	Me	H	**1g**	12	75 (**3g**)
7[d]	H	Me	H	**1h**	36	24[e] (**3h**)
8	Ph	Me	Me	**1i**	5	92 (**3i**)
9	Ph	Me	Cl	**1j**	18	85 (**3j**)
10	Ph	Boc	H	**1k**	24	72 (**3k**)

[a] **1** (0.40 mmol), **2** (1.0 mmol), $Pd(dba)_2$ (4.0 μmol), and $PMePh_2$ (4.8 μmol) were stirred in toluene (0.8 mL) at 50 °C unless otherwise noted. [b] Isolated yield based on **1**. [c] 3 mol % of the catalyst was used. [d] At room temperature using **1h** (0.30 mmol) and **2** (0.60 mmol). [e] ^1H NMR yield based on **1h**.

bissilylation and gave **3i** and **3j** in good yields (entries 8 and 9). The bissilylation was also applicable to *N*-Boc-substituted **1k** to give **3k** in good yield (entry 10). It should be noted that all the bissilylated compounds were formed as a single *trans* diastereomer, whose stereochemistry was confirmed from NMR analysis and X-ray structural analysis of **3b** (Figure 1).

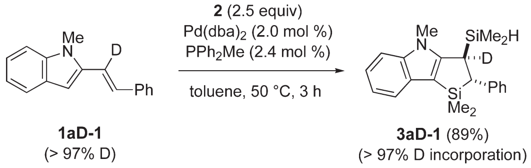
The reaction of *N*-Boc-2-(α-styryl)indole (**1l**) with **2** was then examined (Scheme 2). The reaction proceeded smoothly even at 15 °C to give **5l** in a quantitative yield, indicating that monosilylation took place selectively via silylene-1,3-diene [4+1] cycloaddition. The bissilylated product did not form even when the reaction was carried out at higher temperatures or with prolonged reaction times. Although **5l** was unstable to silica gel chromatography, it could be converted to the more stable silole **6** by oxidation with tetrabromo-*p*-benzoquinone (*p*-bromanil) in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA).[8b,12,13]

In sharp contrast to 2-alkenylindoles **1**, no conversion was observed in the reaction of 3-(*β*-styryl)-*N*-methylindole (**7**) with **2** under the identical conditions (eq 1).

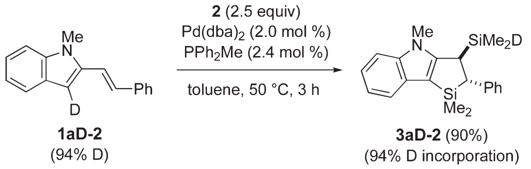


(1)

To obtain mechanistic insight into the bissilylation, deuterium-labeled indoles were subjected to the reaction (eqs 2 and 3). No migration of the deuterium was observed in the reaction of indole **1aD-1**, which has a group (*E*)-*β*-deuterio-*β*-styryl group, which gave **3aD-1** as a single diastereomer (eq 2). In contrast, the reaction of 3-deuterioindole **1aD-2** proceeded with the migration of deuterium to the silicon atom that was introduced at the *β*-position of the styryl group (eq 3).



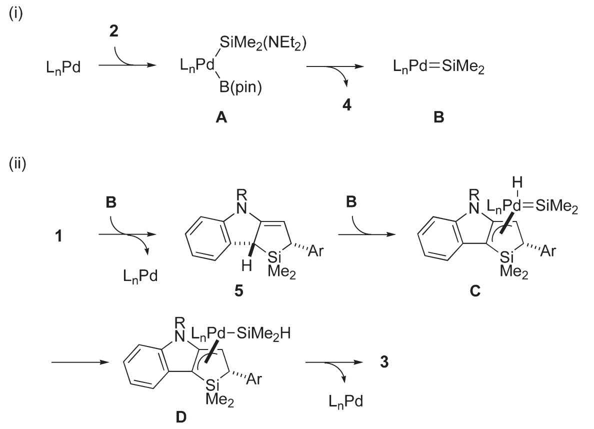
(2)



(3)

A possible mechanism of the bissilylative cyclization is shown in Scheme 3. The silylene-palladium species **B** is formed through

Scheme 3. Possible Reaction Mechanism



oxidative addition of the Si−B bond of **2** to Pd(0), followed by elimination of aminoborane **4** (Scheme 3, i).[14,15] Stereospecific formation of dihydrosilole **5** then takes place through silylene-1,3-diene [4+1] cycloaddition between **B** and **1** (Scheme 3, ii).[8b] Sequentially, the second **B** reacts with **5** to form π-allylpalladium **C** via oxidative addition of the allylic C−H bond. The conversion of (hydride)(silylene)palladium **C** to the (hydrosilyl)palladium complex **D** takes place,[16] and then **3** is formed by reductive elimination from **D**. This mechanism is consistent with both the stereochemical course of the reaction and the results of the deuterium labeling experiments.

In conclusion, we have established a new catalytic silylene-based transformation utilizing silylboronic ester as a silylene source. In this transformation, 2-alkenylindoles react with silylene as a four-atom component in the [4+1] cycloaddition, giving five-membered silacycles fused with the indole. Remarkable bissilylative cyclization takes place with high diastereoselectivity in the reaction of 2-(1-alkenyl)indoles. The synthetic utility of the bissilylated indoles and the applicability of the reaction to other alkenyl heteroaromatic compounds are now under investigation in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Experimental details and characterization data of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) West, R.; Gaspar, P. P. In *The Chemistry of Organic Silicon Compounds*; Rappoport, Z.; Apeloig, Y., Eds.; Wiley: Weinheim, 1998; Vol. 2, p 2463.

(2) For recent reviews, see: (a) Tokitoh, N.; Okazaki, R. *Coord. Chem. Rev.* **2000**, *210*, 251. (b) Hill, N. J.; West, R. *J. Organomet. Chem.* **2004**, *689*, 4165. (c) Kira, M.; Iwamoto, T.; Ishida, S. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 258. (d) Takeda, N.; Tokitoh, N. *Synlett* **2007**, 2483. (e) Mizuhata, Y.; Sasamori, T.; Tokitoh, N. *Chem. Rev.* **2009**, *109*, 3479.

(3) For catalytic silylene transfer to alkynes, see: (a) Okinoshima, H.; Yamamoto, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 9263. (b) Okinoshima, H.; Yamamoto, K.; Kumada, M. *J. Organomet. Chem.* **1975**, *86*, C27. (c) Sakurai, H.; Kamiyama, Y.; Nakadaira, Y. *J. Am. Chem. Soc.* **1977**, *99*, 3879. (d) Seyferth, D.; Duncan, D. P.; Vick, S. C. *J. Organomet. Chem.* **1977**, *125*, C5. (e) Seyferth, D.; Vick, S. C.; Shannon, M. L.; Lim, T. F. O.; Duncan, D. P. *J. Organomet. Chem.* **1977**, *135*, C37. (f) Ishikawa, M.; Sugisawa, H.; Harata, O.; Kumada, M. *J. Organomet. Chem.* **1981**, *217*, 43. (g) Seyferth, D.; Vick, S. C.; Shannon, M. L. *Organometallics* **1984**, *3*, 1897. (h) Ishikawa, M.; Matsuzawa, S.; Hirotsu, K.; Kamitori, S.; Higuchi, T. *Organometallics* **1984**, *3*, 1930. (i) Schäfer, A.; Weidenbruch, M.; Pohl, S. *J. Organomet. Chem.* **1985**, *282*, 305. (j) Seyferth, D.; Shannon, M. L.; Vick, S. C.; Lim, T. F. O. *Organometallics* **1985**, *4*, 57. (k) Ishikawa, M.; Matsuzawa, S.; Higuchi, T.; Kamitori, S.; Hirotsu, K. *Organometallics* **1985**, *4*, 2040. (l) Tamao, K.; Yamaguchi, S.; Shiozaki, M.; Nakagawa, Y.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 5867. (m) Ikenaga, K.; Hiramatsu, K.; Nasaka, N.; Matsumoto, S. *J. Org. Chem.* **1993**, *58*, 5045. (n) Belzner, J.; Ihmels, H. *Tetrahedron Lett.* **1993**, *34*, 6541. (o) Ojima, I.; Fracchiolla, D. A.; Donovan, R. J.; Banerji, P. *J. Org. Chem.* **1994**, *59*, 7594. (p) Tanaka, Y.; Yamashita, H.; Tanaka, M. *Organometallics* **1995**, *14*, 530. (q) Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 1097. (r) Palmer, W. S.; Woerpel, K. A. *Organometallics* **1997**, *16*, 4824. (s) Palmer, W. S.; Woerpel, K. A. *Organometallics* **2001**, *20*, 3691. (t) Clark, T. B.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9522.

(4) For catalytic silylene transfer to 1,3-dienes, see: (a) Seyferth, D.; Shannon, M. L.; Vick, S. C.; Lim, T. F. O. *Organometallics* **1985**, *4*, 57. (b) Ohshita, J.; Ishikawa, M. *J. Organomet. Chem.* **1991**, *407*, 157.

(5) For catalytic silylene transfer to alkenes, see: (a) Ćiraković, J.; Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 9370. (b) Driver, T. G.; Woerpel, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 9993. (c) Ćiraković, J.; Driver, T. G.; Woerpel, K. A. *J. Org. Chem.* **2004**, *69*, 4007.

(6) For catalytic silylene transfer to α,β-unsaturated carbonyl compounds, see: (a) Calad, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 2046. (b) Nevárez, Z.; Woerpel, K. A. *Org. Lett.* **2007**, *9*, 3773. (c) Okamoto, K.; Hayashi, T. *Org. Lett.* **2007**, *9*, 5067. (d) Okamoto, K.; Hayashi, T. *Chem. Lett.* **2008**, *37*, 108.

(7) For catalytic silylene transfer to allylic ethers, see: Bourque, L. E.; Cleary, P. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 12602.

(8) (a) Ohmura, T.; Masuda, K.; Suginome, M. *J. Am. Chem. Soc.* **2008**, *130*, 1526. (b) Ohmura, T.; Masuda, K.; Takase, I.; Suginome, M. *J. Am. Chem. Soc.* **2009**, *131*, 16624. For our recent account, see:(c) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29.

(9) Examples on dearomatizing conversion of benzene derivatives with silylene in the absence of transition metal catalysts: (a) Belzner, J.; Ihmels, H.; Kneisel, B. O.; Gould, R. O.; Herbst-Irmer, R. *Organometallics* **1995**, *14*, 305. (b) Belzner, J.; Dehnert, U.; Ihmels, H. *Tetrahedron* **2001**, *57*, 511. (c) Kira, M.; Ishida, S.; Iwamoto, T.; Kabuto, C. *J. Am. Chem. Soc.* **2002**, *124*, 3830.

(10) Ohmura, T.; Masuda, K.; Furukawa, H.; Suginome, M. *Organometallics* **2007**, *26*, 1291.

(11) An attempt to synthesize **5a** failed even in the reaction of **1a** using 1.0 equiv of **2**. The reaction gave **3a** (38% based on **1a**) and **4** (94%) with a small amount of **5a**, which was detected in GC-MS analysis of the crude mixture.

(12) Screening of some quinones including DDQ and *p*-chloranil indicated that *p*-bromanil was the most suitable reagent for the oxidation of **5l**. For properties of activated quinines, see: Fujita, M.; Fukuzumi, S.; Matsubayashi, G.; Otera, J. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1107.

(13) Significant decomposition of **6** was observed when the reaction was carried out without BSA. For DDQ oxidation in the presence of BSA, see: Ryu, I.; Murai, S.; Hatayama, Y.; Sonoda, N. *Tetrahedron Lett.* **1978**, *19*, 3455.

(14) For oxidative addition of Si−B bond to Pt(0), see: Sagawa, T.; Asano, Y.; Ozawa, F. *Organometallics* **2002**, *21*, 5879.

(15) Examples of isolated $L_2M{=}SiR_2$ (M = Pt, Pd, Ni; L = tertiary phosphine) complexes: (a) Feldman, J. D.; Mitchell, G. P.; Nolte, J.-O.; Tilley, T. D. *J. Am. Chem. Soc.* **1998**, *120*, 11184. (b) Feldman, J. D.; Mitchell, G. P.; Nolte, J.-O.; Tilley, T. D. *Can. J. Chem.* **2003**, *81*, 1127. (c) Watanabe, C.; Inagawa, Y.; Iwamoto, T.; Kira, M. *Dalton Trans.* **2010**, *39*, 9414. For reviews on silylene−transition metal complexes, see:(d) Okazaki, M.; Tobita, H.; Ogino, H. *Dalton Trans.* **2003**, 493. (e) Waterman, R.; Hayes, P. G.; Tilley, T. D. *Acc. Chem. Res.* **2007**, *40*, 712.

(16) For conversion of (hydride)(silylene)M to (hydrosilyl)M, see: Watanabe, T.; Hashimoto, H.; Tobita, H. *Angew. Chem., Int. Ed.* **2004**, *43*, 218.