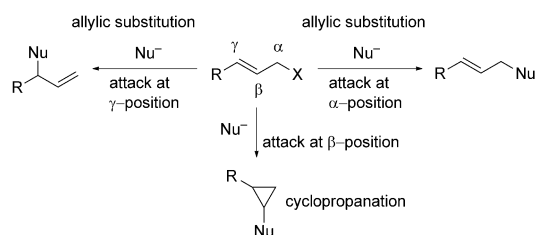


Silylative Cyclopropanation of Allyl Phosphates with Silylboronates**

Ryo Shintani,* Ryuhei Fujie, Momotaro Takeda, and Kyoko Nozaki*

Abstract: A potassium-bis(trimethylsilyl)amide-mediated cyclopropanation of allyl phosphates with silylboronates has been developed. Unlike the reported copper-catalyzed allylic substitution reactions, the nucleophile selectively attacks at the β -position of the allylic substrates under the present reaction conditions. The mechanism of this process has also been investigated, thus indicating the involvement of a silylpotassium species as the active nucleophilic component.

Changing the existing reaction patterns to unusual ones by adding catalysts or reagents represents a powerful approach to the development of new synthetic methods in organic chemistry. In this regard, the nucleophilic attack on an allylic electrophile at its β -position, rather than at the usual α - or γ -position, could lead to cyclopropanes instead of the allylic substitution products (Scheme 1). Except for the use of

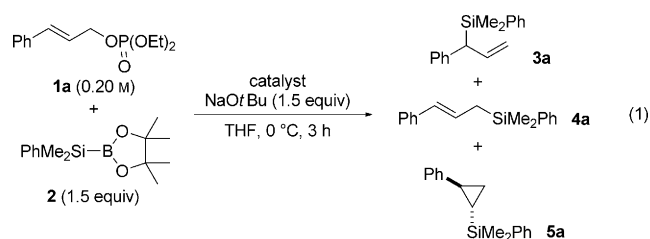


Scheme 1. Allylic substitution versus cyclopropanation in the nucleophilic attack to an allylic electrophile.

Michael acceptors (R = electron-withdrawing group in Scheme 1),^[1,2] which electronically facilitate the selective attack of a nucleophile at the β -position, a limited number of methods have been developed to date for cyclopropanation of less electronically biased allylic electrophiles (e.g., R = aryl, alkyl, H, etc.). For example, palladium-mediated^[3] or palladium-catalyzed^[4] cyclopropanation through π -allylpalladium

intermediates have been reported by using enolate-based carbon nucleophiles for intermolecular reactions, as well as nitrogen^[5] and oxygen^[6] nucleophiles for intramolecular cyclization reactions, but the use of other heteroatom nucleophiles has been scarcely explored. In fact, a copper-catalyzed intermolecular borylative cyclopropanation^[7] and an intramolecular silylative cyclopropanation using elaborate (allyloxy)silyllithiums generated in situ^[8] have only been reported as far as we are aware. In this context, we herein describe the development of a potassium-bis(trimethylsilyl)-amide-mediated carbon–silicon bond-forming cyclopropanation of allyl phosphates with silylboronates, in the absence of any transition-metal catalysts, to provide straightforward access to silicon-containing cyclopropanes with high selectivity.

The reaction of allyl phosphates with silylboronates is known to be promoted by copper catalysts in the presence of a metal alkoxide or hydroxide base to give allylsilanes as the product through an allylic substitution pathway.^[9,10] During the course of our study on the effect of a base on this copper catalysis, we unexpectedly found that a silylative cyclopropanation through nucleophilic attack at the β -position could take place when no copper catalysts were employed. Thus, a reaction of cinnamyl diethyl phosphate (**1a**) with 1.5 equivalents of the silylboronate **2**^[11,12] in the presence of 5 mol % of CuI and 1.5 equivalents of NaOtBu in THF at 0 °C gave only allylic substitution products as a mixture of the γ -substitution product **3a** (34 % yield) and α -substitution product **4a** (51 % yield) as shown in Equation (1) (THF = tetrahydrofuran).



catalyst = CuI (5 mol %): **3a** 34%, **4a** 51%, **5a** 0%
catalyst = none: **3a** 0%, **4a** 17%, **5a** 51%

In contrast, when this reaction was conducted in the absence of a copper catalyst under otherwise identical conditions, the cyclopropane *trans*-**5a** was obtained as the major product (51 % yield) along with **4a** (17 % yield).^[13] Subsequently, we found that the use of KOtBu^[14] instead of NaOtBu improved the selectivity towards **5a** (Table 1, entry 1 versus entry 2), and high selectivity of **5a** was realized by employing KN(SiMe₃)₂^[15] (**5a/4a** = 99:1; entry 3). In comparison, the use of the related NaN(SiMe₃)₂ or LiN(SiMe₃)₂ resulted in somewhat lower selectivity of **5a** (entries 4 and 5). In addition, the use of a phosphate as the leaving group

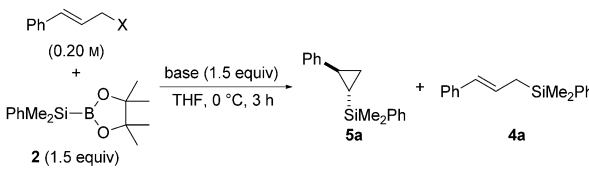
[*] Dr. R. Shintani, R. Fujie, Prof. Dr. K. Nozaki
Department of Chemistry and Biotechnology
Graduate School of Engineering, The University of Tokyo
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656 (Japan)
E-mail: shintani@chembio.t.u-tokyo.ac.jp
nozaki@chembio.t.u-tokyo.ac.jp

Dr. M. Takeda
Department of Chemistry, Graduate School of Science
Kyoto University, Kyoto 606-8502 (Japan)

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Table 1: Silylative cyclopropanation versus allylic substitution: Effect of bases and leaving groups.

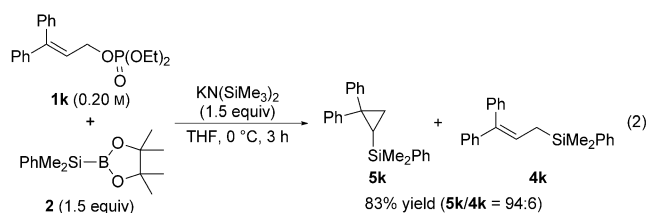


Entry	Substrate	Base	Yield [%] ^[a] 5a + 4a	5a/4a ^[a]
1	1a (X=OP(O)(OEt) ₂)	NaOtBu	68	75:25
2	1a	KOtBu	54	85:15
3	1a	KN(SiMe ₃) ₂	77	99:1
4	1a	NaN(SiMe ₃) ₂	83	77:23
5	1a	LiN(SiMe ₃) ₂	57	78:22
6	6 (X=Cl)	KN(SiMe ₃) ₂	22	< 1:99
7	7 (X=OCO ₂ Et)	KN(SiMe ₃) ₂	0	—

[a] Determined by ¹H NMR spectroscopy.

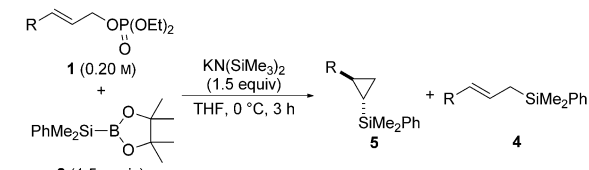
was essential for the present silylative cyclopropanation. For example, cinnamyl chloride (**6**) gave only **4a** in 22% yield (entry 6) and cinnamyl ethyl carbonate (**7**) did not give any substitution or cyclopropanation products because of the decomposition of **7** under these reaction conditions (entry 7).

Under the reaction conditions described in Table 1, entry 3, several substituted phenyl groups are tolerated at the γ -position of allyl phosphates **1** for the reaction with **2** to give the corresponding cyclopropanes **5** as the major product, although the use of the electron-rich substrate **1e** results in somewhat lower selectivity (Table 2, entries 2–5). Substrates with naphthyl, thienyl, pyridyl, or alkenyl groups can also be employed with high selectivity toward the cyclopropanes **5**, albeit in a low yield for the pyridyl cyclopropane **5i** because of the partial decomposition of **1i** during the reaction (**5/4** $\geq$ 92:8; entries 6–10).^[16] In addition to these γ -monosubstituted allyl phosphates, the γ,γ -disubstituted allyl phosphate **1k** is a suitable substrate and provides the cyclopropane **5k** selectively over the allylsilane **4k** in 83% combined yield as shown in Equation (2).



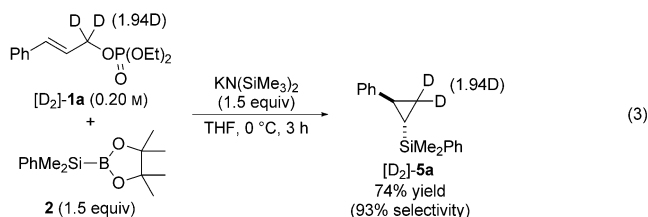
Having established the potassium bis(trimethylsilyl)-amide-mediated silylative cyclopropanation of allyl phosphates with a silylboronate, we turned our attention to understanding how this reaction takes place. At first, we confirmed that the silylation does occur at the β -position of allyl phosphates by employing the α,α -bis(deuterated) substrate [D₂]-**1a** as illustrated in Equation (3). To gain insights into the nature of the active nucleophilic component, we

Table 2: Silylative cyclopropanation of the allyl phosphates **1** with silylboronate **2**: Scope.



Entry	R	5 ^[a]	Yield [%] ^[b] 5 + 4	5/4 ^[c]
1	Ph (1a)	5a	71	99:1
2	Ph-Ph (1b)	5b	75	99:1
3	Ph-Cl (1c)	5c	68 ^[d]	> 99:1
4	Ph-OMe (1d)	5d	75	99:1
5	Ph-O-Ph (1e)	5e	79	77:23
6	Ph-Ph-Ph (1f)	5f	73	96:4
7	Ph-Ph-Ph (1g)	5g	84	96:4
8	Ph-S-Ph (1h)	5h	63	99:1
9 ^[e]	Ph-pyridyl (1i)	5i	38 ^[f]	92:8
10 ^[g]	Ph-alkenyl (1j)	5j ^[h]	71	93:7

[a] Obtained as a *trans* isomer unless otherwise noted. [b] Yield of isolated product. [c] Determined by ¹H NMR spectroscopy. [d] Calculated yield of **5c** after silica gel chromatography (contained inseparable PhMe₂SiSiMe₂Ph; 10% based on **2**). [e] The reaction was conducted at –20 °C for 4.5 h. [f] Yield of **5i** + **4i** as determined by ¹H NMR analysis after silica gel chromatography. [g] The reaction was conducted at –20 °C for 6 h. [h] **5j** was obtained as a mixture of *trans/cis* = 94:6.



monitored a [D₈]THF solution of a 1:1 mixture of silylboronate **2** and potassium bis(trimethylsilyl)amide by ¹¹B NMR spectroscopy at 0 °C [Eq. (4)]. As a result, two broad peaks at δ = 8.4 and 25.0 ppm were observed with the area ratio of 1:1.4. Based on the relevant literature precedents,^[13b,c,17] these peaks could be assigned as tetracoordinated anionic boron species **8** and the desilylated three-coordinate boron species **9**,

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