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Stereoselective Synthesis of Allylsilanes Bearing Tetrasubstituted Olefin via 2,2-Diborylethylsilane

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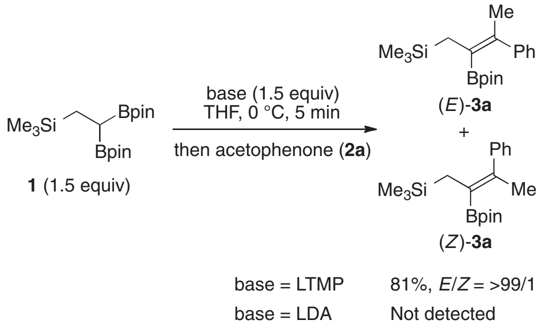
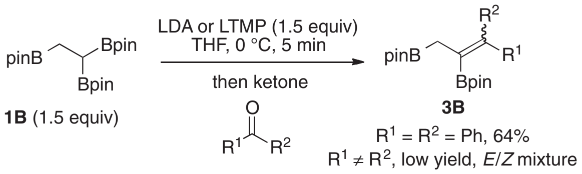
The regio- and stereoselective synthesis of allylsilane derivatives bearing a tetrasubstituted olefin was achieved using 2,2-diborylethylsilane as a key intermediate. The regioselective deprotonation of a 2,2-diborylethylsilane with LTMP and the subsequent nucleophilic addition to ketones gave corresponding allylsilanes in good to excellent yield with excellent stereoselectivity.

Allylation intermediates are important synthons for the synthesis of various functionalized molecules. There have been many efforts to synthesize easily available allylation reagents, such as allylboranes and allylsilanes.[1] Despite their attractive features as an allylic intermediate, there are not many examples to synthesize an allylborane or an allylsilane bearing a tetrasubstituted olefin.[2] We previously reported the highly stereoselective synthesis of tetrasubstituted alkenylboronates via the deprotonation/nucleophilic addition of 1,1-diborylalkanes[3] to ketones.[4] DFT calculations can support the stereoselective *syn*-elimination after nucleophilic addition of 1,1-diborylalkanes to ketones. As a part of our studies, we are interested in the stereoselective synthesis of an allylborane or an allylsilane bearing a tetrasubstituted alkenylboronate moiety. We describe here the stereoselective synthesis of allylsilanes bearing a tetrasubstituted olefin via the nucleophilic addition of a 2,2-diborylethylsilane to ketones, which could not be obtained via other conventional approaches.

The deprotonation of 2,2-diborylethylsilane **1** using a base and the subsequent nucleophilic addition to acetophenone (**2a**) was carried out (Scheme 1). To our delight, the regioselective deprotonation of 2,2-diborylethylsilane **1** using lithium 2,2,6,6-tetramethylpiperazide (LTMP) and the following nucleophilic addition to acetophenone (**2a**) occurred to give the corresponding product (*E*)-**3a** in 81% yield.[5] In contrast, the use of lithium diisopropylamide (LDA) as a base did not give the desired product **3a** at all. The geometry of **3a** was confirmed by NOESY experiment. We carefully checked the crude products, but the stereoisomer (*Z*)-**3a** could not be detected. The tentative reaction using ethane-1,1,2-triboronate **1B** and benzophenone mediated by LDA gave the corresponding product **3B** in moderate yield; the use of LTMP gave a lower yield (Scheme 2). Furthermore, the reaction of unsymmetrical ketones mediated by LDA or LTMP gave products in low yields as a mixture of stereoisomers along with unidentified by-products; the examination of reaction conditions did not improve the yields and stereoselectivities. Thus, we focus on the reaction of 2,2-diborylethylsilane **1** and ketones using LTMP.



Scheme 1. Addition of 2,2-diborylethylsilane.



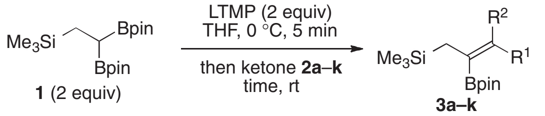
Scheme 2. Addition of ethane-1,1,2-triboronate.

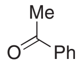
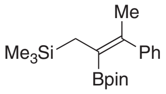
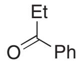
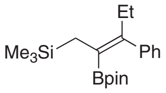
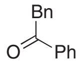
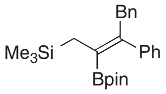
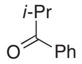
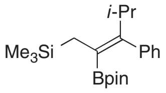
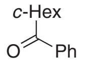
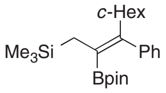
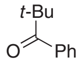
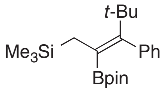
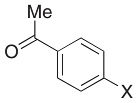
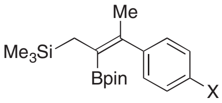
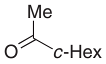
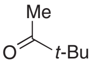
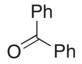
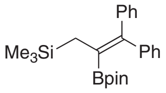
The optimized conditions using **1** (2 equiv) and LTMP (2 equiv) achieved good to excellent yields of allylsilanes using aryl ketones (Table 1).[6] The reaction using phenyl ketones **2a**–**2f** realized excellent stereoselectivities (Entries 1–6). The electron-withdrawing group or -donating group could be compatible to give the corresponding products **3g** and **3h** in moderate to high yields, respectively (Entries 7 and 8). Although the reaction using a 1,1-diborylalkane and an aliphatic ketone gave a desired product as shown in our previous report,[3] the reaction using 2,2-diborylethylsilane **1** and aliphatic ketones, such as **2i** and **2j** gave unidentified by-products in each case (Entries 9 and 10). The symmetric ketone, benzophenone (**2k**), gave the desired product **3k** in excellent yield (Entry 11).

We tested the Suzuki–Miyaura cross-coupling reaction of the product **3c** in the presence of Pd-catalyst (Scheme 3). The coupling reaction with 4-iodoanisole in the presence of $[Pd(PPh_3)_4]$ (5 mol %) and KOH (2.2 equiv) at 60 °C gave the desired product **4** in 55% isolated yield. The trimethylsilyl moiety was intact under the present reaction conditions. The present demonstration represents the synthetic utility for further transformations.

A DFT computation study was performed at the B3LYP/6-31G* level of theory to identify the stereoselectivity (Figure 1).[7] Typical models for lithium alkoxide intermediates, **Int-1** and **Int-2**, are described after the nucleophilic addition to acetophe-

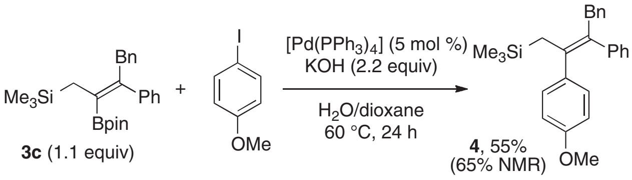
Table 1. Scope of ketones



Entry	Ketone	Time/h	Product	Yield/%[a,b]
1	 **2a**	1	 (*E*)-**3a**	98
2	 **2b**	1	 (*E*)-**3b**[c]	96
3	 **2c**	17	 (*E*)-**3c**	92
4	 **2d**	1	 (*E*)-**3d**	98
5	 **2e**	1.5	 (*E*)-**3e**	74
6	 **2f**	1	 (*E*)-**3f**	71
7	 **2g**, X = CF_3	5	 (*E*)-**3g**	87
8	**2h**, X = OMe	6	(*E*)-**3h**	52
9	 **2i**	9		C. M.[b]
10	 **2j**	9		C. M.[b]
11	 **2k**	1	 **3k**	98

[a]Isolated yields. The geometries were confirmed by NOESY analysis. [b]Complex mixture.

none (**2a**). The intramolecular coordination of the oxygen atom in the pinacolboryl group to the lithium atom is feasible; the optimized geometries gave **OG-1** and **OG-2**, respectively. Therefore, the rotation to path (A) should be predominant and realized the *syn*-elimination through LiO–C–C–B^2 to give



Scheme 3. Suzuki–Miyaura cross-coupling of **3c**.

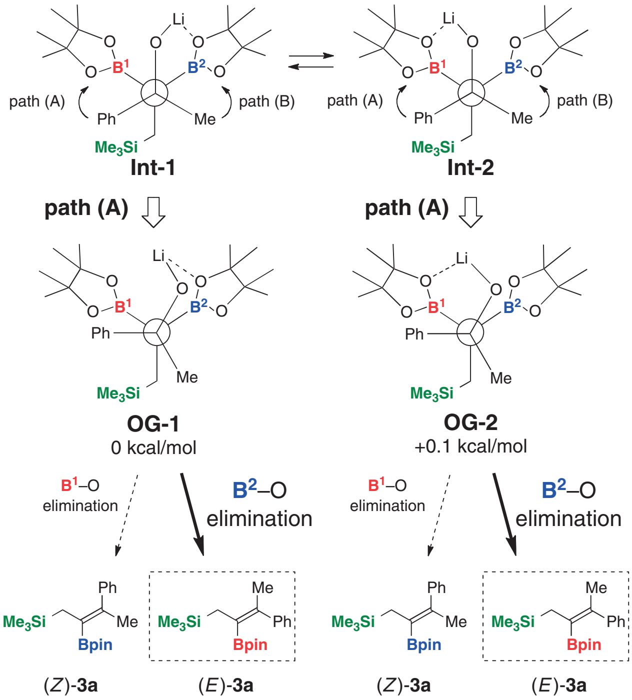


Figure 1. DFT calculations of *syn*-elimination for 2,2-diborylethylsilane (B3LYP/6-31G*).

(*E*)-**3a**. In contrast, DFT calculations of optimized geometries derived from ethane-1,1,2-triboronate **1B** showed that the reaction leads to a mixture of stereoisomers (see the Supporting Information[8]). Further examination of the optimization of four-membered borate intermediates before *syn*-elimination were performed (Figure 2).[9] As a result, the relative energy of ***syn-E*** was 1.8 kcal mol^{-1} higher than that of ***syn-Z***, and the relative energy of (*E*)-**3a** was 0.6 kcal mol^{-1} higher than that of (*Z*)-**3a**. Thus, (*Z*)-**3a** should be obtained as a major isomer because of the thermodynamic stability of borate intermediate ***syn-Z*** and product (*Z*)-**3a**. In this context, the stereoselectivity could be determined at the chelation intermediates **OG-1** and **OG-2** due to its predominant stability.

In conclusion, we have demonstrated the stereoselective synthesis of allylsilanes bearing a tetrasubstituted olefinic moiety derived from 2,2-diborylethylsilane. The use of aromatic ketones gave the desired products with excellent stereoselectivity. In contrast, the reaction of ethane-1,1,2-triboronate gave poor results in yield and stereoselectivity. DFT calculations support their stereoselectivities, although the influence of the silyl moiety in 2,2-diborylethylsilane **1** and boron moiety in ethane-1,1,2-triboronate **1B** was not fully elucidated. We demonstrated the Suzuki–Miyaura cross-coupling reaction of the

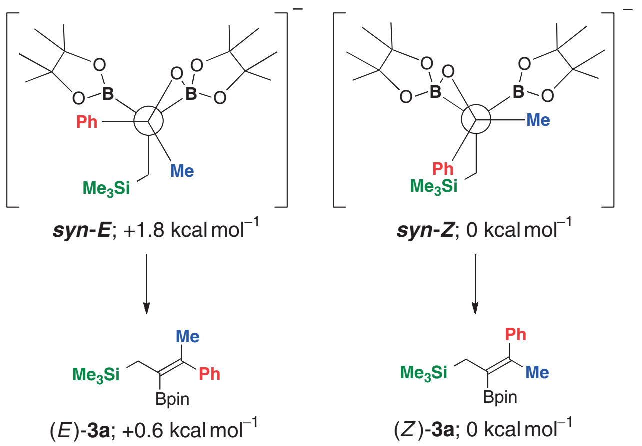


Figure 2. DFT calculations of borate intermediates and products (B3LYP/6-31G*).

allylsilane and the silyl moiety was intact in the coupling product. The further development of products as synthetic intermediates are underway in our laboratory.

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6 The reaction of benzaldehyde gave a mixture of stereoisomers in 59% yield, ca. 2/1 ratio of major and minor isomers.

7 The DFT computational calculations were performed using the Spartan'08 suite for Mac (Wave function, Inc.). Zero-point vibrational energies (ZPEs) were calculated for all structures, and the geometry was verified as true minima using frequency analysis.

8 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

9 The DFT calculations at the B3LYP/6-31+G* level of theory gave similar results, indicating that ***syn-Z*** should be more stable than ***syn-E***.