Palladium-Catalyzed Intramolecular Bis-Silylation of Propargylic Alcohols: A New Stereospecific Access to Chiral Allenylsilanes

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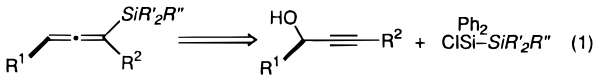
Organic silicon compounds now play indispensable roles in organic synthesis. Hence, development of the methodologies for the stereoselective synthesis of organosilicon compounds has been highly desired from the viewpoint of synthetic organic chemistry.[1]

We have developed bis-silylation of carbon−carbon multiple bonds on the basis of the activation of the Si−Si bonds by a palladium−*tert*-alkyl isocyanide catalyst.[2,3] Very recently, we reported a new synthesis of highly enantioenriched (*E*)-allylsilanes from chiral allylic alcohols with nearly complete overall 1,3-transfer of the chirality.[4] The new synthesis involved diastereoselective intramolecular bis-silylation of carbon−carbon double bonds and subsequent Peterson-type *syn*-elimination. In this paper, we describe a new synthesis of allenylsilanes, which are useful for the synthesis of heterocyclic compounds[5] as well as homopropargylic alcohols,[6] through intramolecular bis-silylation of propargylic alcohols catalyzed by the palladium−isocyanide catalyst.

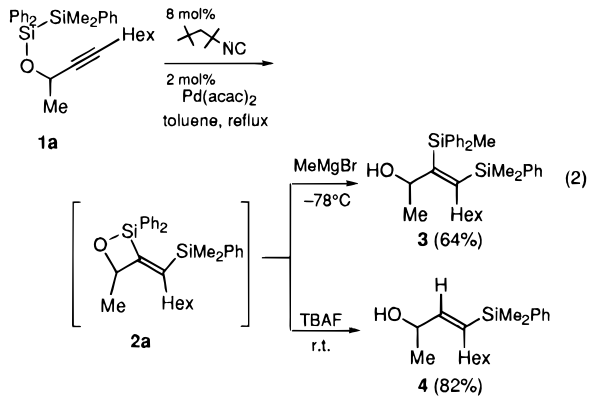
The combination of the intramolecular *cis*-addition of the Si−Si bonds across the carbon−carbon triple bond and subsequent Peterson-type *syn*-elimination successfully led to the stereospecific synthesis of highly enantioenriched allenylsilane (eq 1). A Lewis acid-promoted



(1)

reaction of the optically active allenylsilane thus prepared with aldehyde proceeded stereoselectively to give homopropargylic alcohols with high enantiopurity. In the course of the overall transformation, the chirality of the starting propargylic alcohol was nearly completely transferred to the homopropargylic alcohol.

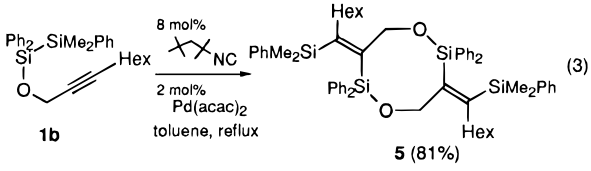
A toluene solution of disilanyl ether **1a** derived from 3-decyn-2-ol was heated in the presence of the palladium catalyst prepared from $Pd(acac)_2$ (2 mol %) and 1,1,3,3-tetramethylbutyl isocyanide (8 mol %) under nitrogen. Intramolecular addition of the Si−Si bond across the carbon−carbon triple bond took place in refluxing toluene for 1 h to give four-membered product **2a** nearly quantitatively. Though the formation of **2a** could be confirmed by ^1H and ^{13}C NMR analyses of the reaction mixture, instability of **2a** prevented its isolation by chromatography on silica gel or by distillation. The Si−O bond in the strained four-membered ring of **2a** was readily cleaved by Grignard reagent at −78 °C to give a ring-opening product **3** (eq 2).[7] Cyclic **2a** also underwent



(2)

protiodesilylation at the silicon atom in the ring by an addition of tetrabutylammonium fluoride (TBAF) to give alcohol **4** in good yield. For the bis-silylation of **1a**, a catalyst prepared from $Pd_2(dba)_3CHCl_3$ (dba = dibenzylideneacetone) and bicyclic phosphate, $P(OCH_2)_3CEt$,[8] was also effective, while the use of a tetrakis(triphenylphosphine)palladium(0) complex catalyst resulted in sluggish reaction (6 h, <40% conversion), being accompanied by unidentified byproducts.

A reaction of disilanyl ether **1b** derived from primary propargylic alcohol afforded eight-membered ring product **5**, which may result from intramolecular bis-silylation followed by dimerization of the resultant four-membered ring product, in good yield (eq 3).[9] Unstrained dimer **5** failed to react with the Grignard reagent under the conditions employed for the reaction of four-membered ring **2**.



(3)

Noteworthy is that the four-membered **2a**, formed by the palladium-catalyzed reaction of **1a**, was found to be

(1) (a) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293−1316. (b) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375−1408. (c) Fleming, I.; Dunogués, J.; Smithers, R. *Org. React.* **1989**, *37*, 57−588.

(2) For carbon−carbon double bonds, see: (a) Suginome, M.; Yamamoto, Y.; Fujii, K.; Ito, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9608−9609. (b) Suginome, M.; Matsumoto, A.; Nagata, K.; Ito, Y. *J. Organomet. Chem.* **1995**, 499, C1−C3. (c) Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487−6498. (d) Murakami, M.; Andersson, P. G.; Suginome, M.; Ito, Y. *J. Am. Chem. Soc.* **1991**, *113*, 3987−3988.

(3) For carbon−carbon triple bonds, see: (a) Murakami, M.; Suginome, M.; Fujimoto, K.; Ito, Y. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1473−1475. (b) Murakami, M.; Oike, H.; Sugawara, M.; Suginome, M.; Ito, Y. *Tetrahedron* **1993**, *49*, 3933−3946. (c) Ito, Y.; Suginome, M.; Murakami, M. *J. Org. Chem.* **1991**, *56*, 1948−1951.

(4) Suginome, M.; Matsumoto, A.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3061−3062.

(5) (a) Becker, D. A.; Danheiser, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 389−391. (b) Danheiser, R. L.; Kwasigroch, C. A.; Tsai, Y.-M. *J. Am. Chem. Soc.* **1985**, *107*, 7233−7235. (c) Danheiser, R. L.; Carini, D. J.; Basak, A. *J. Am. Chem. Soc.* **1981**, *103*, 1604−1606.

(6) (a) Danheiser, R. L.; Carini, D. J.; Kwasigroch, C. A. *J. Org. Chem.* **1986**, *51*, 3870−3878. (b) Danheiser, R. L.; Carini, D. J. *J. Org. Chem.* **1980**, *45*, 3927−3929.

(7) The MeMgBr reaction did not lead to the formation of an allenylsilane even on warming the reaction mixture at room temperature.

(8) The catalytic system was also reported to be effective for bis-silylation of carbon−carbon triple bonds. Yamashita, H.; Catellani, M.; Tanaka, M. *Chem. Lett.* **1991**, 241−244.

(9) Disubstituted alkynes hardly undergo intermolecular bis-silylation under the conditions; see ref 3.

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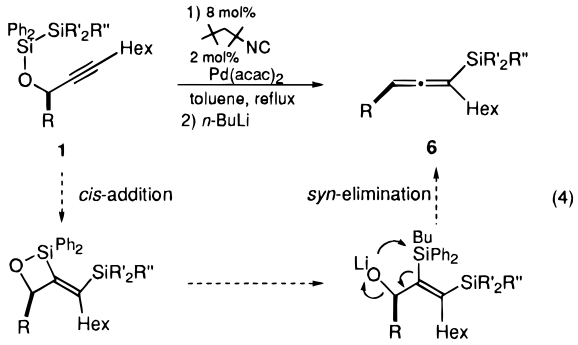
Table 1. One-Pot Synthesis of Allenylsilanes 6 from 1

entry	R	SiR'_2R''	**6** (yield, %)
1[a]	Me	$SiMe_2Ph$	**6a** (86)
2[a]	Me	$SiMe_2Bu$-*t*	**6c** (95)
3[b]	Me	$SiMe_3$	**6d** (79)
4[a]	*c*-hex	$SiMe_2Ph$	**6e** (81)
5[b]	*c*-hex	$SiMe_3$	**6f** (85)
6[b]	Ph	$SiMe_2Ph$	**6g** (94)

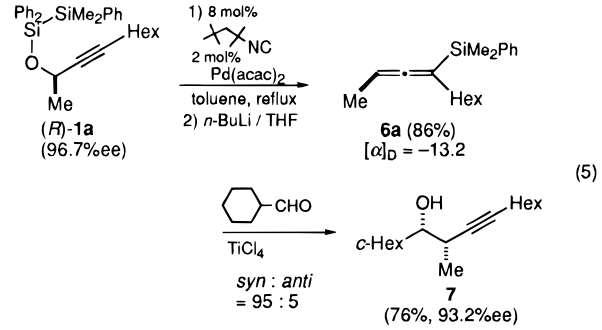
[a] Addition of *n*-BuLi was carried out at 0 °C after toluene was replaced by THF. [b] Addition of *n*-BuLi at −78 °C in toluene was followed by addition of THF.

transformed to allenylsilane **6a** in high yield by treatment with *n*-BuLi in THF (eq 4; Table 1, entry 1). The



formation of **6a** is rationalized by a nucleophilic attack of *n*-BuLi onto the ring-silicon atom of **2a** followed by Peterson-type *syn*-elimination of the silanolate *n*-$BuPh_2SiO^-$.[10,11] Synthesis of various allenylsilanes was summarized in Table 1.[12] In the syntheses of Me_3Si derivatives **6d** and **f**, addition of *n*-BuLi (in hexane) to the THF solution of **2d** and **f** caused undesired nucleophilic attack onto the silicon atom of the Me_3Si group to lower the yields of allenylsilanes. This side reaction was suppressed by a slightly modified procedure, in which an addition of slight excess of *n*-BuLi (in hexane) was carried out in toluene followed by dilution with THF at −78 °C.[13] Stirring the reaction mixture at 0 °C resulted in selective elimination of the silanolate to give allenylsilanes, but the elimination reaction proceeded very sluggishly at −78 °C. According to the modified procedure, allenylsilane **6g** with the phenyl group γ to the silicon substituent was prepared in high yield.

Next, synthesis of highly enantioenriched allenylsilanes starting from chiral propargylic alcohols was successfully achieved (eq 5). Disilanyl ether (*R*)-**1a** with



96.7% ee was reacted according to the procedure described above to give allenylsilanes **6a**, which showed specific rotation of $[\alpha]^{20}_D = -13.2$ ($c = 1.7$, benzene).[14] A $TiCl_4$-mediated reaction of the enantioenriched **6a** with cyclohexanecarboxaldehyde under the conditions reported by Danheiser et al. gave *syn*-homopropargylic alcohol **7** with high diastereoselectivity (95:5).[6] The enantiomeric excess of **7** was determined to be 93.2% ee,[15] indicating that the formation and subsequent reaction of allenylsilane **6a** occurred with >95% stereoselectivity. It is presumed that allenylsilane **6a** with (*R*) configuration was formed via two stereospecific processes, i.e., *cis*-addition of the Si−Si bond to the carbon−carbon triple bond and *syn*-elimination of the silanolate. Probably, subsequent reaction with the aldehyde occurs with high stereoselectivity at the π-face anti to the silyl group to give (1*S*,2*S*)-**7** with high enantiomeric excess, though determination of the absolute configuration of **7** is now underway.

The methodology described herein may make possible a general preparation of highly enantiomerically enriched allenylsilanes from optically active propargylic alcohols.[16]

Supporting Information Available: Detailed experimental procedures and characterization of the new compounds, including ^1H and ^{13}C spectra of intermediate **2a** (7 pages).

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(10) Peterson, D. J. *J. Org. Chem.* **1968**, *33*, 780−784.

(11) In contrast, similar Peterson elimination of *O*-lithio-2-(triphenylsilyl)tridecen-3-ol, prepared by the reaction of undecanal with [α-(triphenylsilyl)vinyl]lithium, was reported not to proceed at room temperature in ether. Chan, T. H.; Mychajlowskij, W.; Ong, B. S.; Harpp, D. N. *J. Org. Chem.* **1978**, *43*, 1526−1532.

(12) For the convenient synthesis of chlorodisilanes via (diethylamino)diphenylsilyllithium, see: (a) Tamao, K.; Kawachi, A.; Nakagawa, Y.; Ito, Y. *J. Organomet. Chem.* **1994**, *473*, 29−34. (b) Tamao, K.; Kawachi, A.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 3989−3990.

(13) This procedure is generally applicable for the synthesis of allenylsilanes. General procedure: To a catalyst prepared from $Pd(acac)_2$ (2.5 mg, 8.2 μmol) and 1,1,3,3-tetramethylbutyl isocyanide (4.6 mg, 33 μmol) in toluene (1 mL) was added disilanyl ether **1** (0.41 mmol) at room temperature. The mixture was stirred under reflux (bath temperature = 120 °C) for 1 h and then cooled to −78 °C. A hexane solution of *n*-BuLi (0.43 mmol) was added at −78 °C and then stirred for 20 min. To the mixture was added THF (2 mL) at −78 °C, and the mixture was allowed to react at 0 °C for 30 min. Extractive workup with ether followed by column chromatography on silica gel (hexane) afforded allenylsilanes **6** in the yields indicated in Table 1.

(14) Several attempts at determination of the enantiomeric excess of the optically active allenylsilane by HPLC or GC with chiral stationary phase have failed so far.

(15) Enantiomeric excess was determined by HPLC analysis with a chiral stationary phase column, SUMICHIRAL OA-4500.

(16) An enantiomerically enriched allenylsilane with an additional stereogenic center α to the allenyl moiety was synthesized by S_N2' displacement of a chiral alkynyloxirane with an organocuprate. Marshall, J. A.; Tang, Y. *J. Org. Chem.* **1994**, *59*, 1457−1464.