[1,5]-Anion Relay/[2,3]-Wittig Rearrangement of 3,3-Bis(silyl) Allyl Enol Ethers: Synthesis of Useful Vinyl Bis(silane) Species
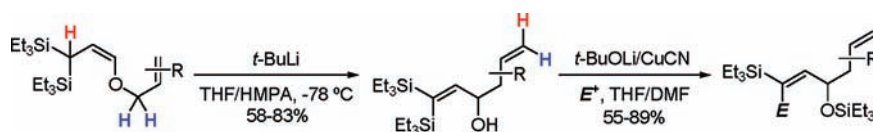
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ABSTRACT

The [1,5]-anion relay/[2,3]-Wittig rearrangement of 3,3-bis(silyl) enol allyl ethers has been developed. This reaction provides an efficient method to synthesize versatile vinyl bissilanes, which can be transformed into trisubstituted vinylsilanes through a [1,4]-Brook rearrangement/alkylation protocol using a wide range of electrophiles.

Bis(silyl) compounds[1] are a special type of organosilane[2] in organic synthesis. Although their great potential for bifunctional reactivity makes them attractive synthons,[3] they have been poorly investigated because of the lack of suitable methods for their synthesis. Recently, we reported a facile retro-[1,4]-Brook rearrangement of 3-silyl allyloxy silanes **1** that generated efficiently a variety of Z-3,3-bis(silyl) enol derivatives **2** (Scheme 1).[4] One focus of our studies on these compounds was the generation of bis(silyl) allyl anion **3**, which could lead to transformations into other useful bis(silyl) building blocks. Because initial attempts based on directed metalation[5] proved unsuccessful, we proposed a conceptually new strategy (Scheme 2).

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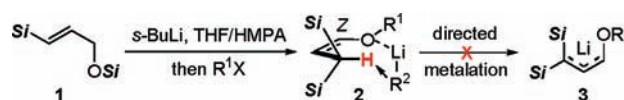[§] These authors contributed equally.

(1) For studies on geminal bis(silyl) species, see: (a) Fleming, I.; Floyd, C. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 969. (b) Brook, A. G.; Chrusciel, J. J. *Organometallics* **1984**, *3*, 1317. (c) Klumpp, G. W.; Mierop, A. J. C.; Vrielink, J. J.; Brugman, A.; Schakel, M. *J. Am. Chem. Soc.* **1985**, *107*, 6740. (d) Lautens, M.; Ben, R. N.; Delanghe, P. H. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2448. (e) Princet, B.; Gariglio, H. G.; Pornet, J. *J. Organomet. Chem.* **2000**, *604*, 186. (f) Hodgson, D. M.; Barker, S. F.; Mace, L. H.; Moran, J. R. *Chem. Commun.* **2001**, 153. (g) Williams, D. R.; Morales-Ramos, Á. I.; Williams, C. M. *Org. Lett.* **2006**, *8*, 4393.
(2) For selective reviews on organosilanes, see: (a) Overman, L. E.; Blumenkopf, T. A. *Chem. Rev.* **1986**, *86*, 857. (b) Panek, M.; Masse, C. E. *Chem. Rev.* **1995**, *95*, 1293. (c) Langkopf, E.; Schinzer, D. *Chem. Rev.* **1995**, *95*, 1375. (d) Fleming, I.; Barbero, A.; Walter, D. *Chem. Rev.* **1997**, *97*, 2063.
(3) For reviews on geminal bimetallic species, see: (a) Marek, I.; Normant, J. F. *Chem. Rev.* **1996**, *96*, 3241. (b) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (c) Marek, I. *Chem. Rev.* **2000**, *100*, 2887.
(4) (a) Song, Z. L.; Lei, Z.; Gao, L.; Wu, X.; Li, L. J. *Org. Lett.* **2010**, *12*, 5298. (b) Gao, L.; Lin, X. L.; Lei, J.; Song, Z. L.; Lin, Z. *Org. Lett.* **2012**, *14*, 158.

The key to this strategy lies in using O-allylated **2** as the substrate. Deprotonation of **2** should occur regioselectively on the allyl group, in which the proton in blue is

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Scheme 1. Initial Attempts To Synthesize Bis(silyl) Allyl Anion by Directed Metalation

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(5) For a review on directed metalation, see: Snieckus, V. *Chem. Rev.* **1990**, *90*, 879.

Scheme 2. [1,5]-Anion Relay/[2,3]-Wittig Rearrangement of Bis(silyl) Allyl Enol Ether
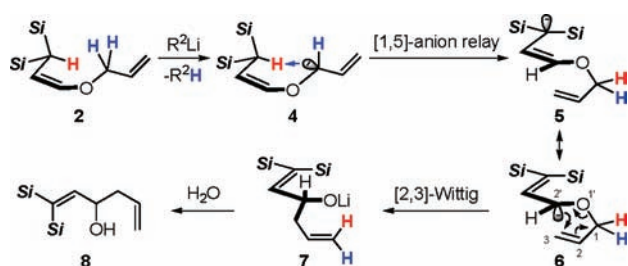
much more sterically accessible than the one in red adjacent to the bis(silyl) group, to generate the oxy allyl anion **4**. Given that silicon can stabilize the α-carbanion through a $p-d\pi$-bonding interaction,[6] a [1,5]-anion relay[7,8] of **4** via a 6-membered ring transition state may proceed to generate the thermodynamically more stable bis(silyl) allyl anion **5**. The process could be further driven by a [2,3]-Wittig rearrangement[9] of the resonance structure **6** to generate allyloxy lithium **7**. Here we report detailed studies applying this novel approach.

The feasibility of the proposed reaction was quickly established using 3,3-bis(triethylsilyl) allyl enol ether **2a**[4a] as the substrate and *t*-BuLi as the base, with 3.0 equiv of HMPA in THF at −78 °C for 2 h. The desired bis(silyl) allylic alcohol **8a** was obtained in 83% yield (Table 1, entry 3). HMPA as a cosolvent proved to be crucial for good efficiency; using no or smaller amounts of HMPA led to either no reaction or to only a moderate yield (entries 1 and 2). In addition, the reaction is also highly dependent on the bis(silyl) group. As shown in entries 4−6, enol ethers

Table 1. Screening of Reactions Conditions
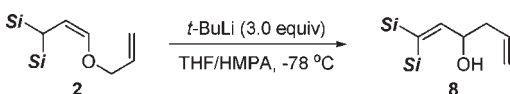
| entry	substrate $(Si)^a$	HMPA (equiv)	product	yield[b]
1	**2a** (Et$_3$Si)	−	−	NR
2	**2a** (Et$_3$Si)	1.5	**8a**	50%
3	**2a** (Et$_3$Si)	3.0	**8a**	83%
4	**2b** (Me$_3$Si)	3.0	**8b**	<5%
5	**2c** (*t*-BuMe$_2$Si)	3.0	**8c**	<5%
6	**2d** (PhMe$_2$Si)	3.0	**8d**	<5%

^{a} Reaction conditions: 0.25 mmol of **2**, 0.75 mmol of *t*-BuLi, and 0.75 mmol of HMPA in THF (2.5 mL) at −78 °C. ^{b} Isolated yields after purification by silica gel column chromatography.

(6) (a) Brinkman, E. A.; Berger, S.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 8304. (b) Chan, T. H.; Wang, D. *Chem. Rev.* **1995**, *95*, 1279.

(7) Reports of a [1,5]-anion relay via an intramolecular proton shift are rare in the literature: (a) Maercker, A.; Eckers, M.; Passlack, M. *J. Organomet. Chem.* **1980**, *186*, 193. (b) Maercker, A.; Stoetzel, R. *Chem. Ber.* **1987**, *120*, 1695.

containing a smaller bis(Me$_3$Si)$_2$CH group (**2b**), larger bis(*t*-BuMe$_2$Si)$_2$CH group (**2c**), or electronically different bis(PhMe$_2$Si)$_2$CH group (**2d**) all showed poor reactivities.

Scheme 3. Reaction of Deuterium-Substituted **2a-D**
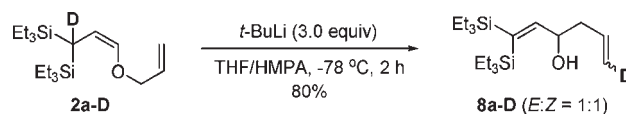
While the desired product was obtained as expected, some key mechanistic issues remained to be elucidated. First, did the reaction proceed by a [1,5]-anion relay or by some other pathways, such as directed metalation and intermolecular proton shift? Second, did product **8a** form by [1,2]- or [2,3]-Wittig rearrangement, since either pathway could yield the same result in this case? To address these questions, the reaction of deuterium-substituted **2a-D** was performed and **8a-D** was obtained as an $E/Z = 1:1$ mixture in 80% yield (Scheme 3). This result unambiguously confirmed that the reaction proceeds by a [1,5]-anion relay/[2,3]-Wittig rearrangement. Further support for the [1,5]-anion relay was obtained when the reaction of **2k-E-E**,[10] having the enol double bond as an *E*-configuration, failed to give the desired product **8k**. Apparently, the oxy allyl anion **4** generated from **2k-E-E** cannot adopt a 6-membered ring transition state.

To gain further mechanistic insight, the reaction of **2a** was quenched with D$_2$O at 15 and 30 min to afford three products **2a**, **2a-D**, and **8a** (Scheme 4). No formation of **9** and **10** implies that the [1,5]-anion relay occurs immediately once the oxy allyl anion **4** forms by the initial deprotonation. The quenching yield of **2a-D** and **8a** at 30 min implies that the [1,5]-anion relay should be faster than the [2,3]-Wittig rearrangement. In addition, formation of **2a-D** and not **11** suggests that, in the bis(silyl) allyl anion, the carbon center attached to the silyl group has a

(8) Anion relay chemistry (ARC), first introduced by Smith III a decade ago, features a negative charge migration in a "through-space" fashion involving the shift of a silyl group from a carbon to an oxygen atom. For reviews, see: (a) Smith, A. B., III; Adams, C. M. *Acc. Chem. Res.* **2004**, *37*, 365. (b) Smith, A. B., III; Wuest, W. M. *Chem. Commun.* **2008**, 5883. For the latest advances from this group, see: (c) Smith, A. B., III; Kim, W. S. *Proc. Natl. Acad. Sci. U.S.A.* **2011**, *108*, 6787. (d) Smith, A. B., III; Tong, R. B.; Kim, W. S.; Maio, W. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 8904. (e) Smith, A. B., III; Han, H.; Kim, W. S. *Org. Lett.* **2011**, *13*, 3328.

(9) For a review of the [2,3]-Wittig rearrangement, see: (a) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 855. For the latest advances, see: (b) Druais, V.; Hall, M. J.; Corsi, C.; Wendeborn, S. V.; Meyer, C.; Cossy, J. *Org. Lett.* **2009**, *11*, 935. (c) Shapland, P. D. P.; Thomas, E. J. *Tetrahedron* **2009**, *65*, 4201. (d) Sasaki, M.; Ikemoto, H.; Kawahata, M.; Yamaguchi, K.; Takeda, K. *Chem.—Eur. J.* **2009**, *15*, 4663. (e) Kitamura, M.; Hirokawa, Y.; Maezaki, N. *Chem.—Eur. J.* **2009**, *15*, 9911. (f) Anderson, J. C.; Davies, E. A. *Tetrahedron* **2010**, *66*, 6300. (g) Ikemoto, H.; Sasaki, M.; Takeda, K. *Eur. J. Org. Chem.* **2010**, *34*, 6643. (h) Hirokawa, Y.; Kitamura, M.; Kato, C.; Kurata, Y.; Maezaki, N. *Tetrahedron Lett.* **2011**, *52*, 581. (i) Chandrasekhar, B.; Prasada, R. J.; Venkateswara, R. B.; Naresh, P. *Tetrahedron Lett.* **2011**, *52*, 5921.

(10) **2k-E-E** with the enol double bond as an *E*-configuration was obtained in 15% yield by reacting **1a** with *E*-crotyl tosylate for 15 h.

higher electron density than that adjacent to an anion-destabilizing OR group. This may be the reason why the [2,3]-Wittig rearrangement proceeds slowly.

Scheme 4. Reaction of **2a** Quenched with D_2O
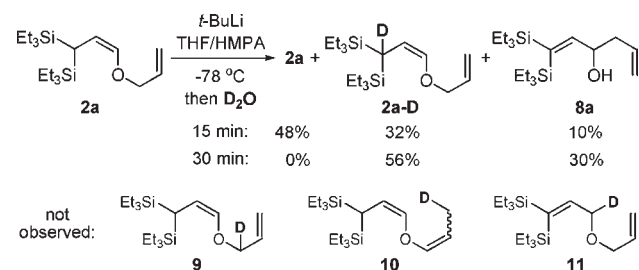
The scope of this reaction was then examined (Table 2). The reaction is generally suitable for enol ethers with substitution at the 2-position of the allyl chain, giving goods yields (entries 1−6). With one substituent at the 3-position, two diastereomers were obtained, with the *syn*-isomer being a major product (entries 7−10).[11] The geometry of the allylic double bond appears to have some impact on the stereochemical outcome, since the reaction of **2k-E** gave a higher diastereoselectivity than that of **2k-Z**.[12] Interestingly, when enol allyl ethers **2n** and **2o** substituted at both the 2- and 3-positions were used, the *anti*-isomers were formed predominantly (entries 11 and 12).[11] It is also noteworthy that when the allyl chain contained a carbanion-stabilizing phenyl or trimethylsilyl group, **2p** failed to undergo the desired reaction (entry 13).[13] Probably, the greater stability of the initially formed allyl anion raises the energy barrier for formation of the 6-membered ring transition state, making the subsequent [1,5]-anion relay much more difficult.

We rationalized the diastereoselectivity of the [2,3]-Wittig rearrangement is based on Nakai's model,[9a] which features a folded-envelope transition state (Scheme 5). Generally, for *E*-alkenes, the G group attached to the carbanion prefers to adopt an equatorial orientation to

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(11) The stereochemistry of the *syn*-isomer of **8k** was assigned by transformation of **8k** to the known vinyliodide compound (Fuwa, H.; Suzuki, T.; Kubo, H.; Yamori, T.; Sasaki, M. *Chem.—Eur. J.* **2011**, *17*, 2678. See Supporting Information for details). The stereochemistry was also determined based on Greeves' observations: In similar structures to ours, H^a in the *syn*-isomers is generally 0.1−0.3 ppm downfield of the equivalent atom in the *anti*-isomers; vicinal coupling constants between H^a and H^b in the *anti*-isomers are 1.0−1.5 Hz higher than those in the *syn*-isomers (Greeves, N.; Lee, W. M. *Tetrahedron Lett.* **1997**, *38*, 6445). This method was also applied to the stereochemical assignment of the *syn*-isomers of **8l** and **8m** and the *anti*-isomers of **8n** and **8o**.

(12) While no isomerization of the allyl chain in **2k-E** was observed, such isomerization occurred partially (from 94:6 to 73:27) via a [1,5]-anion relay in the reaction of **2k-Z-Et** with an Et substituted at the 3-position. (Experiments were performed with **2k-E** and **2k-Z-Et** by quenching the reactions with D_2O at 40 and 30 min, respectively. See Supporting Information for details.) Thus, the real diastereoselectivity obtained from pure **2k-Z** should be slightly lower than the calculated ratio 67:33.

(13) The reaction of **2p-SiMe₃-D**, which is deuterium-substituted at the same position as **2a-D**, gave 3,3-bis(triethylsilyl) aldehyde in 70% yield and left the deuterium untouched. This result implies that the initially formed allyl anion **4** undergoes cleavage of the C−O bond rather than a [1,5]-anion relay.

Table 2. Scope of the [1,5]-Anion Relay/[2,3]-Wittig Rearrangement Process

entry	substrate[a]	product	yield[b, c]
1	**2e:** R = Me		**8e:** 65%
2	**2f:** R = Et		**8f:** 74%
3	**2g:** R = *i*-Pr		**8g:** 80%
4	**2h:** R = Cy		**8h:** 75%
5	**2i:** R = CH₂Cy		**8i:** 70%
6	**2j:** R = CH₂C₅H₉		**8j:** 68%
7	**2k-E**		**8k:** 80% [*dr* = 80:20]
8	**2k-Z** [*Z:E* = 86:14]		**8k:** 70% [*dr* =70:30][d]
9	**2l:** R = Cy		**8l:** 78% [*dr* = 67:33]
10	**2m:** R = *t*-Bu		**8m:** 70% [*dr* = 90:10]
11	**2n:** R = Me		**8n:** 58% [*dr* = 86:14]
12	**2o:** R = Et		**8o:** 65% [*dr* = 86:14]
13	**2p** (R_{ASG} = Ph, or SiMe₃)	—	—

[a] Reaction conditions: **2** (1.0 equiv), *t*-BuLi (3.0 equiv), and HMPA (3.0 equiv) in THF at −78 °C. [b] Diastereoselectivity was determined by ¹H NMR spectroscopy. [c] Isolated yields after purification by silica gel column chromatography. [d] The calculated diastereoselectivity of the reaction from pure **2k-Z** was *syn/anti* = 67:33.

Scheme 5. Model Analysis of Diastereoselectivity in the [2,3]-Wittig Rearrangement
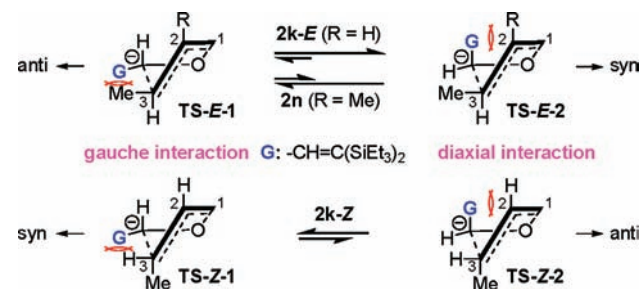
avoid a pseudodiaxial interaction with the R group at the 2-position, giving the *anti*-isomer as the predominant product. The opposite *syn*-selectivity for **2k-E** (R = H) may be due to increased gauche repulsion with the 3-Me group, which forces the bulky G group (—CH=C(SiEt₃)₂) to adopt an axial orientation as in **TS-E-2**. However, when the 2-position contains an additional substituent, such as in **2n**, the diaxial interaction between G and 2-Me groups again dominates, making **TS-E-1** more favorable and

Table 3. Scope of the [1,4]-Brook Rearrangement/Alkylation Reaction

entry	sub[a]	electrophiles	product	yield[b]
1	8a: R = H	X: = Cl / = Br / = OTs	12a	89% / 76% / 80%
2	8a: R = H	R = Me; X = OTs	12b	65%
3	8a: R = H	R = i-Pr; X = OTs	12c	60%
4	8a: R = H	R = Br; X = Br	12d	69%
5	8a: R = H	R = CH₂SiMe₃; X = OTs	12e	80%
6	8a: R = H	Et₃Si / OTs	12f	68%
7	8a: R = H	Me / Br / Me	12g	55%
8	8a: R = H	Et₃Si / Br	12h	60%
9	8a: R = H	PhSSPh	12i	55%
10	8e: R = Me	Cl	12j	75%
11	8g: R = i-Pr		12k	83%

[a] Reaction conditions: **8** (1.0 equiv), electrophile (2.0 equiv), t-BuOLi (3.0 equiv), and CuCN (3.0 equiv) in DMF/THF = 5:3 as cosolvent at 25 °C. [b] Isolated yields after purification by silica gel column chromatography.
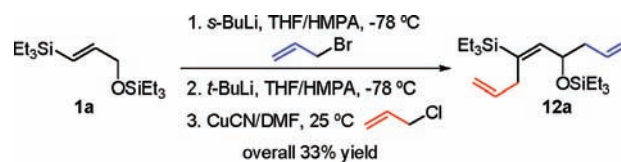
yielding the *anti*-isomer as the major product. In contrast, in the transition states **TS-Z-1** and **TS-Z-2** for **2k-Z**, the

Scheme 6. One-Pot Transformation of **1a** into **12a**

bulky G group appears to suffer the effects of gauche and diaxial interactions with the 3-H and 2-H groups, making **TS-Z-1** slightly favored and giving rise to the observed poor *syn*-selectivity.

Elaboration of the bis(silyl) allylic alcohols to functionally increased trisubstituted vinylsilanes was then explored. The process features a sequential [1,4]-Brook rearrangement[14]/alkylation reaction based on a procedure modified from Takeda.[15] As summarized in Table 3, the reaction is suitable not only for a wide range of allylic electrophiles (entries 2−7, 10, and 11) but also for propargyl bromide (entry 8) and phenyl disulfide (entry 9). Moreover, the leaving group of electrophiles can include several choices such as halides and tosylate (entry 1), with the latter one having not been reported in previous work.

Combining the processes to transform **1a** into **2a**, with subsequent generation of **8a** and **12a**, appeared to be feasible in a one-pot procedure, which would be of substantial interest as a synthetic approach. Therefore we tested this process and obtained the efficient one-pot transformation of **1a** directly into **12a** with overall 33% yield (Scheme 6).[16]

Here we have described a [1,5]-anion relay/[2,3]-Wittig rearrangement of 3,3-bis(silyl) allyl enol ethers to generate versatile 3,3-bis(silyl) allyl alcohols. We have also demonstrated the synthetic value of this approach by efficiently preparing a wide range of trisubstituted vinylsilanes using a sequential [1,4]-Brook/alkylation protocol. We hope this conceptually new strategy can be applied as a general method in related systems. Further investigations in this regard are currently underway.

Supporting Information Available. Experimental procedures and spectral data for products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

(14) For reviews on Brook rearrangement, see: (a) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77. (b) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065. For the latest advances, see: (c) Schmitt, D. C.; Johnson, J. S. *Org. Lett.* **2010**, *12*, 944. (d) Sasaki, M.; Oyamada, K.; Takeda, K. *J. Org. Chem.* **2010**, *75*, 3941. (e) Boyce, G. R.; Johnson, J. S. *Angew. Chem., Int. Ed.* **2010**, *49*, 8930. (f) Song, Z. L; Kui, L. Z; Sun, X. W.; Li, L. *J. Org. Lett.* **2011**, *13*, 1440. (g) Hayashi, M.; Nakamura, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 2249. (h) Li, H.; Liu, L. T.; Wang, Z. T; Zhao, F.; Zhang, S. G; Zhang, W. X; Xi, Z. F. *Chem.—Eur. J.* **2011**, *17*, 7399. (i) Sasaki, M.; Kondo, Y.; Kawahata, M.; Yamaguchi, K.; Takeda, K. *Angew. Chem., Int. Ed.* **2011**, *50*, 6375. (j) Martin, D. B. C.; Vanderwal, C. D. *Chem. Sci.* **2011**, *2*, 649.

(15) (a) Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *Org. Lett.* **2001**, *3*, 3811. (b) Taguchi, H.; Takami, K.; Tsubouchi, A.; Takeda, T. *Tetrahedron Lett.* **2004**, *45*, 429. (c) Tsubouchi, A.; Enatsu, S.; Kanno, R.; Takeda, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 7089. (d) Smith, A. B., III; Kim, W. S.; Tong, R. B. *Org. Lett.* **2010**, *12*, 588.

(16) It is necessary to remove the excess allyl bromide under reduced pressure after the first step to avoid undesired side reactions in the next two steps.