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Efficient Approach to 3,3-Bissilyl Carbonyl and Enol Derivatives via Retro-[1,4] Brook Rearrangement of 3-Silyl Allyloxysilanes

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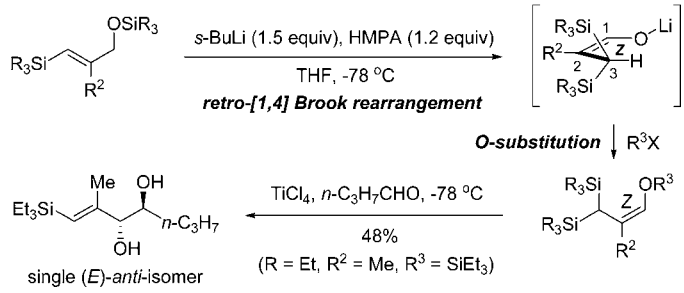
ABSTRACT



A facile and highly stereoselective retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes has been discovered. While basic hydrolysis of the formed (*Z*)-3,3-bissilyl lithium enolates provides 3,3-bissilyl carbonyl compounds efficiently, trapping the species with various electrophiles including alkyl halides leads to the exclusive O-substituted (*Z*)-3,3-bissilyl enol derivatives that can undergo a Sakurai reaction with aldehyde to produce the synthetically useful 1,2-diol diastereoselectively.

Retro-Brook rearrangement,[1] describing an intramolecular silyl migration from an oxygen to a carbon atom, comprises a powerful tactic for the rapid construction of functionalized organosilanes from more accessible silyl ethers. While many investigations of the retro-[1,4] Brook rearrangement[2] have been reported, only two papers have appeared describing the process in allyloxysilane systems. Mitchell[3] first reported a lithium amide-induced retro-[1,4] Brook rearrangement of allyloxysilanes bearing two organometal residues on the vinylic carbons. However, as the author mentioned, the silyl migration is only feasible when the trimethylsilyl group was involved due to the steric effect at silicon. Recently, Tomooka[4] investigated the retro-[1,4] Brook rearrangement of simple allyloxysilanes. The stereochemical course was clarified for the first time by using a silicon-centered chiral silyl group as the migration moiety.

The starting point of this work arises from our interest in geminal bimetallic species, which are useful building blocks and have shown high efficiency in the selective formation

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(1) For reviews, see: (a) West, R. In *Advances in Organometallic Chemistry*; West, R., Stone, F. G. A., Eds.; Academic Press: New York, 1977; Vol. 16, pp 1−31. (b) Brook, A. G.; Bassindale, A. R. In *Rearrangements in Ground and Excited States*; De Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 149−227. (c) Clayden, J. In *Organolithiums: Selectivity for Synthesis*; Clayden, J., Ed.; Pergamon: Oxford, 2002; pp 340−346. (d) Tomooka, K. In *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Ed.; Wiley: Chichester, 2004; Vol. 2, pp 749−828.

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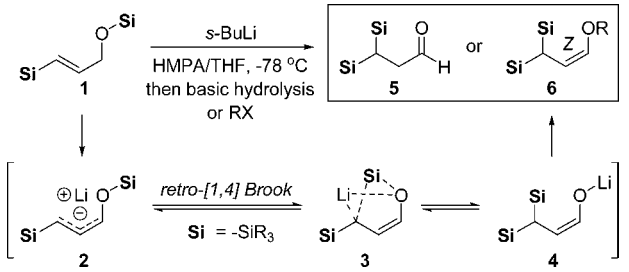
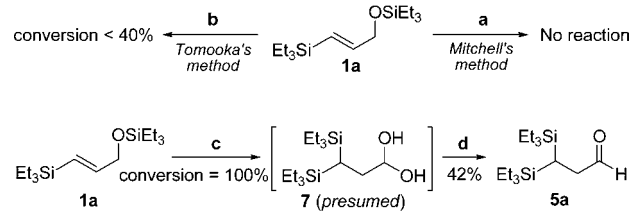
of carbon−carbon bonds.[5] Our particular attention is currently focused on a special type of geminal bissilyl compounds[6] such as 3,3-bissilyl carbonyl and enol derivatives **5** and **6**. Despite potentially being attractive synthons, they have been barely investigated due to the lack of suitable synthetic methods. We envisioned that a direct and practical entry into these species might be achieved via the retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes **1** (Scheme 1). Herein, we report the realization of this methodology.

Scheme 1



In accordance with Mitchell's observation, the initial use of LDA as base proved to be unworkable for the rearrangement of **1a** possessing the sterically hindered triethylsilyl groups. Tomooka's protocol using *t*-BuLi with 5.0 equiv of HMPA as cosolvent was also not effective and led to less than 40% conversion. Delightfully, when *s*-BuLi was used instead of *t*-BuLi, **1a** was consumed completely in several seconds at −78 °C and converted into a new compound after quenching with 10% aq HCl (Scheme 2). To our surprise,

Scheme 2[a]

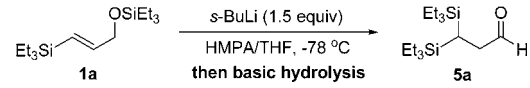


[a] **a**. LDA (1.5 equiv), THF, −78 °C to rt. **b**. *t*-BuLi (1.5 equiv), HMPA (5.0 equiv)/THF, −78 °C. **c**. *s*-BuLi (1.5 equiv), HMPA (5.0 equiv)/THF, −78 °C then 10% aq HCl. **d**. further hydrolysis during concentration and chromatography.

this initial formed product appears to be quite stable with the acidic hydrolysis condition even for several hours, but it can be converted slowly into the desired aldehyde **5a** during concentration and chromatography on silica gel. Since the compound has been ruled out to be either retro-[1,2] Brook rearrangement or 1,3-hydrogen shift products, we presumed it might be the hydrate **7** generated by hydrolysis of the lithium enolate intermediate **4**.

Given the observed good acid stability of **7**, we predicted basic hydrolysis would be feasible to generate the desired aldehydes. As expected, quenching the reaction with 10 equiv of H_2O followed by stirring at room temperature for 3 h gave rise to the aldehyde **5a** in 62% yield (Table 1, entry 1). It is

Table 1. Screening of Reaction Conditions



entry	HMPA	workup	temp[a]	time	yield[b]
1	5.0 equiv	H_2O (10 equiv)	rt	3 h	62%
2	**1.2 equiv**	**H_2O (10 equiv)**	**rt**	**3 h**	**91%**
3	0.3 equiv	H_2O (10 equiv)	rt	3 h	N.D.
4	1.2 equiv	H_2O (10 equiv) LiOH (3 equiv)/H_2O	50°C	1 h	30%
5	1.2 equiv	(20 equiv)	rt	2 h	75%

[a] Temperature of the basic hydrolysis step. [b] Isolated yields after purification by silica gel column chromatography.

noteworthy that despite that Tomooka has emphasized the importance of a large excess of HMPA for the high selectivity of retro-[1,4] Brook rearrangement in simple allyloxysilane systems[4] here 1.2 equiv appeared to be effective enough to facilitate the silyl migration, providing an even much higher 91% yield (entry 2). However, using a catalytic amount of HMPA only resulted in the partial retro-

(2) For studies on the retro-[1,4] Brook rearrangement, see: (a) Evans, D. A.; Takacs, I. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371. (b) Rucker, C. *Tetrahedron Lett.* **1984**, *25*, 4349. (c) Mora, J.; Costa, A. *Tetrahedron Lett.* **1984**, *25*, 3493. (d) Lautens, M.; Delanghe, P. H. M.; Goh, J. B.; Zhang, C. H. *J. Org. Chem.* **1992**, *57*, 3270. (e) Marumoto, S.; Kuwajima, I. *J. Am. Chem. Soc.* **1993**, *115*, 9021. (f) Jiang, X. L.; Bailey, W. F. *Organometallics* **1995**, *14*, 5704. (g) Braun, M.; Mahler, H. *Liebigs Ann.* **1995**, 29. (h) Bures, E.; Spinazze, P. G.; Beese, G.; Hunt, I. R.; Rogers, C.; Keay, B. A. *J. Org. Chem.* **1997**, *62*, 8741. (i) Bousbaa, J.; Ooms, F.; Krief, A. *Tetrahedron Lett.* **1997**, *38*, 7625. (j) Gibson, C.; Buck, T.; Walker, M.; Brüeckner, R. *Synlett* **1998**, 201. (k) Kleinfeld, S. H.; Wegelius, E.; Hoppe, D. *Helv. Chim. Acta* **1999**, *82*, 2413. (l) Comanita, B. M.; Woo, S.; Fallis, A. G. *Tetrahedron Lett.* **1999**, *40*, 5283. (m) Simpkins, S. M. E.; Kariuki, B. M.; Arico, C. S.; Cox, L. R. *Org. Lett.* **2003**, *5*, 3971. (n) Nahm, M. R.; Xin, L. H.; Potnick, J. R.; Yates, C. M.; White, P. S.; Johnson, J. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 2377. (o) Yamago, S.; Fujita, K.; Miyoshi, M.; Kotani, M.; Yoshida, J. *Org. Lett.* **2005**, *7*, 909. (p) Mori, H.; Matsuo, T.; Yoshioka, Y.; Katsumura, S. *J. Org. Chem.* **2006**, *71*, 9004. (q) Mori, Y.; Futamura, Y.; Horisaki, K. *Angew. Chem., Int. Ed.* **2008**, *47*, 1091.

(3) (a) Mitchell, T. N.; Schütze, M.; Giebelmann, F. *Synlett* **1997**, 187. (b) Mitchell, T. N.; Schütze, M. *Tetrahedron* **1999**, *55*, 1285.

(4) Nakazaki, A.; Nakai, T.; Tomooka, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2235.

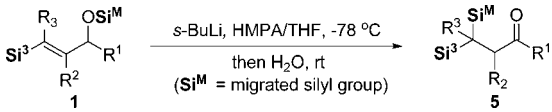
(5) For reviews, see: (a) Marek, I.; Normant, J. F. *Chem. Rev.* **1996**, *96*, 3241. (b) Marshall, J. A. *Chem. Rev.* **1996**, *96*, 31. (c) Marek, I. *Chem. Rev.* **2000**, *100*, 2887. (c) For recent advances, see: Shimizu, M.; Kitagawa, H.; Kurahashi, T.; Hiyama, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 4283. (d) Hirashita, T.; Hayashi, Y.; Mitsui, K.; Araki, S. *J. Org. Chem.* **2003**, *68*, 3467, and references therein.

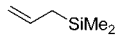
(6) For studies on geminal bissilyl species, see: (a) Fleming, I.; Floyd, C. D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 969. (b) Ahlbrecht, H.; Farnung, W.; Simon, H. *Chem. Ber.* **1984**, *117*, 2622. (c) Brook, A. G.; Chrusciel, J. J. *Organometallics* **1984**, *3*, 1317. (d) Klumpp, G. W.; Mierop, A. J. C.; Vrielink, J. J.; Brugman, A.; Schakel, M. *J. Am. Chem. Soc.* **1985**, *107*, 6740. (e) Lautens, M.; Ben, R. N.; Delanghe, P. H. M. *Angew. Chem., Int. Ed.* **1994**, *33*, 2448. (f) Lautens, M.; Delanghe, P. H. M.; Goh, J. B.; Zhang, C. H. *J. Org. Chem.* **1995**, *60*, 4213. (g) Lautens, M.; Ben, R. N.; Delanghe, P. H. M. *Tetrahedron* **1996**, *52*, 7221. (h) Princet, B.; Anselme, G.; Pornet, J. *Synth. Commun.* **1999**, *29*, 3326. (i) Princet, B.; Gariglio, H. G.; Pornet, J. *J. Organomet. Chem.* **2000**, *604*, 186. (j) Hodgson, D. M.; Barker, S. F.; Mace, L. H.; Moran, J. R. *Chem. Commun.* **2001**, 153. (k) Onyeozili, E. N.; Maleczka, R. E. *Tetrahedron Lett.* **2006**, *47*, 6565. (l) Williams, D. R.; Morales-Ramos, A. I.; Williams, C. M. *Org. Lett.* **2006**, *8*, 4393.

[1,2] Brook rearrangement, and no retro-[1,4] one occurred (entry 3). More vigorous workup conditions including stirring at 50 °C (entry 4) or adding an extra 3.0 equiv of LiOH (entry 5) led to the faster hydrolysis, but the yields dramatically decreased.

Having established the optimal reaction conditions, we further examined the scope of substrates. Not limited to (*E*)-3-silyl allyloxysilane, **1a** with *Z*-configuration is also suitable, giving the comparably high yield (Table 2, entry 1).

Table 2. Scope of 3-Silyl Allyloxysilanes



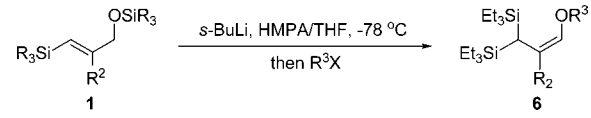
entry	sub[a]	Si^M	Si^3	R^1	R^2	R^3	prod	yield[b]
1	**1a** (*Z*)	Et_3Si	H	H	H	Et_3Si	**5a**	90%
2	**1b**	Me_3Si	Me_3Si	H	H	H	**5b**	74%
3	**1c**	t-$BuMe_2Si$	t-$BuMe_2Si$	H	H	H	**5c**	73%
4	**1d**	$PhMe_2Si$	$PhMe_2Si$	H	H	H	**5d**	93%
5	**1e**	Ph_2MeSi	Ph_2MeSi	H	H	H	**5e**	50%
6	**1f**	Ph_3Si	Ph_3Si	H	H	H	**5f**	75%
7	**1g**	Et_3Si		H	H	H	**5g**	60%
8[c]	**1h**	Et_3Si	Et_3Si	Me	H	H	**5h**	67%
9[c]	**1i**	Me_3Si	Me_3Si	H	Me	H	**5i**	72%
10[c]	**1j**	Me_3Si	Me_3Si	H	Allyl	H	**5j**	53%
11	**1k**	Me_3Si	Me_3Si	H	H	Ph	—	—

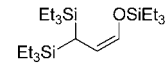
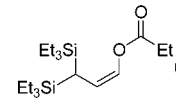
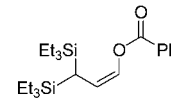
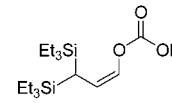
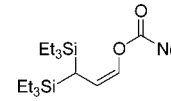
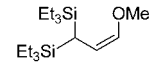
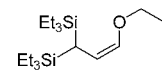
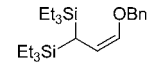
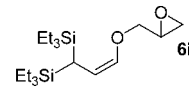
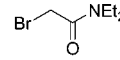
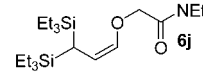
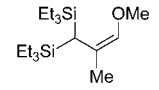
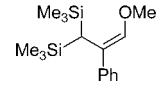
[a] Reaction conditions: allyloxysilane (0.15 M), *s*-BuLi (1.5 equiv), HMPA (1.2 equiv) in THF at −78 °C, then H_2O (10 equiv), warmed to rt, 3 h. [b] Isolated yields after purification by silica gel column chromatography. [c] TMEDA (1.5 equiv) was added.

Moreover, a wide range of silyl groups were found capable to undergo the smooth migration, even though the formed bissilyl moieties are much hindered (entries 2−6). Formation of the aldehyde **5g** (entry 7), in which the migrated silyl group contains an allyl substitution, presents a more attractive result given the potential of further intramolecular transformations. Reactions of 3-silyl allyloxysilanes bearing substitution at the 1- or 2-position can also proceed successfully when the more reactive *s*-BuLi/TMEDA complex was used to facilitate the deprotonation step (entries 8−10). However, with substitution and even the anion-stabilizing phenyl group, located at the 3-position, the silyl migration was totally suppressed probably due to the difficulty of forming the sterically constrained 3-quaternary carbon.

Reactions quenched with various electrophiles were further examined by using allyloxysilane **1a** as the model substrate. As summarized in Table 3, reactions with trialkylsilyl chlorides (Table 3, entry 1) and acyl chlorides (entries 2−5) provided the corresponding functionalized 3,3-bissilyl enol

Table 3. Reactions with Electrophiles



entry	substrate[a]	R^3X	product[b]		yield[c]
1	**1a** (R = Et; R^2 = H)	Et_3SiCl		**6a**	95%
2	**1a**	EtCOCl		**6b**	93%
3	**1a**	PhCOCl		**6c**	92%
4	**1a**	EtOCOCl		**6d**	90%
5	**1a**	$(i\text{-Pr})_2NCOCl$		**6e**	92%
6	**1a**	MeI		**6f**	84%
7	**1a**	AllylBr		**6g**	63%
8	**1a**	BnBr		**6h**	90%
9	**1a**			**6i**	68%
10	**1a**			**6j**	75%
11[d]	**1l** (R = Et; R^2 = Me)	MeI		**6k**	60%
12[d]	**1m** (R = Me; R^2 = Ph)	MeI		**6l**	58%

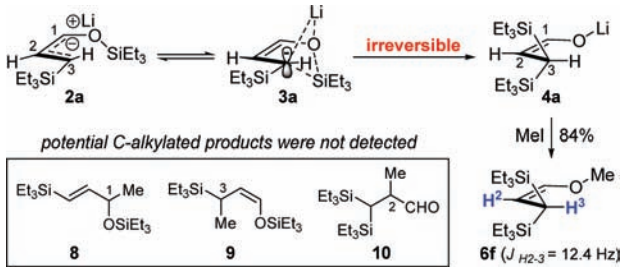
[a] Reaction conditions: allyloxysilane (0.15 M), *s*-BuLi (1.5 equiv), HMPA (1.2 equiv) in THF at −78 °C, then R^3X (3.0 equiv), warmed to rt, 4 h. [b] The stereoselectivity was determined by ^1H NMR spectroscopy, and the configuration was determined by NOE experiments of **6f**. [c] Isolated yields after purification by silica gel column chromatography. [d] TMEDA (1.5 equiv) was added.

derivatives smoothly and in good to excellent yields. Generation of the exclusive (*Z*)-configuration supports formation of the five-membered pentacoordinated silicate **3**[7] to be reasonable during the course. The particularly notable results were obtained when alkyl halides were used as

electrophiles (entries 6−12). All reactions present the reliable and exclusive O-alkylated selectivity, and no C-alkylated products were detected at all. This result is in sharp contrast to the previous observations by Still[8] and Tomooka[4] since they have all found that quenching reactions of simple allyloxysilanes with iodomethane only provided the γ-C-alkylated product,s and none of the retro-Brook rearranged products were formed.

Rationalization of this excellent O-alkylated selectivity is proposed as follows. Given the coupling constant (J = 12.4 Hz) of H^2 and H^3 in **6f** as well as no NOE being observed between them, we speculated the most favorable conformation of lithium enolate could be expected as **4a** that involves the minimum allylic strain and nonbonded interaction (Scheme 3). Thus, regeneration of the pentacoordinated

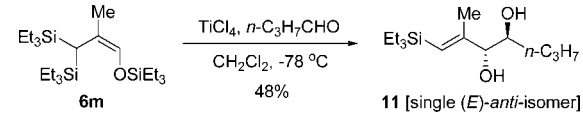
Scheme 3



silicate **3a** and allylic anion **2a** via a reverse process would be quite difficult, thereby prohibiting C-alkylation at the 1- and 3-position to give **8** and **9**, respectively. In fact, we have found that the whole silyl migration proceeded very fast; moreover, **4a** can be stored at either −78 or 10 °C for several hours while still maintaining the good reactivity with electrophiles. That is to say, formation of **4a** is both a kinetic and a thermodynamic process. On the other hand, due to the bulky bissilyl moiety shields, both sides of 2-position in **4a**, C-alkylation to give aldehyde **10** would be unfeasible, as well. As a result, alkyl halides are forced to approach the oxygen anion completely with generating the exclusive O-alkylated products.

The wide existence of polyketide natural products then led us to explore the allylation reactivity of 3,3-bissilyl enol derivatives with aldehydes. The preliminary result is shown in Scheme 4. By treatment of silyl enol ether **6m** with $TiCl_4$

Scheme 4



and *n*-butanal, an expected Sakurai reaction,[5b,9] rather than Mukaiyama aldol addition, occurred to give 1,2-diol **11** in 48% yield and as a single (*E*)-*anti*-isomer.[10]

We have described a facile and highly stereoselective retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes. This route provides a practical entry to a diverse array of 3,3-bissilyl carbonyl and enol derivatives. The synthetic values of these building blocks have also been demonstrated by the Sakurai reaction with aldehyde to generate the 1,2-diol diastereoselectively. Detailed studies on the rearrangement and other applications of this methodology are currently underway.

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

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(10) The stereochemistry of **11** was determined by NOE experiments of its acetonide. See the Supporting Information for details.