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Studies on retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes. Observation of the formation of unusual 3,3-bissilyl enols

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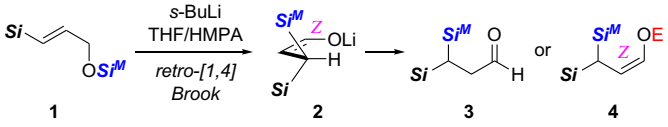
ABSTRACT

Detailed investigations of the retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes are described. Based on control experiments and NMR studies, rationalizations are proposed for the formation of 3,3-bissilyl enols, unusual compounds that are stable to acidic hydrolysis but that can be transformed into the corresponding aldehydes under basic hydrolysis conditions. These studies further show that the 3,3-bissilyl enolates can be *O*-alkylated by alkyl halides with complete chemoselectivity. This reaction provides a practical entry to various 3,3-bissilyl aldehydes and enol derivatives. As a demonstration of the synthetic utility of this approach, 3,3-bissilyl aldehyde was converted into bissilyl divinyl ketone, which can undergo an SiO_2-promoted Nazarov reaction to give cyclic β-silyl enone smoothly.

1. Introduction

Geminal bimetallic compounds are useful building blocks that support highly efficient formation of carbon–carbon bonds.[1] Within the germinal bimetal family, bissilyl compounds[2] are a special type of organosilane[3] that appear to be attractive synthons because of their great potential for bifunctional reactivity. However, investigations of these compounds have been limited because of the lack of practical methods to synthesize them. Indeed, the attachment of two large silyl groups to one carbon center is quite challenging. Solving this problem requires efficient formation of a carbon–silicon bond in a sterically bulky system. Our interest in these compounds led us to focus on the well-known retro-Brook rearrangement,[4] which involves an intramolecular silyl group migration from an oxygen to a carbon atom. The most appealing feature of this reaction is that functionalized organosilane can be rapidly constructed from more accessible silyl ethers. Recently, we communicated a facile retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes **1** promoted by organolithium (Scheme 1).[5] The reaction not only provides a practical approach to synthesize 3,3-bissilyl aldehydes **3** and (*Z*)-3,3-bissilyl enol derivatives **4**, but it also shows some unusual characteristics. Here we report detailed studies that provide a deeper understanding of this reaction.



1 2 3 4

Scheme 1. Retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes.

2. Results and discussion

Although the retro-Brook rearrangement has been studied extensively, few studies have examined the allyloxysilane system. Mitchell et al. reported a retro-[1,4] Brook rearrangement of 3-silyl allyloxysilane containing an $(n\text{-Bu})_3Sn$ group at the 2-position (Eq. 1).[6] This reaction suffers from two limitations. First, the $(n\text{-Bu})_3Sn$ group is required in order to facilitate the silyl migration, but such a substrate is toxic and apparently difficult to prepare. Second, when both silyl groups are bulkier than the trimethylsilyl group, the reaction is sluggish. These disadvantages limit the usefulness of this approach when researchers wish to use different bissilyl groups in order to examine their steric and electronic effects on a given transformation.

To avoid these disadvantages, we reasoned that silyl group migration in 3-silyl allyloxysilanes might be feasible in the presence of a stronger base, such as organolithiums like *s*-BuLi, and polar cosolvents like HMPA or DMPU, which would reduce aggregation of the initially formed allyl anion. As expected, **1a** containing two triethylsilyl groups reacted completely after several seconds at −78 °C in THF (Scheme 2). After quenching with 10% aq HCl, a new

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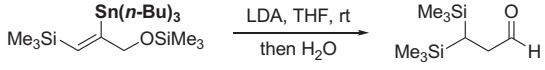
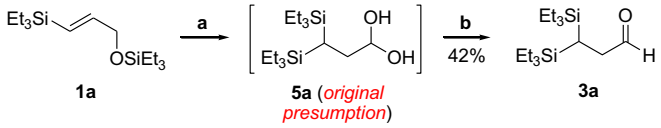
compound was obtained and appeared to be stable to acidic hydrolysis conditions, even after several hours. To our surprise, the product proved not to be the expected aldehyde **3a**, since **3a** formed in 42% yield after concentration of the original reaction mixture and chromatography on silica gel. Since we could rule out that the reaction product was the result of retro-[1,2] Brook rearrangement or a 1,3-hydrogen shift, we presumed it might be the hydrate **5a** generated by acidic hydrolysis of lithium enolate **2a** (Scheme 1).[5]



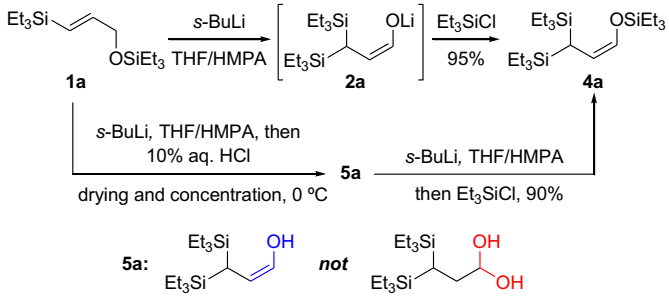
1. The (n-Bu)$_3$Sn group is necessary for silyl group migration.
2. Silyl groups bulkier than Me$_3$Si cannot undergo migration.



a. *s*-BuLi (1.5 equiv), HMPA (5.0 equiv)/THF, -78 °C then 10% aq HCl. b. concentration and chromatography on silica gel.

Scheme 2. Initial presumption that **5a** is a hydrate.

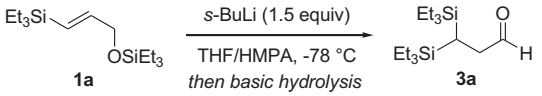
To determine whether this presumption was correct, the following control experiments were performed (Scheme 3). In the first



Scheme 3. Control experiments implying that **5a** is an enol.

experiment, the reaction was quenched with triethylsilyl chloride, generating silyl enol ether **4a** exclusively in the *Z*-configuration in 95% yield. This result supports the idea that *Z*-lithium enolate **2a** forms through the retro-[1,4]-Brook rearrangement of **1a**. In the second experiment, the reaction was quenched with 10% aq HCl,

Table 1
Screening of reaction conditions



Entry	HMPA	Workup	Temp[a]	Time	Yield[b]
1	5.0 equiv	satd aq NH_4Cl	25 °C	3 h	45%
2	5.0 equiv	satd aq $NaHCO_3$	25 °C	3 h	53%
3	5.0 equiv	30 equiv	25 °C	3 h	55%
4	5.0 equiv	10 equiv	25 °C	3 h	62%
5	0.3 equiv	10 equiv	25 °C	3 h	—
6	1.2 equiv	10 equiv	25 °C	3 h	91%
7	1.2 equiv	10 equiv	50 °C	1 h	30%
8	1.2 equiv	20 equiv/LiOH (3.0 equiv)	25 °C	2 h	75%
9	1.2 equiv	*i*-PrOH (10 equiv)	25 °C	3 h	—

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

and subsequent drying and concentrating at 0 °C generated the proposed hydrate **5a**. Treating **5a** again with *s*-BuLi and quenching with triethylsilyl chloride afforded the corresponding silyl enol ether **4a** in 90% yield. This result suggested to us that **5a** was not the proposed hydrate, but rather an enol. In fact, some stable enols of simple ketone compounds have been observed and even isolated.[7] Generally, bulky substituents on the enol are required in order to prevent hydrolysis to the corresponding ketone. However, stable enols of aldehydes have rarely been reported. To obtain more reliable evidence that our reaction had generated the unusual 3,3-bisslilyl enol, ^{1}H NMR analysis was performed on crude enol **5f** containing a bistriphenylsilyl group. The spectrum clearly showed signals due to enol **5f**, albeit contaminated with signals from the corresponding aldehyde **3f** (Fig. 1).

Because the reason why the acidic hydrolysis gives the stable enol was not clear at the moment, we screened a series of hydrolysis conditions to obtain the desired 3,3-bissilyl aldehydes. Using satd aq NH_4Cl or satd aq $NaHCO_3$ led to no obvious transformation from the enol into aldehyde **3a**, which was generated in moderate yields upon subsequent concentration and silica gel chromatography (Table 1, entries 1 and 2). Interestingly, quenching the reaction with 30 equiv of H_2O gave slightly higher yield, and most of the enol was transformed into the aldehyde (entry 3). This result suggests that more basic hydrolysis conditions favor tautomerization toward the aldehyde. As expected, a higher yield of 62% was obtained using 10 equiv of H_2O with stirring at room temperature for 3 h (entry 4). Further testing with HMPA showed that while using a catalytic amount led to only partial [1,2]-Brook rearrangement (entry 5), using 1.2 equiv gave a much higher yield (91%, entry

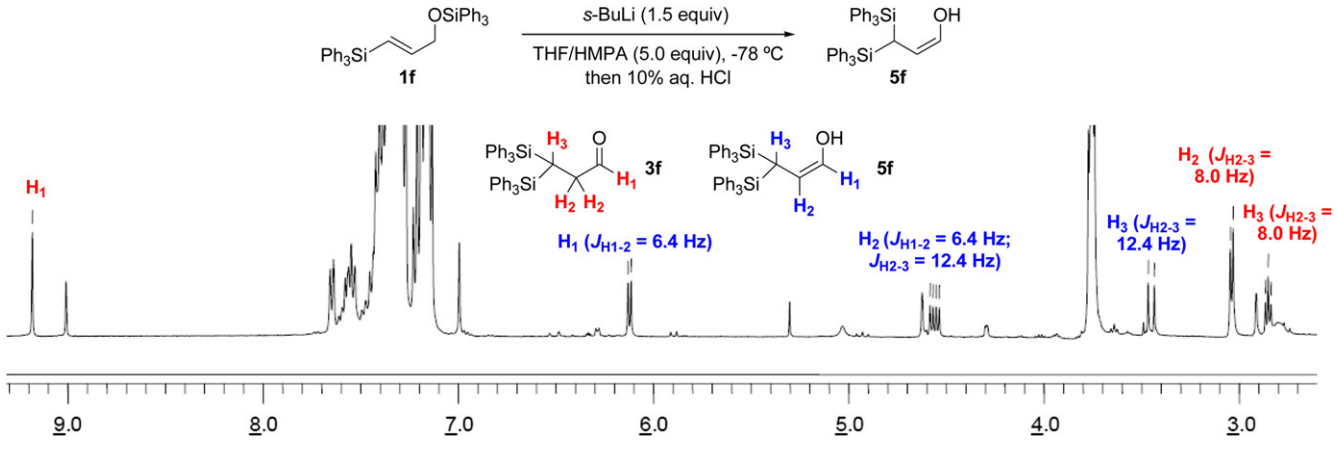
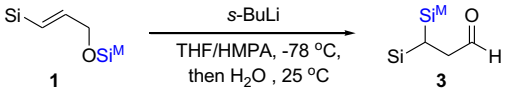
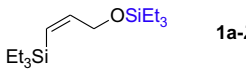
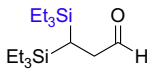
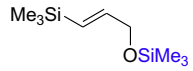
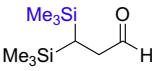
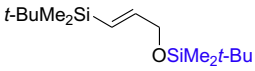
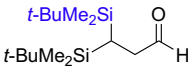
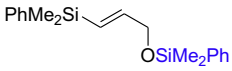
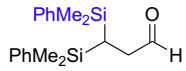
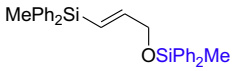
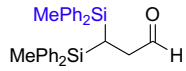
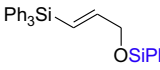
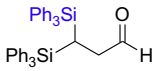
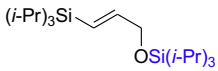
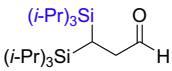
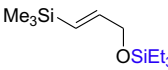
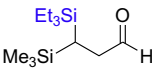
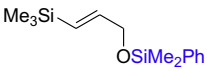
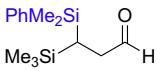
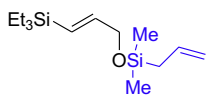
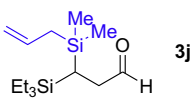
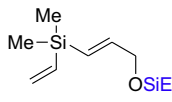
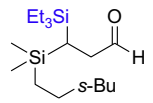


Fig. 1. ^{1}H NMR spectrum of 3,3-bistriphenylsilyl enol **5f** contaminated with the corresponding aldehyde **3f**.

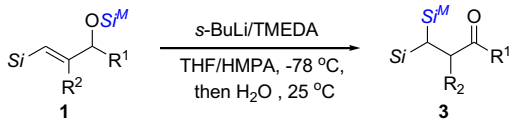
Table 2
Scope of 3-silyl allyloxysilanes[a]

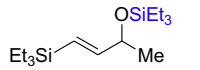
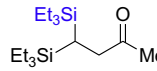
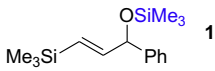
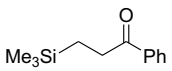
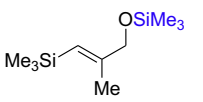
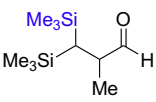
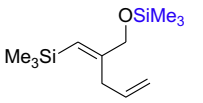
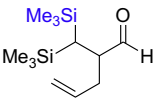
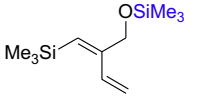
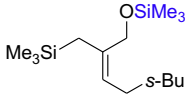
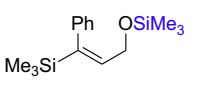
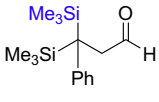


Entry	Allyloxysilane		Product		Yield[b]
1		**1a-*Z***		**3a**	90%
2		**1b**		**3b**	74%
3		**1c**		**3c**	73%
4		**1d**		**3d**	93%
5		**1e**		**3e**	50%
6		**1f**		**3f**	75%
7		**1g**		**3g**	—
8		**1h**		**3h**	87%
9		**1i**		**3i**	82%
10		**1j**		**3j**	60%
11		**1k**		**3k**	21%

[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.

Table 3
Scope of 3-silyl allyloxysilanes substituted at the 1-, 2- or 3-position[a]



Entry	Allyloxysilane		Product		Yield[b]
1		**1l**		**3l**	67%
2		**1m**		**3m**	50%
3		**1n**		**3n**	72%
4		**1o**		**3o**	53%
5		**1p**		**3p**	23%
6		**1q**		**3q**	—

[a] Reaction conditions: allyloxysilane (0.15 M), *s*-BuLi (1.5 equiv), TMEDA (1.5 equiv), HMPA (1.2 equiv) in THF at −78 °C, then H2O (10 equiv), warmed to rt, 3 h.
[b] Isolated yields after purification by silica gel column chromatography.

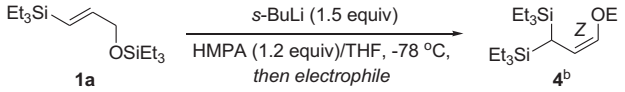
6) than using 5.0 equiv (62%, entry 4). This result is in sharp contrast to Tomooka's observation[8] that a large excess of HMPA is generally necessary for the retro-[1,4] Brook rearrangement of simple allyloxysilanes. More vigorous workup conditions, such as stirring at 50 °C (entry 7) and adding an extra 3.0 equiv of LiOH (entry 8), resulted in lower yields, even though the hydrolysis proceeded faster. In addition, quenching the reaction with *i*-PrOH gave a complex mixture (entry 9). The lithium isopropoxide produced probably acted as a strong base and destroyed the bissilyl or aldehyde groups.

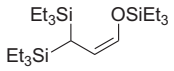
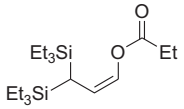
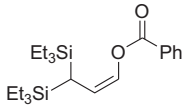
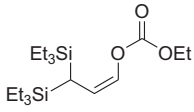
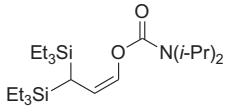
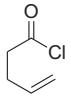
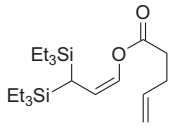
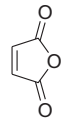
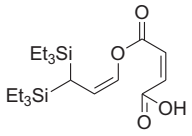
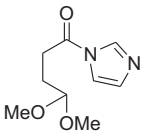
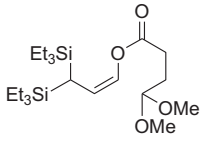
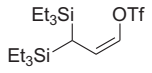
The scope of this synthetic approach was examined (Table 2). The reaction was suitable for **1a**–**z** with a *Z*-configuration, giving **3a** in relatively high yield (Table 2, entry 1). Moreover, a wide range of bissilyl groups could be constructed by smooth silyl migration (entries 2–6), except for the extremely bulky bistriisopropylsilyl group (entry 7). The approach could also be used to synthesize bissilyl groups containing two different silyl species (entries 8–11). The resulting aldehyde **3j** is an attractive compound given its potential to undergo intramolecular functionalization[9] and directed transformations.[10] Reaction of **1k** was complex and led to only 21% yield of the aldehyde **3k**, in which the vinyl group in the 3-silyl substitution was added by *s*-BuLi before or after silyl migration.

Reactions of substrates with a substituent at the 1-, 2- or 3-position were further tested using the more reactive *s*-BuLi/TMEDA complex to facilitate the initial deprotonation step. While the desired 3,3-bissilyl ketone **3l** was formed in 67% yield from **1l** (Table 3, entry 1), reaction of **1m** led only to a 1,3-hydrogen shift and gave ketone **3m** in 50% yield after hydrolysis of the resulting silyl enol ether (entry 2). Compounds **1n** and **1o**, which have methyl and allyl substitutions at the 2-position, were also suitable for this approach (entries 3 and 4). However, in the reaction of **1p**, only the addition of *s*-BuLi to the vinyl group was observed; no silyl group migration occurred (entry 5). Further attempts to obtain the aldehyde **3q** proved unsuccessful (entry 6). It seems reasonable to assume that the difficulty of forming a sterically constrained quaternary carbon center at the 3-position suppresses the silyl migration completely.

Trapping the 3,3-bissilyl enolate **2a** by various electrophiles, including trialkylsilyl chlorides (Table 4, entry 1), acyl chlorides (entries 2–6), anhydrides (entry 7), acyl imidazole (entry 8) and $PhNTf_2$ (entry 9) provided the corresponding 3,3-bissilyl enol derivatives exclusively in the *Z*-configuration and in good to excellent yields.

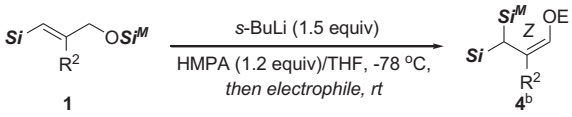
Table 4
Synthesis of 3,3-bissilyl enol compounds[a]

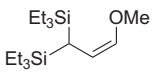
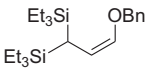
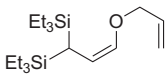
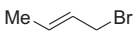
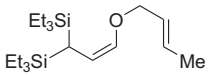
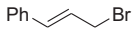
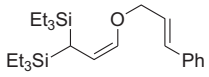
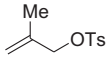
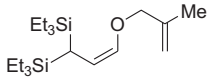
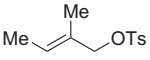
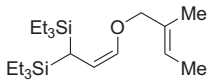
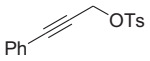
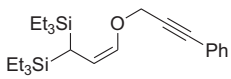
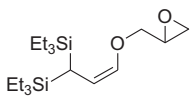
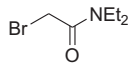
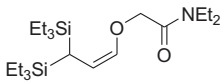
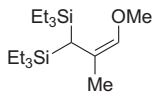
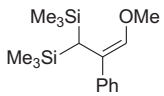


Entry	Electrophile	Product		Yield[c]
1	Et_3SiCl		**4a**	95%
2	EtCOCl		**4b**	93%
3	PhCOCl		**4c**	92%
4[b]	EtOCOCl		**4d**	90%
5	$(i\text{-Pr})_2NCOCl$		**4e**	92%
6			**4f**	70%
7			**4g**	52%
8			**4h**	50%
9	$PhNTf_2$		**4i**	60%

[a] Reaction conditions: allyloxysilane (0.15 M), *s*-BuLi (1.5 equiv), HMPA (1.2 equiv) in THF at −78 °C, then electrophile (3.0 equiv), 15 min.
[b] The stereoselectivity was determined by ^1H NMR spectroscopy, and the configuration was determined based on NOE experiments with **4j** in Table 5.
[c] Isolated yields after purification by silica gel column chromatography.

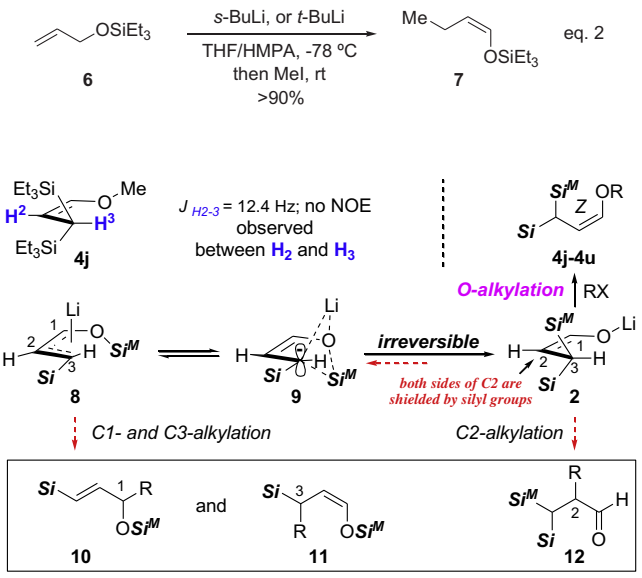
Table 5
Synthesis of 3,3-bissilyl enol compounds by selective O-alkylation[a]



Entry	Electrophile	Product		Yield[c]
1	MeI		**4j**	84%
2	BnBr		**4k**	90%
3			**4l**	63%
4[b]			**4m**	60%
5			**4n**	52%
6			**4o**	61%
7			**4p**	61%
8			**4q**	45%
9			**4r**	68%
10			**4s**	75%
11[d]	MeI		**4t**	60%
12[d]	MeI		**4u**	58%

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

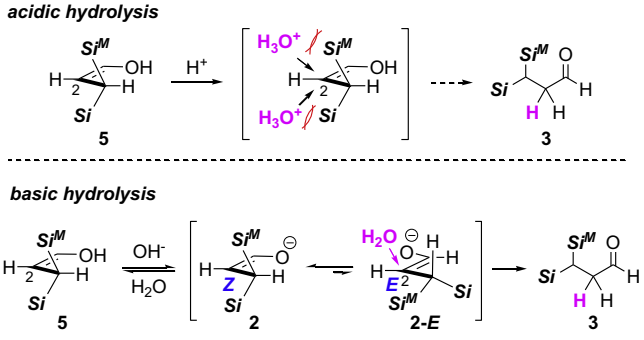
Alkylation of the lithium enolate was further investigated. The reaction could be performed with various electrophiles, such as alkyl halides (Table 5, entries 1, 9–12), benzyl bromide (entry 2), allyl halides and tosylates (entries 3–7), as well as propargyl tosylate (entry 8), giving functionally diverse *Z*-3,3-bissilyl enol ethers in moderate to good yields. The most surprising result was that all reactions reliably showed exclusive O-alkylation selectivity. We did not observe formation of either **10** or **11** from the C1- or C3-alkylation of allyl anion **8**, or formation of aldehyde **12** from the C2-alkylation of enolate **2** (Scheme 4). This is in marked contrast to previous results obtained in the reaction of simple allyloxysilane **6** with iodomethane (Eq. 2). Macdonald, Still[11] and Tomooka[8] all observed that only the C3-alkylated product **7** formed and neither retro-[1,2] nor retro-[1,4] Brook rearrangement occurred. To account for the unusual chemoselectivity displayed in our reaction, we propose the following mechanistic explanation.



Scheme 4. Modeling to explain the exclusive O-alkylation of 3,3-bissilyl enolate **2** by alkyl halides.

First, we found that the 1,4-silyl migration proceeded very fast and generally finished after several seconds. Given that the silyl group can stabilize the α-carbanion through a *p*–*d* π-bonding interaction,[12] the observed kinetic favorability may be because the C3-position in allyl anion **8** is much more electron-dense than the C1-position attached to an anion-destabilizing $OSiR_3$ group. Second, the entire process appears to be thermodynamically favorable, as the resulting lithium enolate can be stored at either −78 °C or 10 °C for several hours and still show good reactivity with electrophiles. This thermodynamic favorability implies that the reaction involves one or more irreversible processes. Based on the observed coupling constant (J=12.4 Hz) and the absence of an NOE between H_2 and H_3 in **4j**, we propose that the *Z*-lithium enolate adopts the most favorable conformation as **2**, thereby minimizing allylic strain and nonbonded interactions (Scheme 4). For this reason, regenerating allyl anion **8** through a reverse process via the pentacoordinated silicate **9** would be very difficult. For the same reason, the corresponding C1- and C3-alkylation to give **10** and **11**, respectively, would be prevented. At the same time, the bulky bissilyl moiety shields both sides of the 2-position in **2**, making C2-alkylation to give aldehyde **12** impossible. As a result, alkyl halides are forced to approach the oxygen anion completely, generating exclusively *O*-alkylated products **4**.

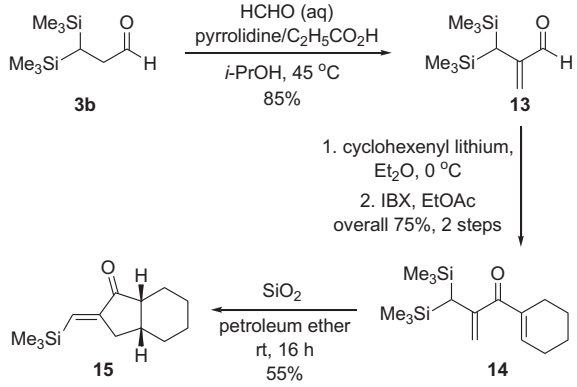
The above mechanistic analysis may also explain why the enol is stable to acidic hydrolysis, but can be transformed into an aldehyde by basic hydrolysis. As shown in Scheme 5, under acidic hydrolysis conditions, protonation of the enol double bond, which is shielded



Scheme 5. Proposal to explain why acidic hydrolysis gives the enol, while basic hydrolysis gives the aldehyde.

by the bulky bissilyl group, would form the desired aldehyde **3** only with great difficulty. However, under basic hydrolysis conditions, there would be an equilibrium between the enol **5** and *Z*-enolate **2**. The *Z*-enolate **2** could be subsequently converted into the *E*-enolate **2**-***E*** via a series of tautomerizations and bond rotations. Although this configurational conversion may be unfavorable, the subsequent protonation of **2**-***E*** from the side opposite to the silyl groups should be feasible, and this could drive the entire process slowly toward formation of the aldehyde **3**.

The synthetic utility of 3,3-bissilyl aldehyde was explored by examining the silicone-assisted Nazarov reaction[13] of divinyl ketone **14**. As shown in Scheme 6, Mannich reaction of **3b** with formaldehyde generated enal **13** in 85% yield,[14] and this was further transformed into **14** in overall 75% yield by addition to cyclohexenyl lithium and IBX oxidation of the resulting allylic alcohol. While general Lewis acids and Brønsted acids yielded complex mixtures, SiO_2 proved effective at promoting a smooth Nazarov reaction of **14**, giving the 5,6-membered ring-fused β-silyl enone **15** in 55% yield and with excellent stereochemical control of both the ring junction and *exo*-cyclic double bond.[15]



Scheme 6. An SiO_2-promoted Nazarov reaction of bissilyl divinyl ketone **14**.

3. Conclusion

We have described detailed studies of the retro-[1,4] Brook rearrangement of 3-silyl allyloxysilanes. Control experiments and NMR studies have been used to rationalize the observed formation of unusual 3,3-bissilyl enols, which are stable to acidic hydrolysis but can be transformed into the corresponding aldehyde by basic hydrolysis. These studies further show that the 3,3-bissilyl enolates can be *O*-alkylated by alkyl halides with complete chemoselectivity. The synthetic utility of the 3,3-bissilyl aldehydes has been demonstrated by preparing cyclic β-silyl enone from a bissilyl divinyl ketone via an SiO_2-promoted Nazarov reaction. Further applications of this methodology are being investigated.

4. Experimental section

4.1. General conditions

^1H NMR spectra were recorded at 400 MHz (Varian) and ^{13}C NMR spectra were recorded at 100 MHz (Varian) using $CDCl_3$ (except where noted) with TMS or residual solvent as standard. Infrared spectra were obtained using NaCl plates on a VECTOR22. High-resolution mass spectral analyses were performed on a Waters Q-TOF Premier apparatus. HMPA, TMEDA, CH_2Cl_2 and Et_3N were distilled from CaH_2. Et_2O and THF were distilled from sodium. TLC was performed on glass-backed silica plates and visualized using UV, $KMnO_4$ stains, $H_3PO_4{\cdot}12MoO_3$/EtOH stains, and H_2SO_4

(concd)/EtOH stains. Column chromatography was performed using silica gel (300–400 mesh) and a mobile phase of EtOAc/petroleum ether.

4.2. General procedure for the synthesis of 3,3-bissilyl aldehydes

To a solution of **1a** (86 mg, 0.3 mmol) in anhyd THF (1.5 mL) and anhyd HMPA (64 μL, 0.36 mmol) under argon was added *s*-BuLi (0.45 mL of a 1.0 M solution in pentane, 0.45 mmol) at −78 °C. After stirring for 5 min, H_2O (30 μL, 3.0 mmol) was added and the resulting solution was warmed to room temperature with stirring for another 3 h. The organic layer was diluted with Et_2O (5.0 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5–10% of EtOAc/petroleum ether) afforded pure **3a** (63 mg, 91%) of as a colorless oil.

*4.2.1. 3,3-Bistriethylsilyl aldehyde (**3a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.56 (q, 12H, J=8.0 Hz), 0.84 (t, 1H, J=6.0 Hz), 0.95 (t, 18H, J=8.0 Hz), 2.55 (dd, 2H, J=1.6, 6.0 Hz), 9.73 (t, 1H, J=1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ -1.7, 4.2, 7.8, 41.0, 202.4; IR (neat) cm^{-1} 2954s, 2881s, 2734m, 1709s, 1461m, 1417m, 1380m; HRMS (MALDI, *m*/*z*) calcd for $C_{15}H_{34}OSi_2Na$ (M+Na)$^+$: 309.2040, found 309.2047.

4.3. General procedure for the synthesis of 3,3-bissilyl enol derivatives in Table 4

To a solution of **1a** (86 mg, 0.3 mmol) in anhyd THF (1.5 mL) and anhyd HMPA (64 μL, 0.36 mmol) under argon was added *s*-BuLi (0.45 mL of a 1.0 M solution in pentane, 0.45 mmol) at −78 °C. After stirring for 5 min, triethylsilyl chloride (135 mg, 0.9 mmol) was added and the resulting solution stirred at −78 °C for another 15 min. Then the reaction was quenched with satd aq $NaHCO_3$ (3.0 mL) and extracted with Et_2O (2×5 mL). The combined organic phases were dried over Na_2SO4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5–10% of EtOAc/petroleum ether) afforded pure **4a** (114 mg, 95%) of as a colorless oil.

*4.3.1. 3,3-Bistriethylsilyl triethylsilyl enol ether (**4a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.53 (q, 12H, J=8.0 Hz), 0.63 (q, 6H, J=8.0 Hz), 0.93 (t, 9H, J=8.0 Hz), 0.94 (t, 9H, J=8.0 Hz), 0.97 (t, 9H, J=8.0 Hz), 1.89 (d, 3H, J=12.0 Hz), 4.26 (dd, 1H, J=5.6, 12.4 Hz), 6.15 (d, 1H, J=5.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 4.6, 6.4, 6.6, 6.8, 7.5, 7.9, 107.2, 135.3; IR (neat) cm^{-1} 3024w, 2954s, 2910s, 2880s, 1636m, 1461m, 1414m, 1270m, 1238m, 1101s; HRMS (MALDI, *m*/*z*) calcd for $C_{21}H_{48}OSi_3Na$ (M+Na)$^+$: 423.2905, found 423.2906.

4.4. General procedure for the synthesis of 3,3-bissilyl enol derivatives in Table 5

To a solution of **1a** (86 mg, 0.3 mmol) in anhyd THF (1.5 mL) and anhyd HMPA (64 μL, 0.36 mmol) under argon was added *s*-BuLi (0.45 mL of a 1.0 M solution in pentane, 0.45 mmol) at −78 °C. After stirring for 5 min, CH_3I (56 μL, 0.9 mmol) was added and the resulting solution was warmed to room temperature with stirring for another 4 h. Then the reaction was quenched with satd aq $NaHCO_3$ (3.0 mL) and extracted with Et2O (2×5 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 5–10% of EtOAc/petroleum ether) afforded pure **4j** (79 mg, 84%) of as a colorless oil.

*4.4.1. 3,3-Bistriethylsilyl methyl enol ether (**4j**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.57 (q, 12H, J=8.0 Hz), 0.94 (t, 18H, J=8.0 Hz), 1.72 (d, 1H, J=12.4 Hz), 3.51 (s, 3H), 4.24 (dd, 1H, J=6.0, 12.4 Hz), 5.80 (d, 1H, J=6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 7.8, 8.6, 59.0, 105.4, 143.5; IR (neat) cm^{-1} 3024w, 2953s, 2912s, 1644m, 1460m, 1415m, 1377m, 1267m, 1236m, 1107s; HRMS (MALDI, *m*/*z*) calcd for $C_{16}H_{36}OSi_2$ Na (M+Na)$^+$: 323.2197, found 323.2210.

4.5. Preparation of bissilyl divinyl ketone 14 and the subsequent SiO_2-promoted Nazarov reaction to give cyclic β-silyl enone 15

To a mixture of aqueous formaldehyde solution (37% formaldehyde in water, 24 mmol) and **3b** (4 g, 20 mmol) in *i*-PrOH (2 mL) were added pyrrolidine (0.5 mL, 6 mmol) and propionic acid (0.45 mL, 6 mmol). The reaction mixture was stirred at 45 °C for 10 h. The mixture was quenched with satd aq $NaHCO_3$ (10 mL) and extracted with Et_2O (3×20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 0–0.2% of EtOAc/petroleum ether) afforded pure **13** (3.6 g, 85%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (s, 18H), 1.87 (s, 1H), 5.86 (s, 1H), 6.07 (s, 1H), 9.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.2, 16.5, 130.9, 150.8, 194.6; IR (neat) cm^{-1} 2960 (s), 2855 (m), 1696 (s), 1608 (m), 1256 (s), 1051 (m), 845 (s), 691 (m); HRMS (MALDI, *m*/*z*) calcd for $C_{10}H_{23}OSi_2$ (M+H)$^+$: 215.1282, found 215.1286.

To a solution of **13** (1.5 g, 7.0 mmol) in dry ether (10 mL) was added cyclohexenyl lithium (14 mL of a ~1.0 M solution in Et_2O, 14.0 mmol)[16] at 0 °C. After stirring for 20 min, the reaction mixture was quenched with satd aq NH_4Cl (20 mL) and extracted with Et_2O (3×10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 0.7%–0.9% of EtOAc/petroleum ether) afforded the pure alcohol (1.74 g, 85%) of as a colorless oil. The resulting alcohol (273 mg, 0.92 mmol) was dissolved in ethyl acetate (13.5 mL) and IBX (386 mg, 1.38 mmol) was added. The resulting suspension was immersed in an oil bath set to 80 °C and stirred vigorously open to the atmosphere overnight. The reaction mixture was cooled to room temperature and filtered through a medium glass frit. The filter cake was washed with EtOAc (3×5 mL) and the combined filtrates were concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 0–0.25% of EtOAc/petroleum ether) afforded pure **14** (325 mg, 88%) of as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 18H), 1.62–1.68 (m, 4H), 1.75 (s, 1H), 2.22–2.27 (m, 4H), 5.44 (s, 1H), 5.56 (s, 1H), 6.64 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.2, 21.6, 22.0, 24.5, 25.7, 121.5, 137.8, 139.4, 148.0, 199.7; IR (neat) cm^{-1} 2949s, 2859w, 1640s, 1598w, 1249m, 1203w, 844m; HRMS (MALDI, *m*/*z*) calcd for $C_{16}H_{30}OSi_2Na$ (M+Na)$^+$: 317.1727, found 317.1743.

To a suspension of flame-activated silica gel (210 mg, 200–300 mesh) in dry petroleum ether (5 mL) was added **14** (20 mg, 0.07 mmol). After stirring at room temperature for 16 h, the reaction mixture was filtered. The filtrates were concentrated under reduced pressure. Purification of the crude residue via silica gel flash column chromatography (gradient eluent: 0–0.5% of EtOAc/petroleum ether) afforded **15** (8.3 mg, 55%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (s, 9H), 0.90 (m, 1H), 1.07 (m, 1H), 1.20 (m, 1H), 1.47–1.50 (m, 2H), 1.56 (m, 1H), 1.68 (m, 1H), 2.14 (m, 1H), 2.28–2.33 (m, 2H), 2.42 (d, 1H, J=16.4 Hz), 2.62 (ddd, 1H, J=2.8, 6.0, 16.4 Hz), 6.75 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.1, 22.6, 23.0, 24.1, 29.5, 33.3, 34.8, 48.7, 134.3, 150.6, 206.0; IR (neat) cm^{-1} 2929s, 2852m,

1722s, 1616w, 1249m, 1165w, 860m, 840m; HRMS (MALDI, *m*/*z*) calcd for $C_{21}H_{48}OSi_3Na$ $(M+Na)^+$: 245.1338, found 245.1333.

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Supplementary data

Experimental procedures and spectral data for products (PDF) can be found in the online version of this article. Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tet.2012.06.005.

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