Generation and Reactions of α-Silyloxiranyllithium in a Microreactor

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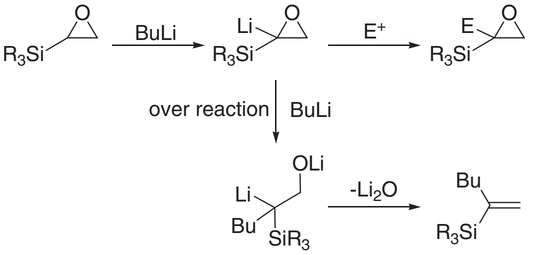
α-Triphenylsilyloxiranyllithium was effectively generated by the reaction of epoxyethyltriphenylsilane with *n*-BuLi in a microflow reactor at 0 °C, though it is well known that an over reaction cannot be avoided even at lower temperatures in a conventional macrobatch reactor. Subsequent reactions with various electrophiles in the microflow reactor gave the corresponding α-substituted epoxysilanes.

Epoxysilanes[1] have been used as versatile synthetic intermediates.[2] For example, regiospecific and stereospecific opening of epoxysilanes with a variety of nucleophiles gives diastereomerically pure hydroxysilanes, which undergo syn or anti elimination to give the corresponding alkenes stereoselectively.[3] Therefore, development of general and straightforward methods for synthesizing epoxysilanes is very important. In general, epoxidation of vinylsilanes with H_2O_2 or peroxy acids have been utilized for this purpose.[1] On the other hand, the generation of oxiranyllithium species by the deprotonation of epoxysilanes with BuLi also serves as a useful method for construction of various substituted epoxysilanes.[4,5] However, α-silyloxiranyllithiums are highly unstable and undergo an over reaction with BuLi. Therefore, oxiranyllithiums are usually generated at very low temperatures. This requirement limits synthetic applications of the α-silyloxiranyllithium methodology.

We have recently reported that microflow systems[6–8] are useful for conducting reactions involving highly unstable short-lived intermediates.[9] For example, α-aryloxiranyllithiums were effectively generated in a microflow reactor.[9f] We report herein that α-silyloxiranyllithiums could be easily generated in a microflow reactor.

We chose to study the reaction of epoxyethyltriphenylsilane (**1**) with butyllithium.[10] In a macrobatch reactor, it is known that the reaction should be carried out at low temperatures such as −78 °C to avoid the over reaction.[5a] In fact, at higher temperatures such as 0 °C, the reaction of **1** with *n*-BuLi (1.5 equiv) followed by treatment with chlorotrimethylsilane in a conventional macrobatch reactor gave 1-trimethylsilyl-1-triphenylsilylepoxyethane (**2**) only in very low yield (4% yield), and 2-triphenylsilyl-1-hexene (**3**), which was produced by reaction of α-silyloxiranyllithium with *n*-BuLi (Scheme 1) in 37% yield.[5c]



Scheme 1. The generation and reaction of α-silyloxiranylllithiums.

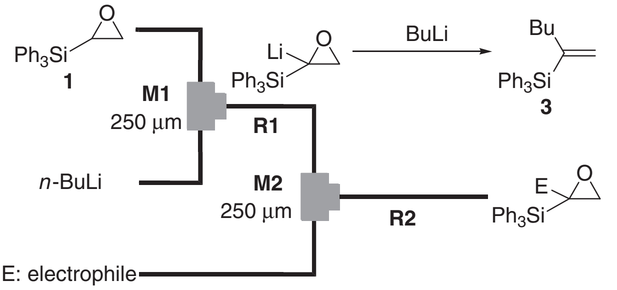


Figure 1. Microflow system for deprotonation of epoxyethyltriphenylsilane (**1**). T-shaped micromixer: **M1** (inner diameter: 250 µm) and **M2** (inner diameter: 250 µm), microtube reactor: **R1** and **R2** ($\phi = 1000$ µm, length = 50 cm), a solution of epoxyethyltriphenylsilane: 0.10 M in THF (6.0 mL/min), a solution of *n*-BuLi: 0.60 M in hexane (1.5 mL/min), a solution of electrophile: 0.36 M in THF (3.0 mL/min).

Next, we examined the reaction in a microflow system consisting of two T-shaped micromixers (**M1** and **M2**) and two microtube reactors (**R1** and **R2**) shown in Figure 1. The yield of **2** was determined by changing the residence time in **R1** and the temperature of the cooling bath in the microflow system. The residence time was adjusted by changing the length of **R1** with a fixed flow rate.

As profiled in Figure 2a, the yield significantly depends on both temperature and residence time (See Supporting Information for the details).[11,12] Figure 2b shows the cross section at 0 and 24 °C. At 24 °C, the yield of **2** increased with an increase in the residence time in **R1** because of the progress of the deprotonation of **1**. The yield became maximum at a residence time of 0.377 s. Further increase in the residence time caused a decrease in the yield of **2** presumably because of the over reaction. At 0 °C, the yield of **2** reached the maximum at a residence time of 3.14 s.

Using the optimized conditions (0 °C, residence time in **R1**: 3.14 s), the reactions of α-silyloxiranyllithium with various electrophiles were examined. As summarized in Table 1, reactions with iodomethane, chlorotrimethylsilane, chlorodimethylsilane, chlorodimethylphenylsilane, benzyl bromide, benzaldehyde, chlorotributylstannane, methyl chloroformate, and dimethylcarbamoyl chloride were successfully carried out to give the corresponding α-substituted epoxysilanes in good yields.

In conclusion, we have developed an efficient method for synthesizing α-substituted epoxysilanes based on generation and reactions of α-silyloxiranyllithium without the over reaction at 0 °C by virtue of short residence times and efficient temperature control in microflow reactors. The scope and limitations of the present method and synthesis of a variety of substituted epoxysilanes are under investigation in our laboratory.

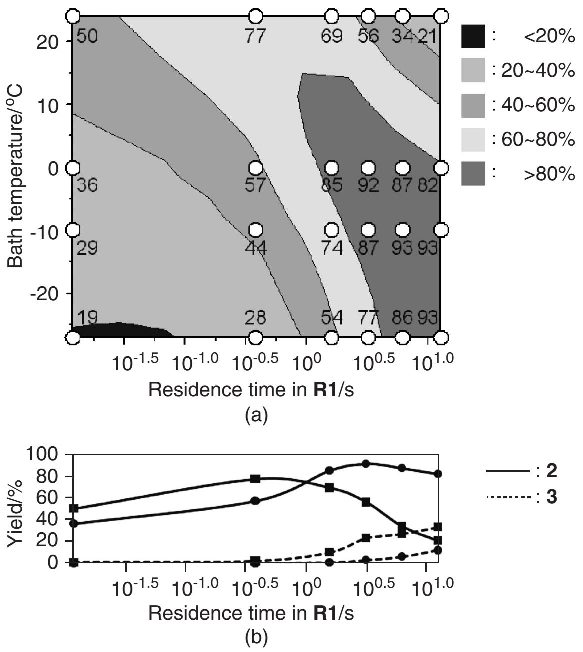
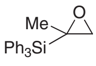
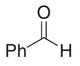
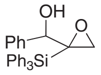
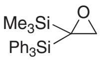
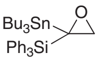
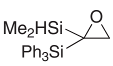
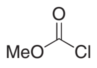
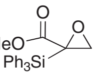
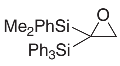
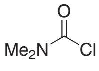
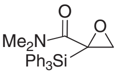
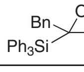


Figure 2. Effects of temperature and residence time on the yield of 1-trimethylsilyl-1-triphenylsilylepoxyethane (**2**): (a) Contour plot with scatter overlay of the yields (%). (b) The yields of **2** and **3**, Cross section at 0 and 24 °C (●: 0 °C, ■: 24 °C).

Table 1. Functionalization of epoxyethyltriphenylsilane via α-silyloxiranyllithium

Electrohpile	Product	Yield/%	Electrohpile	Product	Yield/%
MeI		78[a]			82[a]
Me_3SiCl		92[b]	Bu_3SnCl		93[a]
Me_2HSiCl		87[a]			93[a]
$Me_2PhSiCl$		96[a]			86[a]
BnBr		76[a]			

[a]Isolated yield. [b]Determined by GC.

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10 When deprotonation of epoxyethyltrimethylsilane with *sec*-BuLi followed by reaction with iodomethane was carried out using a microflow system, desired product was obtained in 32% yield (See the Supporting Information for details).

11 When 1.0 equivalent of *n*-BuLi was used, the yield of **2** decreased but that of **3** also decreased (See the Supporting Information for details).

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

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