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The reaction of 1-silylcyclopropyl anions with dichloromethyl methyl ether: the efficient synthesis of cyclopropyl silyl ketones via cyclopropylidene derivatives

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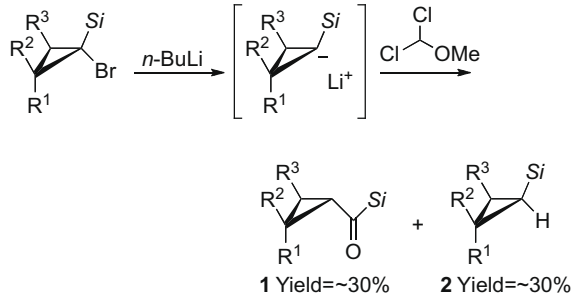
ABSTRACT

The reaction of 1-silylcyclopropyl anions with dichloromethyl methyl ether is described. The reaction with an excess amount of dichloromethyl methyl ether gives the corresponding cyclopropyl silyl ketones in low yields. On the other hand, the reaction under basic conditions proceeded smoothly to afford the corresponding cyclopropylidene derivatives, exclusively. The resulting cyclopropylidene compounds are subjected to hydrolysis or trapping with electrophiles easily to give the cyclopropyl silyl ketone derivatives in good yields.

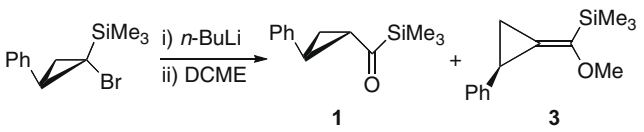
Dichloromethyl methyl ether (DCME) has been used extensively as a carbon monoxide equivalent in the reactions with boranes[1] and borinates,[2] or formylating reagent for aromatic compounds[3] and vinylsilanes[4] in the presence of Lewis acids. In contrast, the reaction of DCME with carbanions under basic conditions is not well-known to our knowledge. Previously we have reported that 1-silylcyclopropyl anions derived from 1-silylcyclopropyl bromides with *n*-butyllithium react with DCME to afford the corresponding cyclopropyl silyl ketones.[5] Cyclopropyl silyl ketones are useful synthetic intermediates. For example, we have reported that the efficient synthesis of silyl-substituted dihydrofurans and stereoselective synthesis of *Z*-homoallyl derivatives using cyclopropyl silyl ketones.[6] However, there have been just a few reports on the preparation of cyclopropyl silyl ketones,[7] so our synthetic method was widely employed. But the low yield was a huge drawback for this procedure. The isolated yield of cyclopropyl silyl ketones **1** was less than 30%[8] and an equivalent amount of the protonated compound **2** was obtained as a by-product (Scheme 1). Here, we wish to describe an improvement of the reaction conditions to proceed the reaction of DCME with carbanions under basic conditions, and also the observation of cyclopropylidene derivatives which are precursors of cyclopropyl silyl ketones **1**. This provides mechanistic evidence. As a result reasonable yields of cyclopropyl silyl ketones **1** were achieved.

The treatment of 2-phenyl-1-trimethylsilylcyclopropyl bromide with *n*-butyllithium gave the corresponding carbanion. The following reaction with DCME was carried out. The reaction proceeded to



Scheme 1. Synthesis of cyclopropyl silyl ketones.

Table 1
Effect of amounts of *n*-BuLi and DCME



Entry	*n*-BuLi (equiv)	DCME (equiv)	Yield[a] (%)	
			1	**3**
1	1.1	1.2	29	–
2	1.1	0.6	–	45
3	2.5	1.2	–	81

[a] Isolated yield.

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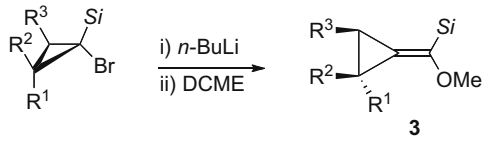
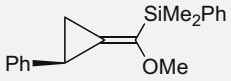
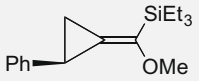
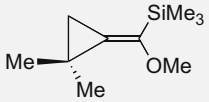
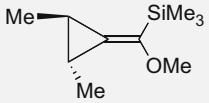
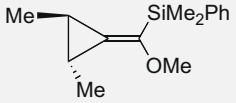
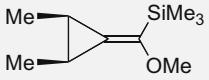
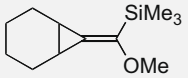
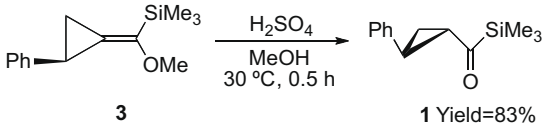
Table 2
Effect of substituents on cyclopropane ring and silicon atom



Entry	Product	Yield[a] (%)
1		74 (>99/1)[b]
2		64 (>99/1)[b]
3		74 (>99/1)[b]
4		70
5		69
6		72
7		76

Molar ratio, cyclopropyl bromide/*n*-BuLi/DCME = 1:2.5:1.2.
[a] Isolated yield.
[b] The *E*/*Z* ratios of the compounds are given in parentheses.

afford the corresponding cyclopropyl silyl ketone **1** or cyclopropylidene derivative **3** according to the reaction conditions. The results are summarized in Table 1. In accordance with the previous study,[5] 1.1 equiv of *n*-butyllithium was used to lithiate the cyclopropyl bromide and then 1.2 equiv of DCME was added to the reaction mixture (entry 1). In this case, the ketone product **1** was isolated in low yield accompanied by the formation of compound **2** as mentioned above previously. Interestingly, when 0.6 equiv of DCME was used, the cyclopropylidene product **3** was formed exclusively in moderate yield with complete *E*-selectivity and the ketone **1** was not obtained at all (entry 2). However, a small amount of silylcyclopropane **2** was also obtained as a by-product. To improve the yield of the cyclopropylidene derivative **3**, the reaction using 2.5 equiv of *n*-butyllithium and 1.2 equiv of DCME was examined, and then the best yield was observed (entry 3).



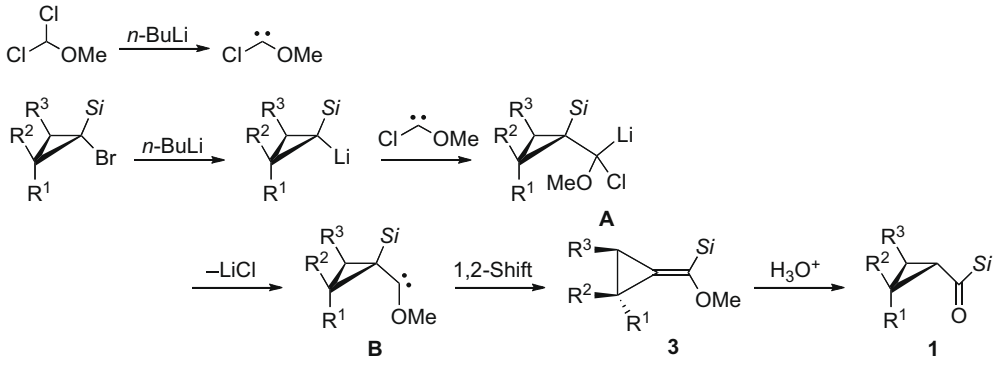
Scheme 2. Conversion of cyclopropylidene derivative into acylsilane with protic acid.

The reaction of other 1-silylcyclopropyl bromides having different groups on the cyclopropane ring or silicon atom was carried out.[9] These results are shown in Table 2. These reactions also proceeded smoothly to furnish the corresponding cyclopropylidene derivatives **3** in good yields, regardless of the kind of the substituents. As previously indicated, of the two possible diastereomeric products, *E*-isomers were selectively obtained (entries 1–3).

These cyclopropylidene derivatives were not very stable and hydrolyzed slowly during attempted chromatography on silica gel to give the cyclopropyl silyl ketones in the purification of crude products. So the hydrolysis of the cyclopropylidene derivative **3** with sulfuric acid in methanol was carried out (Scheme 2). The reaction was complete in 0.5 h at 30 °C and gave the corresponding cyclopropyl silyl ketone **1** in good yield.

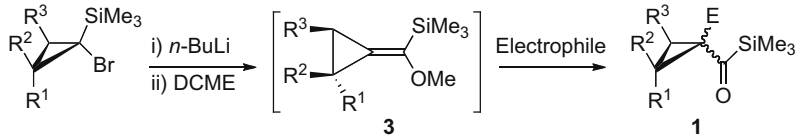
The results mentioned above suggest that more than two equivalents of *n*-butyllithium are required to complete the reaction. Thus, the following mechanism for the reaction was proposed (Scheme 3). *n*-Butyllithium acts as a base and formally eliminates HCl from DCME to give the chloromethoxycarbene.[10] Also, *n*-butyllithium debrominates cyclopropyl bromides and the resulting bromine–lithium exchange affords the corresponding cyclopropyllithium. The reaction of chloromethoxycarbene with the cyclopropyllithium provides lithium carbenoid intermediate **A**.[11] The loss of molecular lithium chloride from **A** gives cyclopropylmethoxycarbene **B**. The 1,2-migration of the silyl group on the adjacent carbon to this carbene center affords the cyclopropylidene derivative **3**.[12] In this migration process, the thermodynamically favored *E*-isomer is produced, exclusively. This cyclopropylidene **3** is easily hydrolyzed to the corresponding silyl ketone derivative **1** under acidic conditions. On the other hand, in the reaction with a smaller amount of *n*-butyllithium (Table 1, entry 1), a part of cyclopropyllithium acts as a base and reacts with DCME. In other words, cyclopropyl anion abstracts a proton from DCME to afford the silyl cyclopropane **2**.

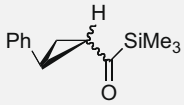
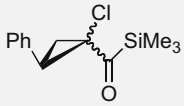
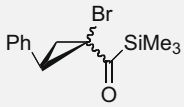
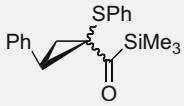
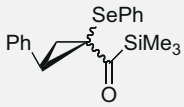
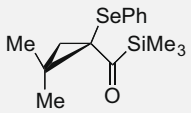
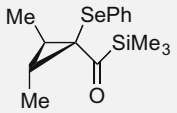
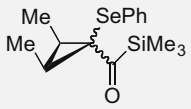
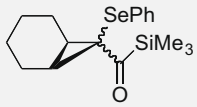
In order to further evaluate the potential of the resulting cyclopropylidene derivatives as synthetic intermediates, the generation of cyclopropylidene derivatives and the following trapping by some



Scheme 3. Plausible reaction mechanism.

Table 3
The one-pot synthesis of cyclopropyl silyl ketones via cyclopropilidene derivatives



Entry	Electrophile	Product	Yield[a,b] (%)
1	H_3O^+		73 (64/36)
2	NCS		64 (76/24)
3	NBS		56 (75/25)
4	PhSCl		48 (86/14)
5	PhSeCl		59 (71/29)
6	PhSeCl		17
7	PhSeCl		63
8	PhSeCl		28 (>99/1)
9	PhSeCl		50 (>99/1)

Molar ratio, cyclopropyl bromide/*n*-BuLi/DCME = 1:2.5:1.2.
[a] Isolated yield.
[b] The diastereomeric ratios of the compounds are given in parentheses.

electrophiles were carried out in a one-pot procedure. The results are summarized in Table 3. The reaction with protic acid as an electrophile gave the corresponding acylsilane in 73% yield (entry 1). Therefore cyclopropyl silyl ketones **1** are conveniently prepared in a one-pot reaction of 1-silylcyclopropyl anions with DCME followed by hydrolysis in good yields. On the other hand, the reaction with NCS, NBS, PhSCl, and PhSeCl proceeded to afford the corresponding cyclopropyl silyl ketones having different substituents on the 1-position of cyclopropane ring in moderate yields.[13] In these reactions, one isomer of the two possible diastereomeric isomers was preferentially formed. At the present time, however, the configurations of these major isomers have not yet been determined.

In conclusion, the reaction of DCME with *n*-butyllithium in the presence of 1-silylcyclopropyl anions was investigated. Under basic conditions the reaction proceeded smoothly to afford the corresponding cyclopropylidene derivatives. The resulting cyclopropylidene compounds were subjected to hydrolysis, which gave the cyclopropyl silyl ketones in good yields. As a result, DCME acts as an insertion reagent of carbon monoxide to C–Si bond of 1-silylcyclopropyl anions under basic conditions. Further studies in our laboratory are aimed at expanding the scope of these reactions. The results will be reported in due course.

Acknowledgment

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8. The yields denoted in Ref. 5 are determined by G.C.
9. Typical procedure for the generation of 1-silylcyclopropyl anions and the following reaction with DCME: A 100-ml four-necked, round-bottomed flask equipped with argon inlet adapter, rubber septum, thermometer, drop funnel, and magnetic stirrer bar was charged with 20 ml of dry THF and 5 mmol of 1-bromo-1-trimethylsilylcyclopropane. This solution was cooled to −90 °C and *n*-butyllithium (1.66 M solution in hexane) 7.5 ml (12.5 mmol) was added slowly over several minutes. The resulting reaction mixture was stirred for 0.5 h, and then a solution of dichloromethyl methyl ether (DCME) (0.69 g, 6 mmol) in THF (2.5 ml) was added. After stirring for 30 min, 1 ml of methanol was added and the reaction mixture was allowed to warm to ambient temperature and then poured into brine. The aqueous layer was extracted with diethyl ether for three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel with hexane/ethyl acetate/triethylamine to give the cyclopropylidene derivative. Selected spectral properties of methoxy-2-phenylcyclopropylidenemethylsilane are as follows. IR (neat) 2958, 1720, 1604, 1496, 1452, 1248, 1203, 1147, 839 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.08–7.25 (m, 5H), 3.82 (s, 3H), 2.52 (dd, J = 4.2 Hz, 7.8 Hz, 1H), 2.01 (t, J = 7.6 Hz, 1H), 1.43 (dd, J = 4.2 Hz, 7.6 Hz, 1H), −0.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.5, 143.9, 128.2, 125.8, 125.5, 107.8, 56.0, 18.4, 18.3, −2.1. HRMS calcd for $C_{14}H_{20}OSi$ (M^+) 232.1284, found 232.1280.
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13. Selected spectroscopic data for 2,3-dimethyl-1-phenylselenocyclopropyl trimethylsilyl ketone (Table 3, entry 7). IR (neat) 3059, 2957, 1617, 1479, 1247, 1077, 844 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32–7.17 (m, 5H), 1.98 (dq, J = 6.3 Hz, 5.9 Hz, 1H), 1.46 (dq, J = 6.3 Hz, 5.9 Hz, 1H), 1.25 (d, J = 6.3 Hz, 3H), 1.08 (d, J = 6.3 Hz, 3H), 0.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 240.9, 132.0, 129.0, 128.3, 125.7, 49.0, 31.5, 22.5, 15.8, 13.3, −1.8. HRMS calcd for $C_{15}H_{22}OSeSi$ (M^+) 326.0605, found 326.0604.