

Sequential Introduction of Carbon Nucleophiles onto Silicon Atoms Using Methyl as a Leaving Group

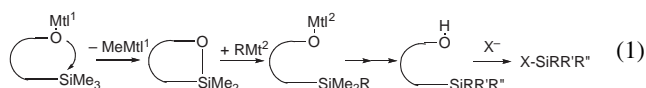
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A molecular structure, which has a trimethylsilyl group in close proximity to a hydroxy group spatially, converts methyl on silicon into a good leaving group.

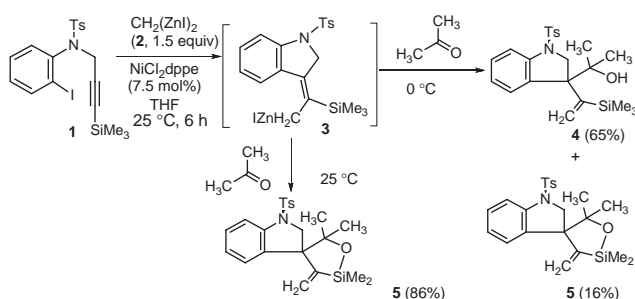
Cleavage of Si–C bonds via a hypercoordinate silicate has been well discussed and studied both from mechanistic and the synthetic viewpoints.¹ The carbanion equivalent, which is released from the hypercoordinate silicate atom, has been used for transition-metal-catalyzed cross-coupling reactions.² In the migration of an organo-group from a hypercoordinate silicate, aryl, benzyl, alkynyl, alkenyl, and allyl groups have higher migration tendency than alkyl groups.³ Among saturated alkyl groups, methyl is the most labile. In some specific substrates, it had been reported that a methyl group on Si can be removed by an intramolecular coordination of an anionic oxygen atom such as metal alkoxide or carboxylate.⁴ To complete this process, the oxygen atom should be placed in the proximity of silicon atom spatially by molecular design. When the coordination is well tuned, the methyl on Si can be replaced with an alkoxide group specifically; an alkoxy group on a Si will be replaced easily with an organolithium or -magnesium reagent. As a result of these transformations, a variety of substituents can be introduced on the Si atom starting from trimethylsilyl-substituted compounds as shown in eq 1. The transformation will be a convenient route to prepare chiral trialkylsilyl halides or alkoxides which have three different alkyl groups on the silicon atom.



In the course of our synthetic studies using bis(iodozincio)methane,⁵ we have found that a nickel-catalyzed arylmetallation to an alkyne, which is followed by a cross-coupling with bis(iodozincio)methane,⁶ affords an allylic zinc species with a tetrasubstituted alkene unit (eq 2).



When this reaction was applied to *N*-(2-iodophenyl)-4-methyl-*N*-[3-(trimethylsilyl)prop-2-ynyl]benzenesulfonamide (**1**), an intramolecular carbometallation lead to the formation of cyclic allylic zinc **3**, which added to acetone to afford the alcohol **4** in 65% yield at 0 °C accompanying a formation of a cyclic silyl ether **5** in 16% yield (Scheme 1). When the reaction temperature was kept at 25 °C for 2 h after addition of acetone, the cyclic silyl ether **5** was obtained in 86% yield. The formation of **5** was considered to be a result of a ring closure of zinc alkoxide of **4** by releasing a methyl from Si atom.



Scheme 1. Preparation of cyclic silyl ether using methyl group as a leaving group.

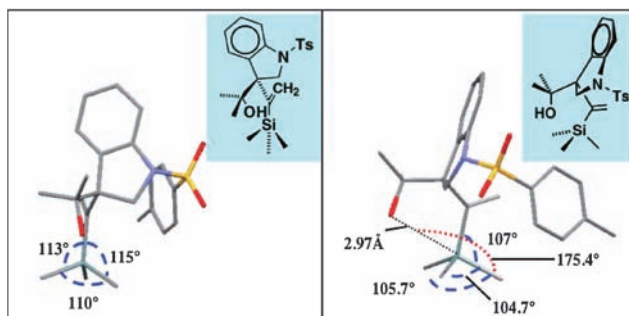
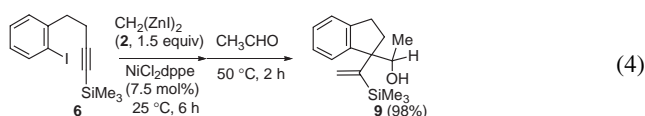
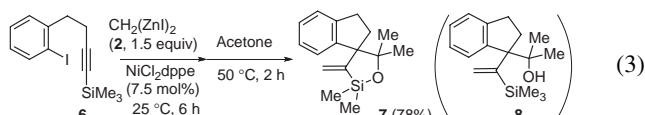


Figure 1. Detailed structural data around Si atom of **4**.

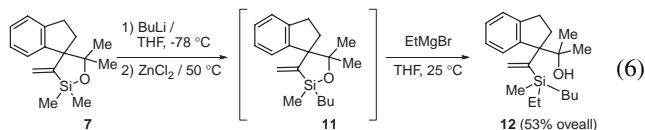
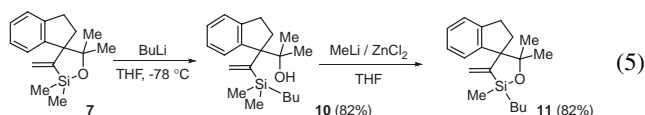
The X-ray analysis of a single crystal of **4** gave structural information as shown in Figure 1.⁷ The notable stereochemical feature of compound **4** is a pyrrolidine ring which has geminal substituents: One is an α -trimethylsilylvinyl group and the other is a 1-hydroxy-1-methylethyl group. Disfavored steric interaction between the pyrrolidine ring and trimethylsilyl group enforces the silyl group to the exo-position. The steric bulkiness of the trimethylsilyl group also effects the conformation of the 1-hydroxy-1-methylethyl group. The hydroxy group, which is smaller than methyl group, will come closer to the trimethylsilyl group. As shown in Figure 1, the data of bond angles around Si atom implied an interaction of hydroxy group and Si atom.⁸ The sum of three bond angle around Si atom was 338°, which is bigger than the typical tetrahedral Si case (328°). The distance between Si and O atom was 2.97 Å, which is shorter than the simple addition of van der Waals radius of Si and O atoms (3.35 Å). Once the hydroxy group is converted into zinc-alkoxide, the corresponding pentacoordinate silicate will be formed smoothly.

As shown in eq 3, alkyne **6**, which is a carbon analog of compound **1**, was also examined in the nickel-catalyzed reaction followed by treatment with acetone at 50 °C resulting formation of the corresponding cyclic ether **7** in 78% yield.⁹ When the reaction was performed at 25 °C, the simple adduct **8** was obtained

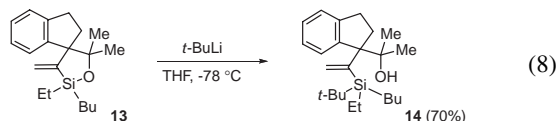
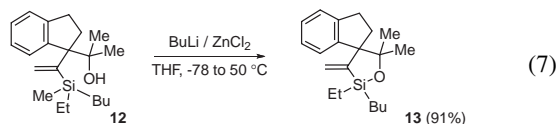
in 80% yield. Treatment of the intermediary allylic zinc species with acetaldehyde at 50 °C afforded the alcohol **9** in 98% yield without the formation of the cyclic ether. Even after treatment for 6 h at 50 °C, the cyclic silyl ether was not detected (eq 4).



As shown in eq 5, the cyclic silyl ether **7** which was formed from **6** in eq 3 was treated with butyllithium to afford the corresponding ring-opening product **10** in 82% yield. When the alcohol **10** was treated with methyllithium and zinc(II) chloride in THF at 50 °C, the cyclic silyl ether **11**, which was formed by elimination of a methyl group, was obtained in 82% yield. The product has two stereogenic centers and obtained as a mixture of diastereomers in 1:1 ratio. In this transformation, the cyclic ether **7**, which would be formed by butyl group elimination from **10**, was not detected. In this case also, methyl group was substituted selectively to give **11**. Without isolation of the alcohol **10**, the sequential treatment with butyllithium, zinc(II) chloride, and ethylmagnesium bromide in THF afforded the corresponding organosilane **12** carrying butyl, ethyl, and methyl groups in 53% overall yield (eq 6).

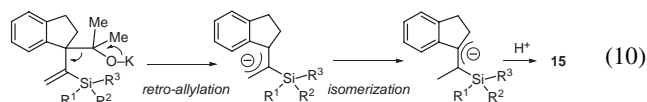
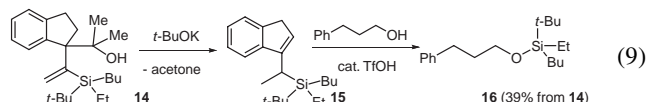


Treatment of alcohol **12** with butyllithium and zinc(II) chloride gave the cyclic ether **13** via a selective elimination of methyl (eq 7). Nucleophilic attack of organolithium reagent onto **13** afforded the corresponding ring-opening product **14**. Considering the structure of the starting material **6**, the production of **14** showed that three methyl groups on Si atom can be used as leaving groups (eq 8).



As shown in eq 9, a device for methyl group migration can be dismantled as follows. Treatment of **14** with *t*-BuOK triggered a retro-allylation (eq 10)¹⁰ accompanying a loss of acetone, followed by an isomerization, and afforded an allylsilane derivative **15**. The allyl moiety in **15** was removed with alcohol

in the presence of acid catalyst and gave **16** in 39% overall yield.¹¹



In this study, three methyl groups on a Si atom can be used as leaving groups, although sp³ carbon–Si bonds is more stable under various reaction conditions. In the present study, we cannot show the preparation of an optically active trialkylsilyl alkoxide, which possesses high potential for organic synthesis.¹² Proper design of a molecule which has similar structure to our device will give a route to them.¹³

References and Notes

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- For the X-ray diffraction, a crystal was mounted on a glass fiber coated with epoxy resin. Measurements were made on a Rigaku Mercury charge-coupled device (CCD) system with graphite monochromated Mo K α radiation. Crystal data: **4**, *M_r* = 429.64, monoclinic C2/c, *a* = 33.095(6), *b* = 10.9080(19), *c* = 13.108(2) Å, β = 95.469(3)°, *V* = 4710.4(14) Å³, *Z* = 8, ρ = 1.212 Mg/m³, λ (Mo K α) = 0.71073 Å, *T* = 296 K, $2\theta_{\text{max}}$ = 54.0°, *R* = 0.0765 for 12076 reflections (*I* > 2 σ (*I*)).
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