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Intramolecular Participation in Alkoxycarbenium Ion Pools

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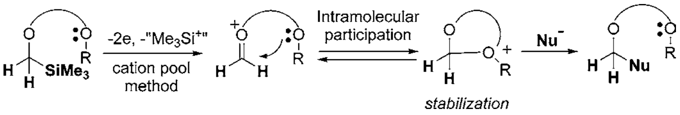
ABSTRACT



Alkoxycarbenium ions having no substituents on the cationic carbon have been accumulated as "cation pools" by the introduction of an ether group in an appropriate position. Intramolecular participation of the ether oxygen is suggested to be responsible for stabilization of the alkoxycarbenium ions.

Alkoxycarbenium ions[1] are important reactive intermediates in organic synthesis. Acidic activation of acetals (or equivalents) is usually utilized to generate alkoxycarbenium ions.[2] The reversibility of the method[3] is disadvantageous from a viewpoint of mechanistic studies. Electron-transfer reactions serve as irreversible methods for generation of alkoxycarbenium ions. For example, alkoxycarbenium ions have been effectively generated by photoelectron-transfer reactions[4] and electrochemical oxidation reactions.[5] Unique electron transfer initiated cyclization (ETIC) involving alkoxycarbenium ions is a recent intriguing synthetic application of the method.[6] We have recently reported the electrooxidative generation of alkoxycarbenium ions using the "cation pool" method.[7] Alkoxycarbenium ions having an alkyl group on the cationic carbons **1** are readily generated from the corresponding α-silyl ethers by low-temperature electrolysis and are ac-

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(1) Recent examples: (a) Mayr, H.; Gorath, G. *J. Am. Chem. Soc.* **1995**, *117*, 7862. (b) Mayer, P. S.; Morton, T. H. *J. Am. Chem. Soc.* **2002**, *124*, 12928. (c) Evans, P. A.; Cui, J.; Gharpure, S. J.; Hinkle, R. J. *J. Am. Chem. Soc.* **2003**, *125*, 11456. (d) Chamberland, S.; Ziller, J. W.; Woerpel, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 5322.

(2) Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC Press: Boca Raton, 1995; Chapter 4.

(3) Denmark, S. E.; Willson, T. M. In *Selectivities in Lewis Acid Promoted Reactions*; Schinzer, D., Ed.; Kluwer Academic Publishers: Dordrecht, 1989; p 247.

(4) C−H bond cleavage: (a) Steenken, S.; Buschek, J.; McClelland, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 2808. C−C bond cleavage: (b) Steenken, S.; McClelland, R. A. *J. Am. Chem. Soc.* **1989**, *111*, 4967. C−Si bond cleavage: (c) Gutenberger, G.; Steckhan, E.; Biechert, S. *Angew. Chem., Int. Ed.* **1998**, *37*, 660. C−Sn bond cleavage: (d) Chen, C.; Mariano, P. S. *J. Org. Chem.* **2000**, *65*, 3252. (e) Mikami, T.; Harada, M.; Narasaka, K. *Chem. Lett.* **1999**, 425. C−S bond cleavage: (f) Saito, I.; Takayama, M.; Sakurai, T. *J. Am. Chem. Soc.* **1994**, *116*, 2653.

(5) C−Si bond cleavage: (a) Yoshida, J.; Murata, T.; Isoe, S. *J. Organomet. Chem.* **1988**, *345*, C23. C−Sn bond cleavage: (b) Yoshida, J.; Ishichi, Y.; Nisiwaki, K.; Shiozawa, S.; Isoe, S. *Tetrahedron Lett.* **1992**, *33*, 2599. (c) Yoshida, J.; Ishichi, Y.; Isoe, S. *J. Am. Chem. Soc.* **1992**, *114*, 7594. C−O bond cleavage: (d) Noyori, R.; Kurimoto, I. *J. Org. Chem.* **1986**, *51*, 4320. C−S bond cleavage: (e) Mandai, T.; Irei, H.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1984**, *25*, 2371. (f) Mandai, T.; Yasunaga, H.; Kawada, M.; Otera, J. *Chem. Lett.* **1984**, 715. (g) Amatore, C.; Jutand, A.; Mallet, J. M.; Meyer, G.; Sinay, P. *J. Chem. Soc., Chem. Commun.* **1990**, 718. (h) Balavoine, G.; Gref, A.; Fischer, J.-C.; Lubineau, A. *Tetrahedron Lett.* **1990**, *31*, 5761. (i) Yoshida, J.; Sugawara, M.; Tatsumi, M. Kise, N. *J. Org. Chem.* **1998**, *63*, 5950. (j) Nokami, J.; Osafune, M.; Ito, Y.; Miyake, F.; Sumida, S.; Torii, S. *Chem. Lett.* **1999**, 1053. C−Se and C−Te bond cleavage: (k) Yamago, S.; Kokubo, K.; Hara, O.; Masuda, S.; Yoshida, J. *J. Org. Chem.* **2002**, *67*, 8584.

(6) (a) Kumar, V. S.; Floreancig, P. E. *J. Am. Chem. Soc.* **2001**, *123*, 3842. (b) Kumar, V. S.; Aubele, D. L.; Floreancig, P. E. *Org. Lett.* **2002**, *4*, 2489. (c) Wang, L.; Seiders, J. R., II; Floreancig, P. E. *J. Am. Chem. Soc.* **2004**, *126*, 12596.

(7) (a) Yoshida, J.; Suga, S.; Suzuki, S.; Kinomura, N.; Yamamoto, A.; Fujiwara, K. *J. Am. Chem. Soc.* **1999**, *121*, 9546. (b) Suga, S.; Okajima, M.; Yoshida, J. *Tetrahedron Lett.* **2001**, *42*, 2173. (c) Suga, S.; Okajima, M.; Fujiwara, K.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 7941. (d) Suga, S.; Suzuki, S.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 30. (e) Yoshida, J.; Suga, S. *Chem. Eur. J.* **2002**, *8*, 2650. (f) Suga, S.; Watanabe, M.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 14824. (g) Suga, S.; Kageyama, Y.; Babu, G.; Itami, K.; Yoshida, J. *Org. Lett.* **2004**, *6*, 2709. (h) Szuki, S.; Matsumoto, K.; Kawamura, K.; Suga, S.; Yoshida, J. *Org. Lett.* **2004**, *6*, 3755. (i) Suga, S.; Suzuki, S.; Maruyama, T.; Yoshida, J. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1545. (j) Suga, S.; Nishida, T.; Yamada, D.; Nagaki, A.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 14338. (k) Nagaki, A.; Kawamura, K.; Suga, S.; Ando, T.; Sawamoto, M.; Yoshida, J. *J. Am. Chem. Soc.* **2004**, *126*, 14338. (l) Okajima, M.; Suga, S.; Itami, K. Yoshida, J. *J. Am. Chem. Soc.* **2005**, *127*, 6930. (m) Maruyama, T.; Suga, S.; Yoshida, J. *J. Am. Chem. Soc.* **2005**, *127*, 7324. (n) Suga, S.; Tsutsui, Y.; Nagaki, A.; Yoshida, J. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1206.

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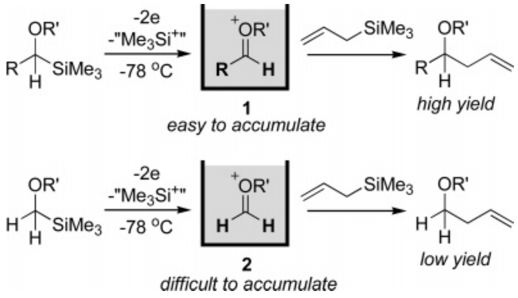
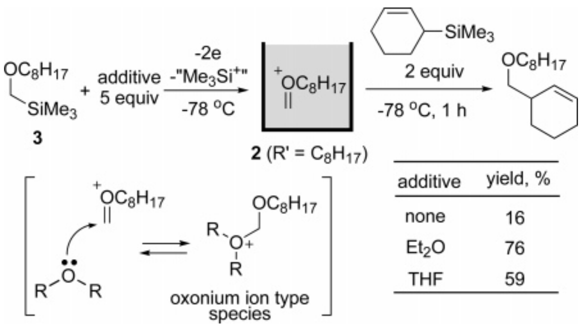
Scheme 1



cumulated in the absence of nucleophiles (Scheme 1).[8] Decrease of the oxidation potential by the introduction of the silyl group and facile cleavage of the C−Si bond seem to be responsible for the effective generation of alkoxycarbenium ions.[9] The alkoxycarbenium ions thus generated are well characterized by NMR and react with a variety of carbon nucleophiles such as allyltrimethylsilane to give the C−C bond formation products. Alkoxycarbenium ions having no substituents on the cationic carbon such as **2** were, however, difficult to accumulate as "cation pools" probably because of their instability owing to lack of electron donating alkyl substituents. In this paper, we describe a study of the generation and accumulation of cation **2** by using intramolecular ether participation.

First, the electrochemical oxidation of α-silyl ether **3** to generate the alkoxycarbenium ion **2** ($R' = C_8H_{17}$) was examined under standard conditions of the "cation pool" method (solvent, CH_2Cl_2; supporting electrolyte, Bu_4NBF_4; the anode, graphite felt; the cathode, platinum plate; temperature, −78 °C) (Scheme 2). After the electrolysis cyclohexenyltrimethylsilane was added to thus-generated solution. Only 16% of the allylated product was obtained. The poor yield may be attributed to the instability of **2**.

Scheme 2

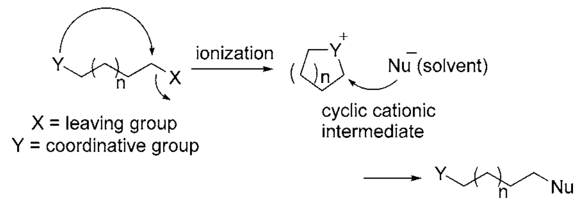


additive	yield, %
none	16
Et_2O	76
THF	59

The stabilization of carbenium ions by ether participation is well-known. For example, the use of an ether additive leads to well-defined living cationic polymerization.[10] The efficient stabilization of the growing cation by nucleophilic participation of the ether has been proposed. Thus, we envisaged that similar ether participation could assist in formation and accumulation of cation **2**. The reaction was carried out, again, this time in the presence of 5 equiv of Et_2O. After treatment with cyclohexenyltrimethylsilane, the desired product was obtained in 76% yield. The use of THF instead of Et_2O was also effective providing the product in 59% yield. Presumably ether participation stabilized **2** by forming an oxonium ion type species (Scheme 2).

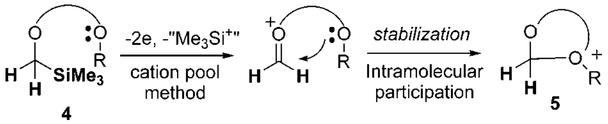
Intramolecular participation to stabilize carbenium ions is also well-known.[11] For example, the introduction of a coordinative group in an appropriate position leads to rate enhancement of solvolysis because ionization of the starting materials is assisted by the intramolecular participation (Scheme 3).

Scheme 3



Thus, we envisioned that intramolecular participation of ether may stabilize alkoxycarbenium ions having no substituents on the cationic carbon to afford an oxonium ion type intermediate **5**, and such cations could be accumulated as "cation pools" (Scheme 4).

Scheme 4



α-Silyl ethers **4a**−**d** were synthesized according to the method that we reported previously (Scheme 5).[12] Bromination of (methoxymethyl)trimethylsilane by NBS followed by a substitution with a methoxyalkyl alcohol gave the corresponding [methoxyalkoxy(methoxy)methyl]trimethylsilanes. The acetal was reduced with $Et_3SiH/BF_3{-}OEt_2$ to afford the α-silyl ethers having an ether tether.

α-Silyl ethers **4a**−**d** thus obtained were electrochemically oxidized under the standard cation pool conditions (Table 1). When the electrolysis was completed, cyclohexenyltri-

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[8] Suga, S.; Suzuki, S.; Yamamoto, A.; Yoshida, J. *J. Am. Chem. Soc.* **2000**, *122*, 10244.

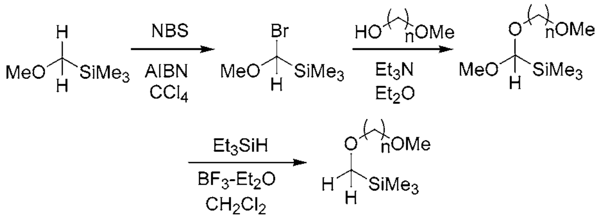
[9] (a) Yoshida, J.; Maekawa, T.; Murata, T.; Matsunaga, S.; Isoe, S. *J. Am. Chem. Soc.* **1990**, *112*, 1962. (b) Yoshida, J.; Nishiwaki, K. *J. Chem. Soc., Dalton Trans.* **1998**, 2589.

[10] For a representative example, see: Kishimoto, Y.; Aoshita, S.; Higashimura, T. *Macromolecules* **1989**, *22*, 3877.

[11] March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley: New York, 1992; p 308.

[12] Suga, S.; Miyamoto, K.; Watanabe, M.; Yoshida J. *Appl. Organomet. Chem.* **1999**, *13*, 469.

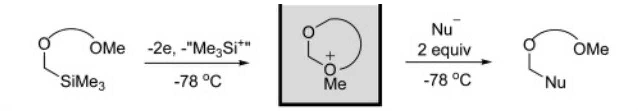
Scheme 5

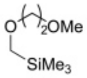
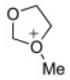
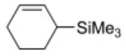
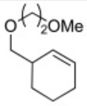
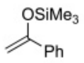
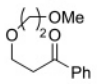
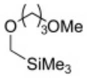
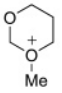
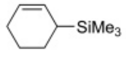
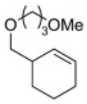
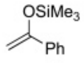
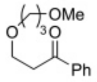
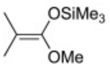
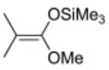
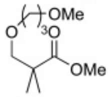
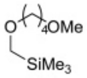
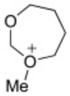
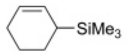
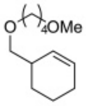
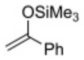
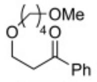
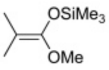
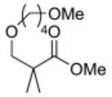
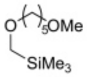
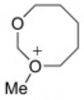
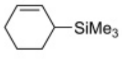
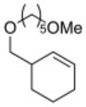


4a: n=2 **4c**: n=4
4b: n=3 **4d**: n=5

methylsilane (2 equiv) was added, and the mixture was stirred for 15−120 min at −78 °C before the reaction was quenched with triethylamine. The reactions gave the corresponding allylated products in good to moderate yields, indicating that alkoxycarbenium ions **5a**−**d** were generated and accumulated. The reactions of **5a** and **5b**, in which the intramolecular participation leads to the formation of five or six-membered ring, took an hour or more to complete. Since the reaction of alkoxycarbenium ions without such participation (**1**, R = C_8H_{17}, R′ = CH_3) usually completes within a few minutes,[8] reactions of **5a** and **5b** were extremely slow. These observations indicate that the intramolecular participation did take place to stabilize the alkoxycarbenium ions. On the other hand, cation **5c**, in which seven-membered ring forming participation might take place, smoothly reacted with cyclohexenylsilane within 15 min. The result indicates that the participation is weaker in this case because the seven-membered ring formation is usually less effective than five- or six-membered ring formation.

Table 1. Oxidative Generation of Alkoxycarbenium Ions from α-Silyl Ethers Having an Internal Ether and Their Reactions of Carbon Nucleophiles[a]



substrate	alkoxy-carbenium ion	nucleophile (Nu⁻)	product	reaction time (min)	yield (%)[b]
 **4a**	 **5a**			60	64
				15	27
 **4b**	 **5b**			15 60 120	39 77 93
				15	60[c]
				15	56
 **4c**	 **5c**			15 120	72 69
				15	38
				15	32
 **4d**	 **5d**			15	41

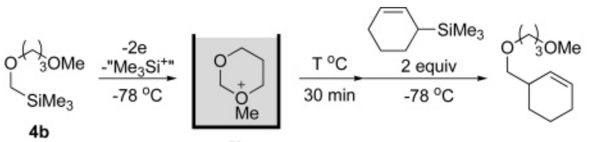
[a] Reactions were normally carried out with 0.4 mmol of α-silyl ethers and 2 equiv of carbon nucleophiles. [b] Isolated yield. [c] Determined by GC analysis.

It has been reported that the formation of a five or six-membered ring by ether participation accelerates solvolysis,[13] which seems to be inconsistent with the trend observed in the present study. But it was revealed that the solvolysis involves two steps; i.e., the formation of a carbenium ion (ionization step) and its reaction with a nucleophile (Scheme 3). Usually the ionization step is the rate determining step and is accelerated by the intramolecular participation. In contrast, we observed the reaction of the carbenium ion with a nucleophile, which corresponds to the second step of the solvolysis. Our results indicated that the reaction of the carbenium ion with a nucleophile was decelerated by the intramolecular participation because such participation stabilizes the carbenium ion.

Other carbon nucleophiles such as a ketene silyl acetal and an enol silyl ether were also found to react with **5** to afford the desired products, although the yields were low in some cases.

The thermal stability of the alkoxycarbenium ions was investigated (Scheme 6). The pool of alkoxycarbenium ion **5b** produced by the anodic oxidation of **4b** at −78 °C was allowed to warm to a second temperature (*T*, °C). After being

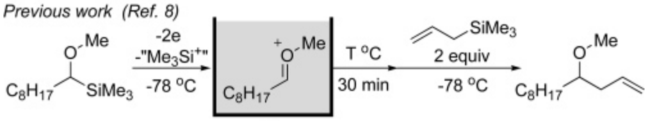
Scheme 6



4b **5b**

T, °C	-78	-47	-25	0	20
yield	93	93	79	66	15

Previous work (Ref. 8)



1
(R = C_8H_{17},
R′ = CH_3)

T, °C	-78	-47	-25	0	20
yield	80	79	46	4	nd

kept there for 30 min, the pool was allowed to react with cyclohexenyltrimethylsilane at −78 °C until the reaction completed. The results are summarized in Scheme 6. Our previous results for the alkoxycarbenium ion **1**, which has an alkyl group on the cationic carbon are also listed in Scheme 6 for comparison.[8] Obviously, **5b** is more stable than **1**. A large portion of **1** decomposed at 0 °C within 30 min; however, **5b** is still alive under the same conditions. Although a further study is needed to get a deeper insight into the stability and reactivity of alkoxycarbenium ions, the ether participation must play an important role.

In conclusion, we have succeeded in accumulating the alkoxycarbenium ions having no substituent on the cationic carbon using intramolecular participation of ether. The length of the tether significantly affects the reactivity and the stability of the cationic intermediates. Further studies are in progress to elucidate deeper mechanistic insights of carbenium ion chemistry by taking advantage of the "cation pool" methods, in which carbenium ions are irreversibly generated and accumulated in common organic solvents such as dichloromethane.

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

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(13) (a) Winstein, S.; Allred, E.; Heck, R.; Glick, R. *Tetrahedron* **1958**, *3*, 1. (b) Allred, E. L.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 3991. (c) Allred, E. L.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 4012.