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Electrooxidative Generation and Accumulation of Alkoxycarbenium Ions and Their Reactions with Carbon Nucleophiles

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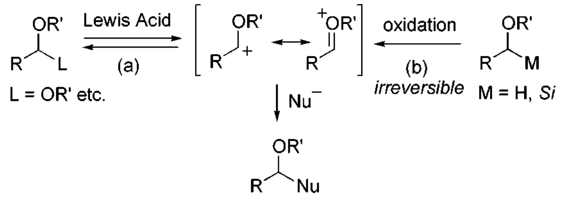
Alkoxycarbenium ions are carbenium ions stabilized by a neighboring alkoxy group and are important reactive intermediates in organic synthesis.[1] For example, the Lewis acid promoted reactions of acetals and related compounds with carbon nucleophiles such as allylsilanes and enol silyl ethers are considered to proceed through alkoxycarbenium ion intermediates (Scheme 1 (a)).

Scheme 1. Generation of Alkoxycarbenium Ion

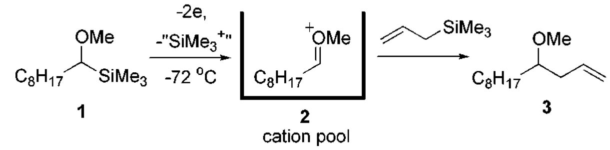


Although highly stabilized alkoxycarbenium ions, such as benzylic alkoxycarbenium ions and di- and tri(alkoxy)carbenium ions, are well-characterized spectroscopically,[2] it is difficult to characterize simple alkylalkolxycarbenium ions. Extensive NMR studies on the mechanism of the reaction of acetals with Lewis acids revealed the presence of Lewis acid−acetal complexes, but failed to detect alkoxycarbenium ions.[3]

Although alkoxycarbenium ions in superacid solution have been investigated extensively,[4] to our knowledge, there is no report on the characterization of simple alkylalkoxycarbenium ions in reaction media that are normally used in organic synthesis. Thus, we initiated a project to study alkoxycarbenium ions using the “cation pool” method. This technique involves the *irreversible* electrooxidative generation (Scheme 1 (b)) and accumulation of carbocations.[5]

In the “cation pool” method, anodic oxidations are used to generate and accumulate relatively high concentrations of carbocations at low temperature in the absence of nucleophiles. In the next step the carbocations are then allowed to react with nucleophiles. This one-pot method has an advantage over the conventional processes because nucleophiles that might be otherwise oxidized during an in situ process can be used without any difficulty.

Scheme 2. Generation of Alkoxycarbenium Ion Pool from α-Silyl Ether and Its Reaction with Allyltrimethylsilane



As precursors of alkoxycarbenium ions in the cation pool method, dialkyl ethers should be the first choice (Scheme 1 (b), M = H)[6] in the analogy with the reported oxidative generation of iminium cation pool from amine derivatives. The oxidation potentials of dialkyl ethers, however, are very positive, and hence, it is rather difficult to oxidize ethers selectively without affecting the reaction media.[7] The regioselectivity is another problem, because two regioisomeric alkoxycarbenium ions are generally formed from unsymmetrical dialkyl ethers.

The pre-introduciton of a silyl group solves these problems.[8] The oxidation potentials of α-silyl ethers (Scheme 1 (b), M = Si) are much less positive than the corresponding dialkyl ethers,[9] and their anodic oxidation takes place smoothly, giving rise to selective cleavage of the C−Si bond which eventually leads to the generation of an isomerically pure alkoxycarbenium ion.

Thus, α-silyl ether (**1**) was oxidized in a divided cell equipped with a carbon felt anode and a platinum plate cathode in deuterated dichloromethane in the presence of tetrabutylammonium tetrafluoroborate as electrolyte at −72 °C (Scheme 2).

After 2.5 F/mol of electricity was consumed, the solution thus obtained was analyzed by NMR spectroscopy at −80 °C. ^{1}H NMR exhibited a signal at 9.55 ppm due to the methine proton. ^{13}C NMR exhibited a signal at 231.0 ppm due to the methine carbon.[10] These chemical shifts are consistent with those of alkoxycarbenium ions generated in superacid.[4] These values also suggest the presence of a strong positive charge at the carbon, indicating the formation of a solution of an ionic species.

The pool of the alkoxycarbenium ion **2**, thus generated by the low temperature electrolysis, was then allowed to react with allyltrimethylsilane as a carbon nucleophile. The corresponding allylated product **3** was obtained in 80% yield. Noteworthy is that this reaction is extremely fast even at −72 °C. Even under these conditions, the reaction was complete within a few minutes.[11] Other electrolytes such as tetrabutylammonium perchlorate, triflate, hexafluorophosphate in electrolysis gave us poor yields of **3**, probably because of inefficiency in the accumulation of **2**.[12]

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[1] For example, Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*; CRC Press: Boca Raton, 1995; Chapter 4.

[2] Benzylic alkoxycarbenium ions: (a) Rabinovitz, M.; Bruck, D. *Tetrahedron Lett.* **1971**, 245. (b) Amyes, T. L.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 7888. (c) Jagannadham, V.; Amyes, T. L.; Richard, J. P. *J. Am. Chem. Soc.* **1993**, *115*, 8465. (d) Mayr, H.; Gorath, G. *J. Am. Chem. Soc.* **1995**, *117*, 7862. Di- and trialkoxycarbenium ions: (e) Ramsey, B. G.; Taft, R. W. *J. Am. Chem. Soc.* **1966**, *88*, 3058. (f) Steenken, S.; Buschek, J.; McClelland, R. A. *J. Am. Chem. Soc.* **1986**, *108*, 2808. (g) McClelland, R. A.; Steenken, S. *J. Am. Chem. Soc.* **1988**, *110*, 5860. (h) Steenken, S.; McClelland, R. A. *J. Am. Chem. Soc.* **1989**, *111*, 4967.

[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] (a) Olah, G. A.; Bollinger, J. M. *J. Am. Chem. Soc.* **1967**, *89*, 2993. (b) Olah, G. A.; Sommer, J. *J. Am. Chem. Soc.* **1968**, *90*, 4323. (c) Forsyth, D. A.; Osterman, V. M.; DeMember, J. R. *J. Am. Chem. Soc.* **1985**, *107*, 818.

[5] Yoshida, J.; Suga, S.; Suzuki, S.; Kinomura, N.; Yamamoto, A.; Fujiwara, K. *J. Am. Chem. Soc.* **1999**, *121*, 9546.

[6] Generation of alkoxycarbenium ions by radiation of ethers: See refs 2f and 2g.

[7] For example, Shono, T. In *The Chemistry of Ethers, Crown Ethers, Hydroxyl groups and Their Sulfur Analoges, Part 1*; Patai, S., Ed.; Wiley: Chichester, 1980; Chapter 8.

[8] (a) Yoshida, J.; Murata, T.; Isoe, S. *J. Organomet. Chem.* **1988**, *345*, C23. (b) Yoshida, J.; Matsunaga, S.; Murata, T.; Isoe, S. *Tetrahedron* **1991**, *47*, 615.

[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] There are no signals which could be assigned to species having C−F covalent bond, although tetrafluoroborate is well-known as fluorination reagent. NMR spectra of compounds having O−C−F units are reported: See, Rozov, L. A.; Rafalko, P. W.; Evans, S. M.; Brockunier, L.; Ramig, K. *J. Org. Chem.* **1995**, *60*, 1319.

[11] The Lewis acid promoted reactions of acetals with carbon nucleophiles such as allylsilanes and enol silyl ethers are relatively slower (usually several hours at −78 °C) than our reaction, see: (a) Mukaiyama, T.; Hayashi, M. *Chem. Lett.* **1974**, 15. (b) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941. (c) Murata, S.; Suzuki, M.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 3248. (d) Demmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089.

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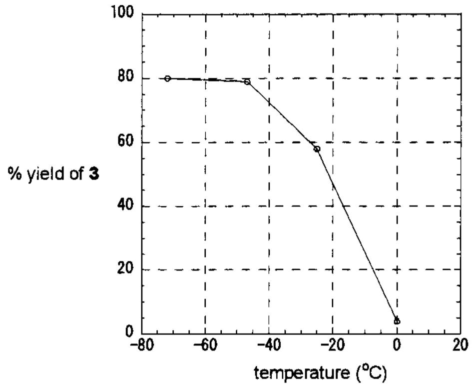


Figure 1. Thermal stability of alkoxycarbenium ion **2**.

The thermal stability of the alkoxycarbenium ion was studied. The pool of **2** produced by the anodic oxidation of **1** at −72 °C was allowed to warm to a second temperature. After being kept there for 30 min, the cation pool was then allowed to react with allyltrimethylsilane. It can be seen from Figure 1 that the alkoxycarbenium ion is stable at temperatures lower than ∼−50 °C. Above this temperature, the yield of **3** decreased significantly. At 0 °C, the alkoxycarbenium ion decomposed almost completely within 30 min. This stability sharply contrasts to the stability of benzylic alkoxycarbenium ions which are stable at room temperature.[2d]

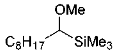
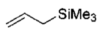
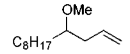
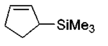
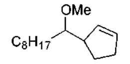
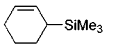
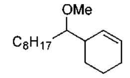
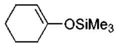
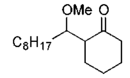
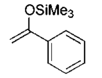
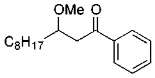
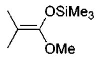
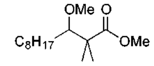
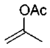
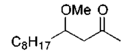
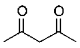
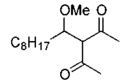
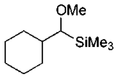
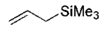
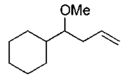
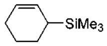
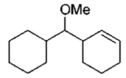
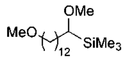
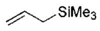
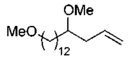
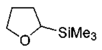
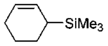
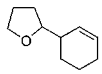
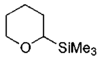
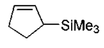
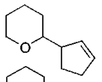
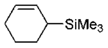
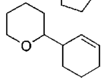
The reaction of the alkoxycarbenium ion pool with other allylsilanes such as cyclopentenylsilane and cyclohexenylsilane also took place smoothly to give the corresponding coupling products in good yields, indicating the effectiveness of substituted allylsilanes as nucleophiles (Table 1). The reaction with enol silyl ethers also proceeded smoothly to give the corresponding carbon−carbon bond formation products. The fact that diastereomeric selectivity is fairly lower than those obtained by the Lewis acid promoted reaction,[13] suggest that alkoxycarbenium ion **2** generated by the present method has somewhat different reactivity.[14]

The reactions of the alkoxycarbenium ion with other carbon nucleophiles were also examined. Ketene silyl acetals and enol acetates were also found to serve as effective carbon nucleophiles. More interesting is the observation that 1,3-dicarbonyl compounds, which are much weaker nucleophiles, were also effective as carbon nucleophiles.

Other alkoxycarbenium ions were also generated from the corresponding α-silyl ethers. Such alkoxycarbenium ions exhibited similar stability and reactivity. The reactions with allylsilanes proceeded smoothly to give the corresponding coupling products as depicted in Table 1. It should be emphasized that the present method can be applied to cyclic ethers, implying the effectiveness in the synthesis of C-glucosides.

In conclusion, we developed an efficient method for the generation and accumulation of alkoxycarbenium ions. The alkoxycarbenium ions can be characterized by NMR spectroscopy and react with various carbon nucleophiles. The research reported here adds a new aspect of the chemistry of alkoxycarbenium ions from viewpoints of both mechanistic studies and synthetic applications. Further work is in progress to explore the full range of stability and reactivity of alkoxycarbenium ions.

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

α-silyl ether	nucleophile	product	% yield [b]
			80 [d]
			84 (62:38)
			83 (ca 3:2)
			69 (67:33)
			68
			71
			70
			55 [c]
			74
			83 (83:17)
			60
			59 (ca 9:1)
			54 (ca 9:1)
			55 [d] (86:14)

[a] Reactions were normally carried out with 0.4 mmol of α-silyl ethers and 2 equiv of carbon nucleophiles. [b] Isolated yield. Diastereomer ratio, determined by ^{1}H NMR, ^{13}C NMR, or GC analysis, is described in the parenthesis. [c] Five equivalents of 1,3-pentanedione was used. [d] Determined by GC analysis.

Acknowledgment. This research was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

Supporting Information Available: Experimental details and spectroscopy data of the products (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(12) The counteranion of **2** which should be supplied from electrolyte seriously effects on the efficiency of the generation of cation pool: See also ref 5.

(13) Over 9:1 ratio was obtained in TMSOTf-catalyzed reaction: See ref 11c.

(14) Another possibility to be considered is that the Lewis Acid promoted reaction involves a covalently bonded intermediate.