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METHOXY(TRIMETHYLSILYL)METHANE AND METHOXYBIS(TRIMETHYLSILYL)METHANE[1] AS NEW REAGENTS FOR HOMOLOGATION

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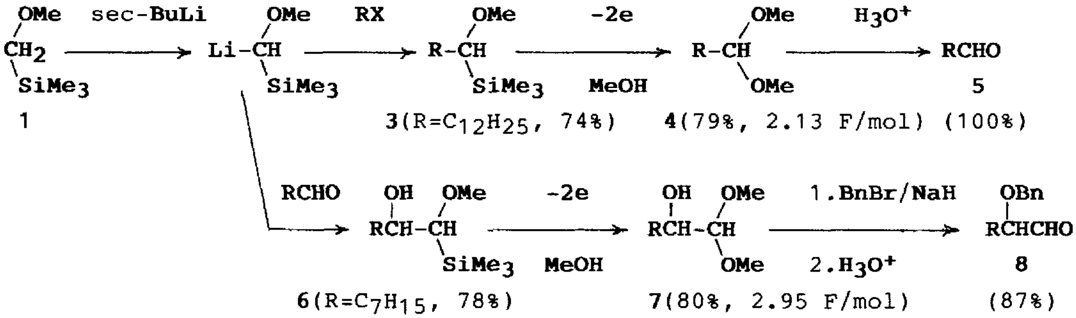
Summary: New synthons of formyl anion (methoxy(trimethylsilyl)methane (**1**)) and alkoxylcarbonyl anion (methoxybis(trimethylsilyl)methane (**2**)) have been developed using oxidative cleavage of the carbon-silicon bond by anodic oxidation.

E. J. Corey introduced the concept "synthons" in 1967,[2] and since then various types of umpoled synthons have been developed.[3] Although numerous studies on synthons of acyl, formyl, and alkoxycarbonyl anions have been reported so far,[3] development of a new methodology which has compatibility toward a wide range of reactions and requires milder conditions for the generation of carbonyl functionalities such as aldehydes and esters has been still desired. Herein we wish to report on new synthons of acyl and alkoxycarbonyl anions using electrochemical oxidation of organosilicon compounds.[4]

Recent investigation in our group revealed that substitution of a silyl group at the α position of ethers caused significant decrease in their oxidation potentials and that the electrochemical oxidation of α-silyl ethers resulted in facile and selective cleavage of the carbon-silicon bond.[5] We applied this concept to the development of new synthons of formyl and alkoxycarbonyl anions.

Deprotonation of methoxy(trimethylsilyl)methane (**1**) with sec-butyllithium afforded the anion[6] which readily reacted with organic halides to give 1-methoxy-1-trimethylsilylalkanes (**3**) as shown in Scheme I. The electrochemical oxidation of **3** in 0.2 M Et_4NOTs/methanol in an undivided cell equipped with carbon rod electrodes gave the corresponding dimethyl acetal (**4**).[5] The acetal **4** was readily hydrolyzed to the aldehydes (**5**) with dilute aq HCl in THF. The anion of **1** also reacted with aldehydes to give the 2-hydroxy-1-methoxy-1-trimethylsilylalkanes (**6**)[7], the electrolysis of which gave the acetal (**7**) without affecting the hydroxyl group. Protection of the hydroxyl group followed by acid-catalyzed hydrolysis afforded the 2-benzyloxyaldehydes (**8**). Thus the anion of **1** provides a convenient synthon of the formyl anion.

Scheme I



1

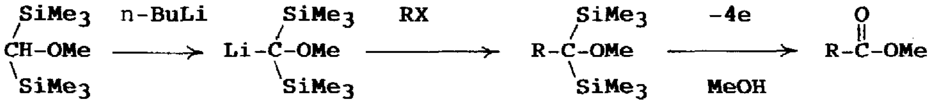
3($R=C_{12}H_{25}$, 74%) 4(79%, 2.13 F/mol) 5 (100%)

6($R=C_7H_{15}$, 78%) 7(80%, 2.95 F/mol) 8 (87%)

$\boxed{^-CH(OMe)(SiMe_3) \equiv {}^-CH(OMe)_2 \equiv {}^-CHO}$

As an extension of the chemistry of **1** we have examined the reactions of the compound having an additional silyl group, i.e. methoxybis(trimethylsilyl)-methane (**2**) and found that the electrochemical oxidation of its alkylation products directly gave the corresponding ester. Thus the anion of **2** provides a convenient synthon of alkoxycarbonyl anion (Scheme II).

Scheme II.



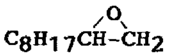
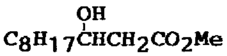
2

$\boxed{^-C(OMe)(SiMe_3)_2 \equiv {}^-COOR}$

Methoxybis(trimethylsilyl)methane (**2**) was prepared by the deprotonation of methoxy(trimethylsilyl)methane (**1**) with sec-butyllithium in THF[5] followed by the reaction with chlorotrimethylsilane (82% yield). It should be noted that deprotonation of **2** can be accomplished even with n-butyllithium which is less strong base than sec-butyllithium. Higher acidity of the methine proton due to the additional α silyl group[8] seems to be responsible for easier deprotonation. (Methoxybis(trimethylsilyl)methyl)lithium thus obtained was subjected to the reaction with various organic halides. Table I summarizes the results. Primary alkyl bromides and iodides reacted smoothly to give the corresponding alkylation products in high yields. Alkyl chlorides also served as good substrates but their reactions were much slower than those with alkyl bromides. Secondary alkyl bromides reacted with the anion of **2**, but yields were lower. The reaction with acyclic terminal epoxides gave 3-hydroxy-1-methoxy-1,1-bis-(trimethylsilyl)alkanes. Cyclic epoxides such as cyclohexene oxides, however, were inactive under similar conditions.

Cyclic voltammetric study revealed that the oxidation potentials of methoxybis(trimethylsilyl)alkanes was about 0.3 V less than those of the compounds having only one silyl group.[9] The constant current electrolysis of methoxybis(trimethylsilyl)alkanes[10] were carried out in 0.2 M $Et_4NOTs/MeOH$

Table I. Alkylation of Methoxybis(trimethylsilyl)methane and Electrochemical Oxidation of Methoxybis(trimethysilyl)alkanes

alkylation [a]		anodic oxidation [c]		
alkylating reagent	yield [b] (%)	electricity [d] (F/mol)	product	yield [e] (%)
$Ph(CH_2)_3Br$	99	4.00	$Ph(CH_2)_3CO_2Me$	91
$Ph(CH_2)_3Cl$	98			
$C_{12}H_{25}Br$	78	4.00	$C_{12}H_{25}CO_2Me$	92
$CH_2=CH(CH_2)_9Br$	92	4.00	$CH_2=CH(CH_2)_9CO_2Me$	75
$THPO(CH_2)_3I$	89	4.90	$THPO(CH_2)_3CO_2Me$	58[e]
$PhCH_2Br$	67	4.00	$PhCH_2CO_2Me$	80
 $C_8H_{17}CH(O)CH_2$	98	4.00	 $C_8H_{17}CH(OH)CH_2CO_2Me$	92

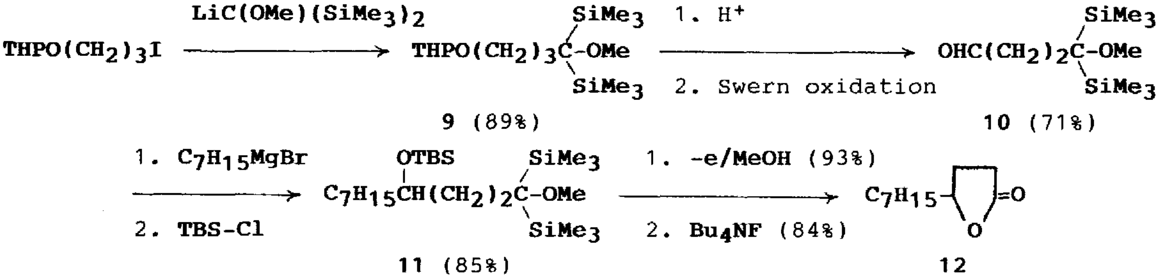
[a] The reactions were normally carried out with methoxybis(trimethylsilyl)methane (2.6 mmol), n-buthyllithium/hexane (2.4 mmol), and an alkylating reagent (2.0 mmol) in 5.0 ml of THF. [b] Isolated yields based on the alkylating agent. [c] The anodic oxidation was normally carried out with methoxybis(trimethylsilyl)alkane (0.5 mmol) in 0.2 M $Et_4NOTs/MeOH$ (10 ml) in an undivided cell equipped with carbon rod anode and cathode. Constant current (10 mA) was passed at room temperature. [d] Isolated yields based on the methoxybis(trimethylsilyl)alkane. [e] The electrolysis was carried out in the presence of a small amount of pyridine.

using an undivided cell equipped with carbon rod electrodes. Monitoring with VPC indicated that the most of the starting material was consumed after electricity of 4 F/mol was passed. Aqueous work-up followed by bulb-to-bulb distillation or flash chromatography on silica-gel afforded the corresponding methyl esters as shown in Table I. Thus the ester functionality can be generated from methoxybis(trimethylsilyl)methyl moiety under mild conditions at room temperature in high yields.

The reaction mechanism seems to be interesting. VPC monitoring of the reaction indicated the formation of the dimethoxy(trimethylsilyl)alkane which was gradually consumed during the course of the reaction. As a matter of fact, with 3.13 F/mol of electricity[11] was obtained 1,1-dimethoxy-1-trimethylsilyltridecane[12] (85% yield) from 1-methoxy-1,1-bis(trimethylsilyl)tridecane. The anodic oxidation of this dimethoxy compound in methanol gave the corresponding methyl ester (2.00 F/mol, 93% yield). The reaction therefore seems to proceed by a two step mechanism which involves the substitution of one silyl group by a methoxyl group with two electron oxidation followed by the substitution of the other silyl group with the second two electron oxidation. The orthoester thus obtained seems to be converted into the ester in situ.

The potentiality of **2** as a reagent for homologation is demonstrated by the following synthesis of γ-undecalactone (Scheme III). The reaction of 1-iodo-3-tetrahydropyraoxypropane with the anion of **2** gave the corresponding alkylation product (**9**). Deprotection of the hydroxyl group followed by Swern oxidation gave the aldehyde **10**, which was alkylated with hexylmagnesium bromide and the resulting alcohol was converted to TBS ether (**11**). The electrochemical oxidation of **11** in methanol followed by the treatment with fluoride anion afforded the lactone (**12**) in high yield.

Scheme III.



The compatibility of α-silylether moiety toward various reactions including acidic removal of THP, Swern oxidation, and Grignard reactions together with its thermal stabilities allows synthetic reactions employing **1** and **2** to be run under a wide range of conditions. Mild reaction conditions of the electrochemical method and easy separation from the volaltile silicon containing by-product are also advantageous. Thus **1** and **2** provide useful alternatives to the conventional synthons of formyl and alkoxycarbonyl anions, respectively.

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References and Notes

(1) Electrochemical oxidation of organosilicon compounds part 6. For part 5 see ref 5.

(2) Corey, E. J., Pure Appl. Chem., **1967**, 14, 19.

(3) (a) Hase, T. A. Ed., "Umpoled Synthons", Wiley: New York, 1987; (b) Seebach, D. Angew. Chem. Int. Ed. Engl., **1979**, 18, 239.

(4) Related work: Mandai, T.; Irie, H.; Kawada, M.; Otera, J. Tetrahedron Lett., **1984**, 25, 2371 and references cited therein.

(5) Yoshida, J.; Murata, T.; Isoe, S, J. Organomet. Chem., **1988**, 345, C23.

(6) Magnus, P.; Roy, G. Organometallics, **1982**, 1, 553.

(7) Magnus reported the reaction of the anion of **1** with carbonyl compounds. Peterson elimination of the resulting compounds gave the aldehyde.[6]

(8) The silyl group is well known to stabilize α-carbanions. See for example: Colvin, E. W, "Silicon in Organic Synthesis", Butterworths: London, 1981.

(9) Peak potentials of **1** and **2** were 1.89 V and 1.57 V (vs. Ag/AgCl), respectively in $LiClO_4$/MeCN.

(10) Oxidation of 1,1-bis(trimethylsilyl)alkan-1-ols with t-butylhypochlorite is reported to give acylsilanes, see: Kuwajima, I.; Abe, T.; Minami, N. Chem. Lett., **1976**, 993.

(11) The electrolysis was carried out in the presence of a small amount of 2,6-lutidine.

(12) Acid catalyzed hydrolysis of **9** gave the corresponding acylsilane. Thus the anion of **2** also provides the synthon of $^{-}C(=O)SiMe_3$. Related work is reported, see: Mandai, T.; Yamaguchi, M.; Nakayama, Y.; Otera, J.; Kawada, M. Tetrahedron Lett., **1985**, 26, 2675.

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