Facile Synthesis of Acylsilanes via Aerobic Oxidation of *gem*-Disilylalkylcopper Compounds

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Received July 26, 2001
Revised Manuscript Received September 27, 2001

Oxidation of organometallic reagents,[1] especially organoborane[2] and organosilicon[3] compounds, is a methodology of great importance in organic synthesis for the preparation of alcohols.

In general, the oxidation of a carbon−metal σ-bond does not provide carbonyl compounds (except from oxidation of vinylmetals). Knochel pioneered the oxidation of dimetallic compounds with oxygen to yield ketones (Scheme 1).[4] Since then, however, few reports of the oxidation of organometals to carbonyl compounds have appeared in the literature.[5]

Acylsilanes are an important class of compounds that are frequently utilized as intermediates in organic synthesis.[6] Herein we wish to report an operationally simple oxidation protocol to prepare various acylsilanes. Oxidation of 1,1-disilylalkylcopper compounds with atmospheric oxygen furnishes acylsilanes in good to excellent yields.

gem-Disilylalkylcopper (**3a**) was easily prepared via transmetalation of 1,1-bis(methyldiphenylsilyl)hexyllithium (**2**), which was obtained by the treatment of 1,1-disilylethene (**1**)[7] with butyllithium in THF. After the addition of aqueous ammonium chloride, the reaction mixture was exposed to air with stirring for 30 min. During this period, the aqueous layer turned blue, indicating the presence of copper(II). After purification, hexanoylsilane (**4a**) was isolated in 84% yield (Table 1).

In the presence of various additives, oxidation by atmospheric oxygen afforded the desired acylsilane. Among copper salts we examined, the THF-soluble complex CuCN•2LiCl proved to be the best.[8] Aqueous NH_4Cl was quite effective as an additive. We confirmed by ^{13}C NMR spectroscopy of the organic phase of the reaction mixture that *gem*-disilylalkylcopper (**3a**) was not hydrolyzed by aqueous ammonium chloride.[9] The stability of *gem*-disilylalkylcopper toward hydrolysis allows us to employ atmospheric air.

Scheme 1

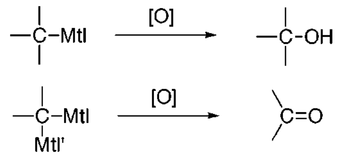
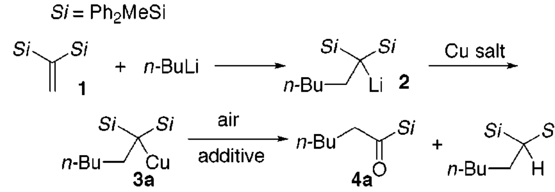


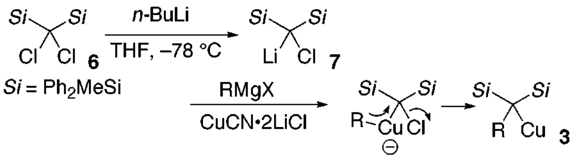
Table 1. Optimization of Aerobic Oxidation Conditions[a]



Cu salt	additive	yield (%) (**4a**/**5**)	Cu salt	additive	yield (%) (**4a**/**5**)
CuCN•2LiCl	NH_4Cl aq	84/4	CuCN	NH_4Cl aq	72/12
CuCN•2LiCl	NH_3 aq	71/5	CuI	NH_4Cl aq	52/18
CuCN•2LiCl	Et_3N	65/5	CuBr	NH_4Cl aq	35/32
CuCN•2LiCl	pyridine	66/5	$CuCl_2$	NH_4Cl aq	0/51

[a] The reaction mixture was exposed to air. After oxidation for 30 min, the reaction was quenched with concentrated HCl.

Scheme 2



Having optimized the oxidation conditions, we directed our attention toward the synthesis of a variety of acylsilanes. However, the current method is limited because only organolithiums can add to 1,1-disilylethene. Accordingly, we investigated an alternative method to prepare 1,1-disilylalkylmetals. To our delight, the treatment of $(Ph_2MeSi)_2CCl_2$ (**6**)[10] with *n*-butyllithium followed by a Grignard reagent in the presence of a copper salt efficiently furnished the requisite organocopper species **3** (Scheme 2).[11] This copper-mediated alkylative metalation of **7** enables incorporation of a variety of alkyl groups into the *gem*-disilylalkylcopper intermediate.[12]

Oxidation of the resultant organocopper species with air yielded the respective acylsilanes in good yields (Table 2).[13] Methyldiphenylsilanol (**8**) was formed as a byproduct in almost quantitative yield. Several features of this reaction are noteworthy. Various primary or secondary Grignard reagents can be employed in the reaction. The use of silylmethylmagnesium successfully afforded α-silyl acylsilane (**4i**). Interestingly, the reaction with crotylmagnesium chloride yielded 3-pentenoylsilane (**4k**) without 2-methyl-3-butenoylsilane (entry 10). The oxidation of disilyl-

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(4) (a) Knochel, P.; Xiao, C.; Yeh, M. C. P. *Tetrahedron Lett.* **1988**, *29*, 6697. (b) Chen, H. G.; Knochel, P. *Tetrahedron Lett.* **1988**, *29*, 6701. (c) Knochel, P.; Xiao, C.; Yeh, M. C. P. *Organometallics* **1989**, *8*, 2831.

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(6) (a) Hodgson, D. M.; Comina, P. J.; Drew, M. G. B. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2279. (b) Nàjera, C.; Yus, M. *Org. Prep. Proc. Int.* **1995**, *27*, 385. (c) Cirillo, P. F.; Panek, J. S. *Org. Prep. Proc. Int.* **1992**, *24*, 555. (d) Page, P. C. B.; Klair, S. S.; Rosenthal, S. *Chem. Soc. Rev.* **1990**, *19*, 195. (e) Ricci, A.; Degl'Innocenti, A. *Synthesis* **1989**, 647.

(7) (a) Seebach, D.; Bürstinghaus, R.; Gröbel, B.-Th.; Kolb, M. *Liebigs Ann. Chem.* **1977**, 830. (b) Inoue, A.; Kondo, J.; Shinokubo, H.; Oshima, K. *Chem. Lett.* **2001**, 956.

(8) Direct oxidation of 1,1-disilylalkyllithium without conversion to the corresponding copper intermediate was ineffective, and afforded a complex mixture.

(9) We observed no significant change to the ^{13}C spectrum of the reaction mixture upon the addition of water.

(10) Yoon, K.; Son, D. Y. *J. Organomet. Chem.* **1997**, *545−546*, 185.

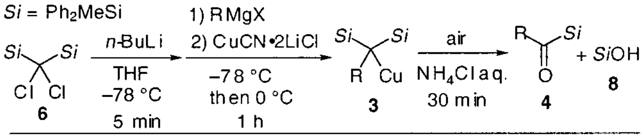
(11) Kondo, J.; Inoue, A.; Shinokubo, H.; Oshima, K. *Angew. Chem.* **2001**, *113*, 2146; *Angew. Chem., Int. Ed.* **2001**, *40*, 2085.

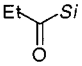
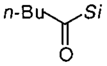
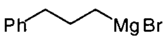
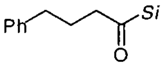
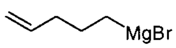
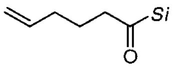
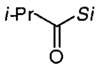
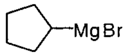
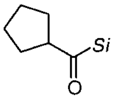
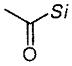
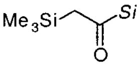
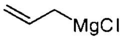
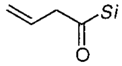
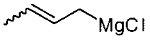
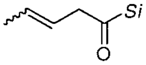
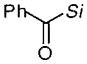
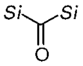
(12) This process is not efficient for $PhMe_2Si$ or Me_3Si analogues. Lithiation of **6** (*Si* = $PhMe_2Si$ or Me_3Si) is sluggish.

(13) **General procedure**: A solution of *n*-BuLi (0.31 mL, 1.6 M in hexane, 0.5 mmol) was added to a THF solution of **6** (239 mg, 0.5 mmol) at −78 °C. After stirring for 20 min, *i*-PrMgBr (0.6 mmol, THF solution) and CuCN•2LiCl (0.6 mmol, 1.0 M THF solution) were introduced and the mixture was stirred for 1 h at 0 °C. Hexane (5 mL) and NH_4Cl aqueous (10 mL) were added, and the mixture was exposed to air with stirring for 0.5 h. Extractive workup and purification afforded **4f** (118 mg, 0.44 mmol) in 88% yield. The procedure can be easily scaled up. The use of 5.0 mmol of **6** provided **4c** in 77% yield.

10.1021/ja016716r CCC: $20.00

Table 2. Preparation of Acylsilanes via Aerobic Oxidation of 1,1-Disilylalkylcopper Compounds



Entry	RMgX	Acylsilane		Yield (%)
1	EtMgBr		**4b**	75
2	*n*-BuMgBr		**4c**	81
3			**4d**	75
4			**4e**	65
5	*i*-PrMgBr		**4f**	88
6			**4g**	84
7	MeMgBr		**4h**	47
8	Me_3SiCH_2MgCl		**4i**	67[a,c]
9			**4j**	72[b,c]
10			**4k**	47
11[d]	PhMgBr		**4l**	68
12[e]	$Ph_2MeSiLi$		**4m**	40

[a] During silica gel column purification of **4i**, the trimethylsilyl group was cleaved, and only **4h** was isolated. [b] The product was partially isomerized to 2-butenoylsilane during silica gel column purification. [c] NMR yield with dibenzyl ether as an internal standard. [d] Air was introduced after an addition of pyridine (1.5 mmol). [e] Oxidation required 2 h for completion.

phenylmethylcopper under the standard conditions caused considerable hydrolysis of the benzylic copper (entry 11).[14] In this case, however, oxidation in the presence of pyridine yielded benzoylsilane (**4l**) in 68% yield. Employing $Ph_2MeSiLi$ yielded disilyl ketone (**4m**)[15] in 40% yield (entry 12).[16]

Our proposed mechanism for this reaction is outlined in Scheme 3. The reaction of the copper species with O_2 in the presence of NH_4Cl furnishes peroxide **9**. After formation of **9**, two pathways are conceivable. Path A involves migration of one of the silyl groups to the internal oxygen with elimination of water (**10** → **11**). In path B, attack of terminal oxygen on silicon yields the product through a four-membered-ring transition state (or intermediate), as is often seen in the Peterson reaction. To determine which route is more plausible, we have carried out ab initio calculations at the B3LYP/6-31G* level.

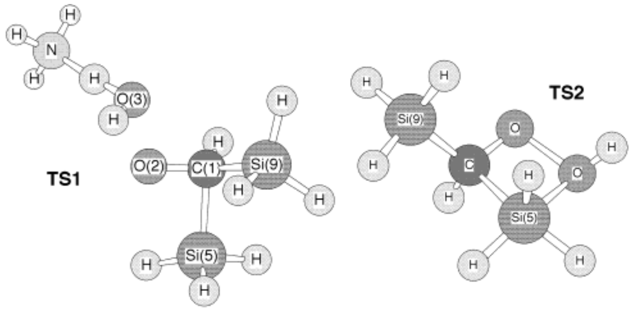
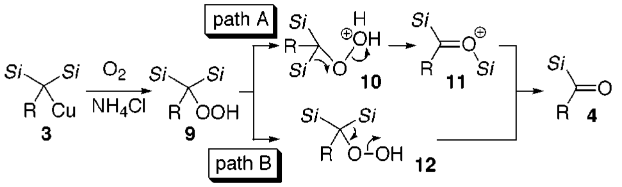


Figure 1. The transition states of **TS1** for path A and **TS2** for path B. The structures were optimized at the B3LYP/6-31G* level.

Scheme 3



In path A, the transition state **TS1** was optimized with NH_4^+ as a proton source (Figure 1). The activation energy was calculated to be 2.8 kcal/mol. The Si(5)−C(1)−O(2) angle of 92.6° and the Si(5)−C(1)−O(2)−O(3) dihedral angle of 167.2° indicate that positive charge on O(2) is stabilized by $(\sigma-p)\pi$ conjugation. In path B, **TS2** has a four-membered-ring structure with 23.6 kcal/mol of the activation energy at the B3LYP/6-31G* level. These results provide strong support that the oxidation of 1,1-dialkylsilylcopper species in aqueous ammonium chloride proceeds via the mechanism outlined in path A.[17]

In conclusion, we have developed a simple and efficient oxidation of organocopper species with atmospheric air to provide a wide variety of acylsilanes. In this reaction, a copper salt plays a dual role to facilitate the migration of an alkyl group from the metal to the adjacent carbon, and to allow for the formation of peroxides without hydrolysis of the disilylalkyl group. This protocol does not require the use of hazardous oxidizing agents, enabling the preparation of various acylsilanes from the corresponding Grignard reagents with only atmospheric air as the oxidant.

Acknowledgment. We thank Dr. Hidehiro Sakurai (Osaka University) for helpful discussions and Mr. Hideki Yorimitsu for help with theoretical calculations. This work was supported by a Grant-in-Aid for Scientific Research (No. 12305058) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. A.I. acknowledges the JSPS Research Fellowship for Young Scientists.

Supporting Information Available: General procedures, spectral data for compounds, and the Cartesian coordinates for **TS1** and **TS2** optimized at the B3LYP/6-31G* level (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA016716R

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(14) Oxidation in the presence of aqueous NH_4Cl provided benzoylsilane in 55% yield and disilylphenylmethane in 16% yield.

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(16) Disilyl ketones are reported to be unstable toward oxygen.[15d,e]

(17) Detailed discussion on the theoretical calculations will be reported in due course.