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SYNTHESIS OF α,α-DIMETHYLALLYLSILANES, A REAGENT OF REGIOSPECIFIC PRENYLATION OF ACETALS AND CARBONYL COMPOUNDS[1]

Akira Hosomi and Hideki Sakurai
Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

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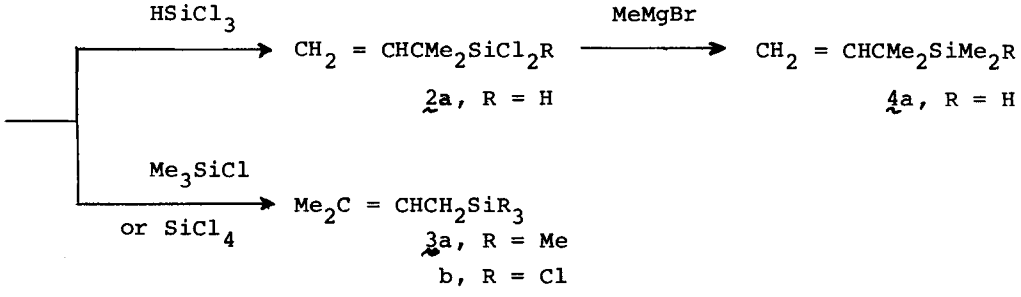
Prenylation is one of the important reacitons for synthesis of various natural products. We have recently demonstrated that allylsilanes are useful synthetic intermediates with a highly nucleophilic double bond, and that allyl transfer took place from allylsilanes to electrophilic carbon centers with regiospecific transposition in the allylic part.[2] Nevertheless, regiospecific prenylation at a primary site could not be attained yet in this reaction, because, to our knowledge, any kind of α,α-dimethylallylsilanes has not been prepared successfully, while γ,γ-dimethylallylsilanes were readily available.[3] We wish to report here a convenient and regioselective route to α,α-dimethylallylsilanes and regiospecific prenylation of acetals and carbonyl compounds.

Interestingly, we have found that the course of the reaction of chlorosilane with the Grignard reagent from 1-chloro-3-methylbut-2-ene(1) and magnesium can be controlled by changing the substituents on the chlorosilane. Thus, with trichlorosilane, the Grignard reagent afforded regioselectively dichloro(α,α-dimethylallyl)-silane(2a) in moderate to high yield, while the reaction with tetrachlorosilane or trimethylchlorosilane gave only a γ,γ-dimethylallylsilane 3(eq. 1). Other chlorosilanes such as methyldichlorosilane gave a mixture of allylsilanes of type 2 and 3. 2a was converted to 4a without isolation.[4]

$$Me_2C = CHCH_2Cl + Mg \longrightarrow [Me_2C = CHCH_2MgCl \longleftarrow Me_2C(MgCl)CH = CH_2]$$

1

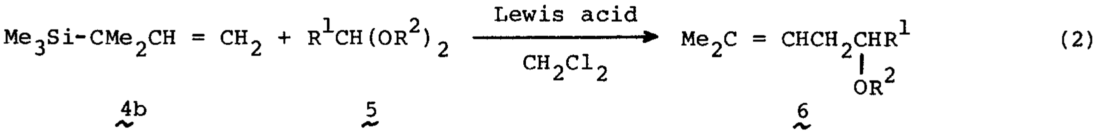


$$\xrightarrow{HSiCl_3} \underset{\textbf{2a},\ R = H}{CH_2 = CHCMe_2SiCl_2R} \xrightarrow{MeMgBr} \underset{\textbf{4a},\ R = H}{CH_2 = CHCMe_2SiMe_2R}$$

$$\xrightarrow[\text{or } SiCl_4]{Me_3SiCl} \underset{\substack{\textbf{3a},\ R = Me \\ \textbf{b},\ R = Cl}}{Me_2C = CHCH_2SiR_3}$$

Hydrosilane 4a[5] was readily converted to (α,α-dimethylallyl)trimethylsilane (4b, R = Me) as follows. First, an ethoxysilane 4c(R = OEt) was obtained quantitatively by the reaction of 4a with ethanol catalyzed by chloroplatinic acid at room temperature, and then 4c was fluorinated by hydrofluoroboric acid(42%, in H_2O) in ethanol to give a fluorosilane 4d(R = F) after usual workup (in 87% yield in one pot reaction from 4a to 4d). The fluorosilane 4d was allowed to react with a small excess of methyllithium in ether to afford a methylsilane 4b(R = Me) in 96% yield.

The methylsilane 4b reveals high reactivity toward acetals with an aid of a Lewis acid[6] to give the corresponding homoallyl ethers with regiospecific transposition in the allylic part(eq. 2). Thus, 4b is a quite useful reagent for prenylation. The results are listed in Table 1.



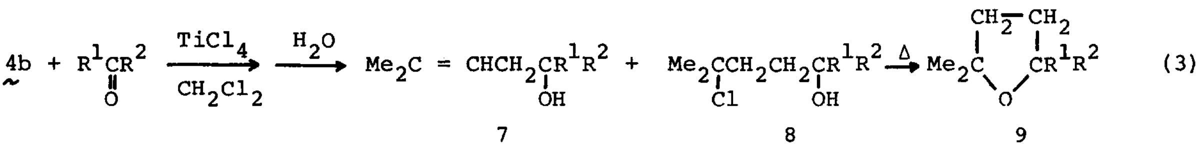
$$Me_3Si\text{-}CMe_2CH = CH_2 + R^1CH(OR^2)_2 \xrightarrow[CH_2Cl_2]{\text{Lewis acid}} Me_2C = CHCH_2\underset{OR^2}{CHR^1} \qquad (2)$$

4b 5 6

The following experimental procedure is typical. To an acetal(1.1 mmol) in dry methylene dichloride(15 ml), a Lewis acid(1.0 mmol) was added by a syringe at -78°C. After several seconds with stirring, the allylsilane 4b(1.0 mmol) was added and the reaction mixture was stirred under a condition shown in the table and hydrolyzed. After usual workup, a homoallyl ether 6 was isolated by the preparative tlc or glc.

In all cases, transfer of allylic group from 4b to acetals took place very rapidly. The prolonged stirring after the addition of 4b brings less satisfactory results because of polymerization or other side reactions.

The reaction of 4b with carbonyl compounds such as aldehydes or ketones[7] is very slow at -78°C. With increasing reaction temprature, however, the regiospecific carbon-carbon bond formation occurs smoothly at a γ-carbon of the allylic group, although products are mainly tetrahydrofuran derivatives 9, along with a small amount of expected homoallyl alcohols 7.(eq. 3) The results are presented in Table 2. It appears probable that 9 can be derived by the cyclization of γ-chloroalcohols 8,[8] possibly formed by addition of hydrogen chloride to 7, under the reaction conditions and/or at a stage of isolation of products. Indeed a γ-chloroalcohol 8, carefully isolated from the reaction mixture of the reaction of β-phenylpropanal with 4b(entry 4), is readily converted to the corresponding 9 by heating.



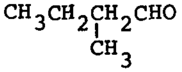
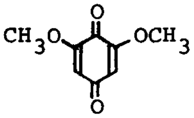
(3)

7 8 9

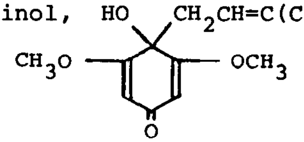
Table 1. Reactions of α,α-dimethylallyltrimethylsilane($4b$) with acetals in the presence of a Lewis acid.

Entry	Acetals	Lewis acid	Conditions	% Yields of 6
1	$CH_3(CH_2)_3CH(OCH_3)_2$	$TiCl_4$	-78°, 10 min.	83
2	$C_6H_5CH(OCH_3)_2$	$BF_3 \cdot OEt_2$	-78°, 30 min. then 0°, 5 min.	85
3	$C_6H_5CH_2CH_2CH(OCH_3)_2$	$TiCl_4$	-78°, 2 min.	93

Table 2. Recations of α,α-dimethylallyltrimethylsilane($4b$) with carbonyl compounds in the presence of titanium tetrachloride.

Entry	Carbonyl compounds	Conditions	Products (% Yield)	
			7	9^a (8)^b
1	 $CH_3CH_2\underset{CH_3}{CH_2}CHO$	r.t., 5 min.	_c	79
2	CH_3CH_2CHCHO	r.t., 5 min.	_c	78[d]
3	$C_6H_5CH_2CH_2CHO$	r.t., 6 min.	_c	81
4	$C_6H_5CH_2CH_2CHO$	r.t., 4 min.	13	(76)
5	$CH_3COCO_2CH_3$	-78°, 1.5 h, then r.t., 15 min.	_e	61
6	$CH_3COCO_2CH_3$	r.t., 4 min.	61	16
7	$CH_3COCO_2CH_3$	r.t., 20 min.	36	30
8		-78°, 10 min.	58[f]	

[a] Determined after isolation as tetrahydrofuran derivatives 9 after heating at ca 200°. [b] Numbers in parenthesis shows the yield of 8. [c] Not observed by glc. [d] The product is dihydroocimenoyl oxide. [e] Not examined. [f] The product is 1-prenyl-2, 6-dimethoxyquinol,

 .

References and Notes

1. Chemistry of Organosilicon Compounds. 112.
2. For recent reports, a) A. Hosomi and H. Sakurai, J. Am. Chem. Soc., **99**, 1673 (1977); b) idem, Tetrahedron Lett., 4041(1977) and references cited therein.
3. a) P. -J. Pillot, J. Dunogues, and R. Calas, Tetrahedron Lett., 1871(1976), reported that **3**a(R = Me) was readily available, but that **4**b(R = Me) is absent in the reaction of the Grignard reagent of **1** with trimethylchlorosilane in ether; b) We found that **3**a was obtained in 80 % yield from **1** and trimethylchlorosilane in THF by in situ Grignard method, and in 77 % yield from tetrachlorosilane in THF-ether followed by methylation with methylmagnesium bromide.
4. **4**a(R = H) was prepared as following: **1**(10.5 g, 0.10 mol) was added slowly to magnesium(2.7 g, 0.11 g-atom) in dry THF(200 ml) with ice-cooling. The Grignard reagent, thus obtained, was added dropwise to a solution of trichlorosilane(40.6 g, 0.30 mol) in a mixed solvent of ether(300 ml) and petroleum ether(800 ml) and the reaction mixture was heated at reflux with stirring for 3 h. Then methylmagnesium bromide(ca. 0.9 mol) in ether, prepared in a separate flask, was added to the reaction mixture, and the resulting mixture was heated at reflux with stirring for 8 h. After hydrolysis and usual work-up, the solvent was removed by distillation. When the residue was distilled, **4**a boiled at 108° was obtained in 76 % yield in more than 99 % isomeric purity.
   From methyldichlorosilane, allylsilanes of type **2** and **3** was obtained in a ratio of 3 : 1 in 64 % yield, along with a small amount of (α,α-dimethylallyl)-methylsilane(5 % yield), according to the similar procedure described above.
5. All new compounds obtained in this work gave correct elemental analysis and spectra data.
6. A. Hosomi, M. Endo, and H. Sakurai, Chem. Lett., 941(1976).
7. A. Hosomi and H. Sakurai, Tetrahedron Lett., 1295(1976).
8. γ-Chloroalcohols **8** are considerably unstable. In only one case, **8** was isolated in nearly pure state. (Table 2, entry 4)

Acknowledgment

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