

Synthesis of Tetrahydrofurans by the Reaction of α,β -Epoxy Alcohol Derivatives with Allylsilanes

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Abstract: In the presence of SnCl_4 , α,β -epoxy alcohol derivatives easily reacted with allylsilanes to give the corresponding tetrahydrofurans in moderate yields. © 1999 Elsevier Science Ltd. All rights reserved.

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The Lewis acid-promoted allylation of allylsilanes to carbonyl compounds (Sakurai-Hosomi reaction) is a most important method for the carbon-carbon bond formation in organic synthesis.¹ In addition, allylsilanes are excellent reagents for the construction of four- and five-membered ring systems.² Several groups have reported the synthesis of carbo- and heterocyclic compounds by the cycloaddition reactions of allylsilanes with activated $\text{C}=\text{X}$ π -bonds.^{3,4} On the other hand, α,β -epoxy alcohols are important starting materials and versatile intermediates in organic synthesis due to their ease of reactivity toward several nucleophiles and availability in optically pure forms.⁵ We report herein the synthesis of tetrahydrofurans by the Lewis acid-promoted reaction of allylsilanes with α,β -epoxy alcohol derivatives.

We chose allyltrimethylsilane (allyl TMS) as the allylsilane and examined the reaction with glycidol benzyl ether (**1**). When the reaction was performed in the presence of TiCl_4 (1.2 equiv.) in CH_2Cl_2 , the allylic product (**10**) and chlorohydrin (**14**)⁶ were obtained in 55% and 22% yields, respectively, and the desired cycloadduct was not detected (Table 1, entry 1). On the other hand, a solution of SnCl_4 (1.2 equiv.) in CH_2Cl_2 was added to a mixture of **1** and allyl TMS in CH_2Cl_2 at -50°C (procedure A)⁷ to give the tetrahydrofuran (**6a**) in 76% yield as a 1:1 mixture of *cis* : *trans* isomers.⁸ On the contrary, a marked decrease in yield was observed when the benzyl group was replaced by other protecting groups such as phenyl, vinyl, and isopropyl (entries 5, 7, and 8). It was found that the benzyloxymethylene moiety in the glycidol benzyl ether plays an important role in the cycloaddition reaction. Namely, while the cycloadduct (**6a**) was produced in 76% yield in the reaction of **1** with allyl TMS, only a 16% (*cis* : *trans* = 1:1) yield of the tetrahydrofuran (**19a**) was obtained when the reaction was carried out using the homoglycidol ether (**18**) instead of **1** under the same reaction conditions (Scheme 1).

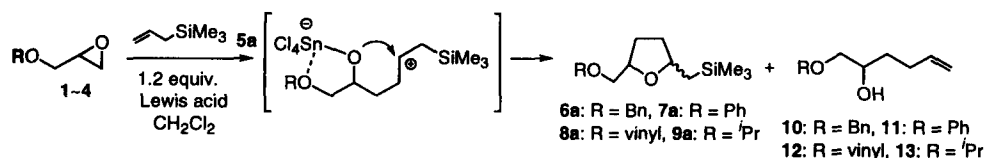
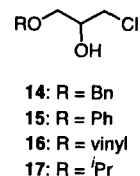
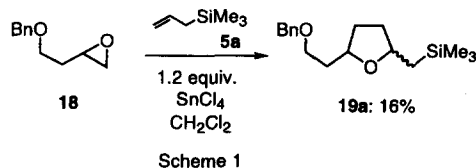


Table 1. Reaction of Glycidol Derivatives with Allyltrimethylsilane

Entry	Glycidol R	Lewis acid	Temp. °C	Time	Products (yield, %) ^a
1	Bn 1	TiCl ₄	-78	5 min	6a (0) 10 (55) 14 (22)
2	Bn	BF ₃ ·OEt ₂	-50	5 min	complex mixture
3	Bn	SnCl ₄	-50	5 min	6a (76) 10 (4) 14 (4)
4	Ph 2	TiCl ₄	-50	5 min	7a (4) 11 (28) 15 (58)
5	Ph	SnCl ₄	-78~-50	1 h	7a (20) 11 (4) 15 (50)
6	Ph	Et ₂ AlCl	-50	1 h	7a (10) 11 (6) 15 (64)
7	vinyl 3	SnCl ₄	-50	5 min	8a (17) — ^b
8	iPr 4	SnCl ₄	-50	30 min	9a (25) — ^b

^aIsolated yield. ^bNot isolated.

The reactions of other allylsilanes were then examined and these results are summarized in Table 2. As for the allylsilanes, allyl DMPS (**5b**) as well as allyl TMS reacted effectively to give the cycloadduct (**6b**) in 70% yield. We found that the yield of the cycloadduct depends on the steric demand of the alkyl substituents on the



silicon atom. Namely, the use of sterically bulky allylsilanes decreased the yield of the cycloadduct and the yield of the chlorohydrin was increased. The change in the chlorohydrin yield probably results because the nucleophilic addition reaction of the allylsilane proceeded slowly when using the bulkier allylsilanes.

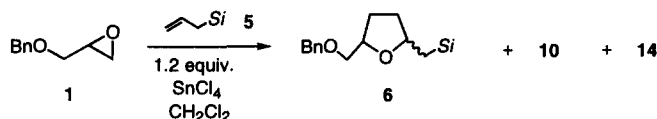


Table 2. Reaction of Glycidol Benzyl Ether (1) with Allylsilanes

Entry	Si	Temp. °C	Time	Yield, % ^a
				6^b 10 14
1	SiMe ₃ 5a	-50	5 min	6a 76 4 4
2	SiMe ₂ Ph 5b	-50~-20	1 h	6b 70 (0) ^c 6 (39) ^c 20 (36) ^c
3	SiMePh ₂ 5c	-50~-20	1 h	6c 54 6 27
4	Si ⁱ Pr ₃ 5d	-50~-20	1 h	6d 20 15 35

^aIsolated yield. ^bcis : trans = ca. 1 : 1. ^cTiCl₄ was used as a Lewis acid.

To extend the scope of this methodology, we examined the reaction with several epoxides. When the epoxide (**20**) reacted with allyl TMS under the same reaction conditions (procedure A), however, the

tetrahydrofuran (**24a**) was obtained in low yield (26%). In order to improve the yield of this cycloaddition reaction, we examined the reaction conditions such as the order of addition of the reagents, reaction temperature, and solvent. Among these conditions, it was found that the order of the addition of the reagents influenced the yield dramatically. Namely, slow addition of the epoxide and SnCl_4 simultaneously to a solution of allyl TMS over 1 h period (procedure B)⁹ resulted in a remarkable enhancement of the yield of the cycloadduct (**24a**) from 26% to 79% (Table 3, entry 1). The epoxide (**20**) also reacted with allyl DMPS to form the cycloadduct (**24b**) in 44% yield (entry 2). A similar tendency was observed in the cycloaddition reactions of the epoxide (**23**) with allylsilanes (entries 6 and 7). Namely, while the cycloaddition reaction proceeded sluggishly under the normal conditions (procedure A), enhancement of the reactivity was observed when the reaction was carried out under slow addition conditions (procedure B). It was also found that introduction of an alkyl group at the 3-position of the α,β -epoxy alcohol derivatives decreased the yield of the cycloadduct and the chlorohydrin was obtained as the major product (entries 3, 4 and 5).

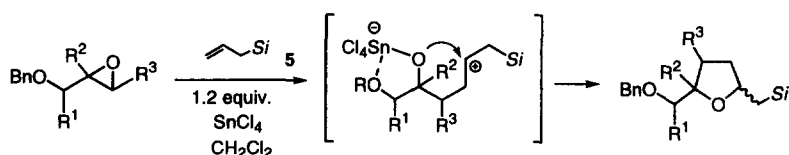


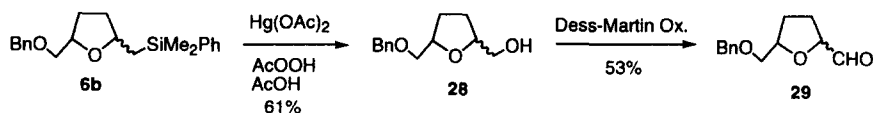
Table 3. Reaction of α,β -Epoxy Alcohol Derivatives with Allylsilanes

Entry	R ¹	R ²	R ³	Epoxide	Allylsilane	Temp. °C	Product yield, % ^{a,b}
1	H	Me	H	20	5a	-50	24a 79 (26) ⁹
2	H	Me	H	20	5b	-50	24b 44
3	H	H	Me	21	5a	-20	25a 32 ^c (26) ⁹
4	H	H	Me	21	5b	-20	25b 16 ^d
5	H	H	Ph	22	5a	-20	26a 9 ^e
6	Me	H	H	23^f	5a	-50	27a 68 (24) ⁹
7	Me	H	H	23^f	5b	-50	27b 54 (21) ⁹

^aIsolated yield. ^b*cis* : *trans* = ca. 1:1. ^cThe chlorohydrin was also obtained in 34%. ^d48%. ^e61%.

^f*threo*-**23** was used. ^gTo a mixture of the epoxide and allylsilane in CH_2Cl_2 was added SnCl_4 (procedure A).

Interestingly, the cycloadduct (**6b**) obtained from **1** and allyl DMPS was converted to tetrahydrofurfural (**29**) using Fleming's procedure¹⁰ followed by the Dess-Martin oxidation¹¹ (Scheme 2).



Scheme 2

In summary, we have demonstrated that the Lewis acid-catalyzed cycloaddition reactions of α,β -epoxy alcohol derivatives with allylsilanes proceeded smoothly to afford the tetrahydrofurans in moderate yields. Further applications of this reaction are now under investigation in our laboratory.

References and notes

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7. A typical procedure A is as follows: To a stirred solution of **1** (82 mg, 0.5 mmol) and allyl TMS (114 mg, 1.0 mmol) in CH₂Cl₂ (4 ml) was added dropwise a solution of SnCl₄ (1.0 M solution in CH₂Cl₂, 0.6 ml, 0.6 mmol) at -50 °C under an argon atmosphere. After being stirred for 5 min, the reaction was quenched at the same temperature by adding a saturated NH₄Cl solution (2 ml). The mixture was stirred vigorously for 10 min and allowed to warm to room temperature. The mixture was extracted with CH₂Cl₂ (20 ml x 3), and the combined organic layers were dried over Na₂SO₄. The solvent was then evaporated under reduced pressure. The residue was purified by silica gel column chromatography (eluent: hexane-AcOEt = 60:1) to give the cycloadduct (**6a**), homoallylalcohol (**10**), and chlorohydrin (**14**) in 76%, 4%, and 4% yields, respectively.
8. Reaction of glycidol benzyl ether (**1**) and allyl TMS using a catalytic amount (0.1 equiv.) of SnCl₄ gave the cycloadduct (**6a**) in low yield (4%) and **1** was recovered in 46% yield.
9. A typical procedure B is as follows: A solution of **20** (89 mg, 0.5 mmol) in CH₂Cl₂ (0.5 ml) and SnCl₄ (1.0 M solution in CH₂Cl₂, 0.6 ml, 0.6 mmol) were added simultaneously to a stirred solution of allyl TMS (228 mg, 2.0 mmol) in CH₂Cl₂ (1.2 ml) over 1 h period at -50 °C under an argon atmosphere. After workup was performed as detailed in procedure A, the cycloadduct (**24a**) was obtained in 79% yield.
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