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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.

Keywords: epoxides; cycloadditions; Sakurai-Hosomi reaction

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 C=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 ℃ (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).

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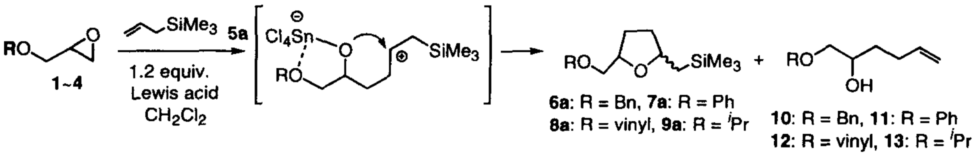
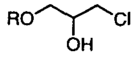


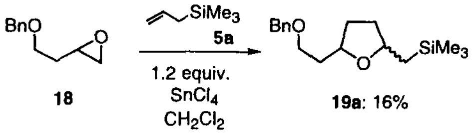
Table 1. Reaction of Glycidol Derivatives with Allyltrimethylsilane

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		$BF_3 \cdot OEt_2$	-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_2AlCl	-50	1 h	**7a** (10)	**11** (6)	**15** (64)
7	vinyl	**3**	$SnCl_4$	-50	5 min	**8a** (17)		—— [b]
8	^{i}Pr	**4**	$SnCl_4$	-50	30 min	**9a** (25)		—— [b]

[a]Isolated yield. [b]Not 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.



Scheme 1

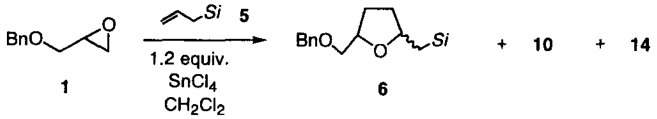


Table 2. Reaction of Glycidol Benzyl Ether (**1**) with Allylsilanes

Entry	*Si*		Temp. °C	Time	Yield, %[a] 6[b]		10	14
1	$SiMe_3$	**5a**	-50	5 min	**6a**	76	4	4
2	$SiMe_2Ph$	**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^iPr_3	**5d**	-50~-20	1 h	**6d**	20	15	35

[a]Isolated yield. [b]*cis* : *trans* = ca. 1 : 1. [c]$TiCl_4$ 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 influeneced 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).

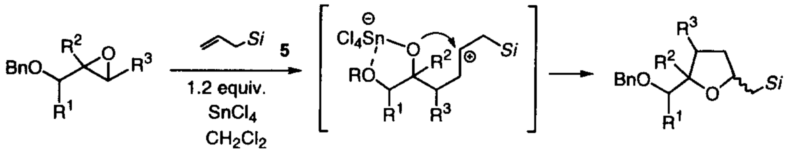
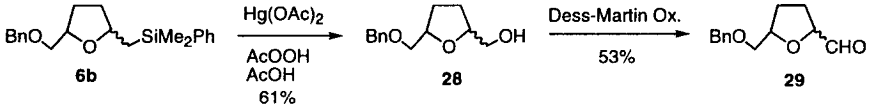


Table 3. Reaction of α,β-Epoxy Alcohol Derivatives with Allylsilanes

	Epoxide					Temp.	Product
Entry	R^1	R^2	R^3		Allylsilane	°C	yield, %[a,b]
1	H	Me	H	**20**	**5a**	-50	**24a** 79 (26)[g]
2	H	Me	H	**20**	**5b**	-50	**24b** 44
3	H	H	Me	**21**	**5a**	-20	**25a** 32[c] (26)[g]
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)[g]
7	Me	H	H	**23**[f]	**5b**	-50	**27b** 54 (21)[g]

[a]Isolated yield. [b]*cis* : *trans* = ca. 1:1. [c]The chlorohydrin was also obtained in 34%. [d]48%. [e]61%. [f]*threo*-**23** was used. [g]To a mixture of the epoxide and allylsilane in CH$_2$Cl$_2$ was added SnCl$_4$ (procedure A).

Interestingly, the cycloadduct (**6b**) obtained from **1** and allyl DMPS was converted to tetrahydrofurfural (**29**) using Fleming's procedure[10] followed by the Dess-Martin oxidation[11] (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.

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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 CH_2Cl_2 (4 ml) was added dropwise a solution of $SnCl_4$ (1.0 M solution in CH_2Cl_2, 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 NH_4Cl solution (2 ml). The mixture was stirred vigorously for 10 min and allowed to warm to room temperature. The mixture was extracted with CH_2Cl_2 (20 ml x 3), and the combined organic layers were dried over Na_2SO_4. 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 $SnCl_4$ 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 CH_2Cl_2 (0.5 ml) and $SnCl_4$ (1.0 M solution in CH_2Cl_2, 0.6 ml, 0.6 mmol) were added simultaneously to a stirred solution of allyl TMS (228 mg, 2.0 mmol) in CH_2Cl_2 (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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