

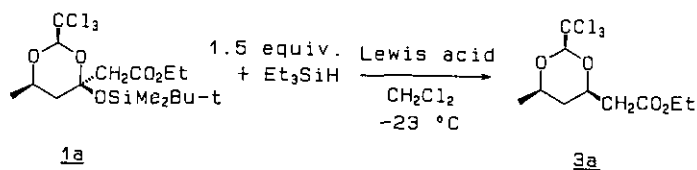
STERESELECTIVE REDUCTION OF t-BUTYLDIMETHYLSILOXY GROUP OF ETHYL
2-TRICHLOROMETHYL-4-t-BUTYLDIMETHYLSILOXY-1,3-DIOXAN-4-ACETATES

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Abstract — t-Butyldimethylsiloxy group of ethyl 4-t-butyldimethylsiloxy-2-trichloromethyl-1,3-dioxan-4-acetates, easily prepared from 2-trichloromethyl-1,3-dioxan-4-ones, was stereoselectively reduced with triethylsilane by using titanium tetrachloride as a promoter to afford ethyl cis-2-trichloromethyl-1,3-dioxan-4-acetates.

In the previous paper, we have reported that, in the presence of a catalytic amount of TrSbCl_6 , 2-trichloromethyl-1,3-dioxan-4-ones were stereoselectively attacked by t-butyldimethylsiloxy-1-ethoxyethene to give silylated cyclic hemiketals, ethyl 4-t-butyldimethylsiloxy-2-trichloromethyl-1,3-dioxan-4-acetates (**1** and **2**).¹⁾ We already reported that siloxy groups of silylated cyclic hemiketals which were derived from lactones with silyl ketene acetal, or γ -, δ - and ϵ -trimethylsiloxy carbonyl compounds were reduced with Et_3SiH in the presence of a catalytic amount of TrSbCl_6 or catalyst system of SbCl_5 , Me_3SiCl and SnI_2 .²⁾ However, these catalysts were not effective in the cases of the siloxy group of **1** and **2** probably due to the strong electronegative trichloromethyl group at 2-position. Thus, several Lewis acids were screened for the reduction of the siloxy group of ethyl 4 α -t-butyldimethylsiloxy-6 α -methyl-2 α -trichloromethyl-4 β -acetate (**1a**) (Table 1). Titanium tetrachloride was superior to the other Lewis acids in terms of yield and selectivity.



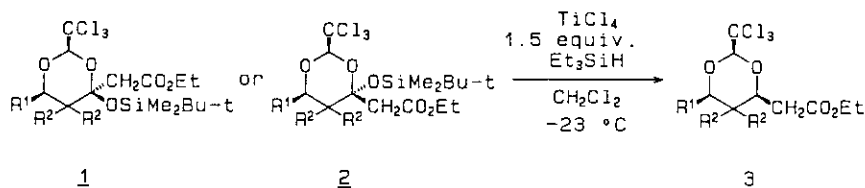
Scheme 1

Table 1. Effect of Lewis Acids

Entry	Lewis acid(equiv.)	Yield / %(2,4-cis/trans) ^{a)}
1	TiCl ₄ (1.1)	62(98:2)
2	TiCl ₄ (3.0)	91(98:2)
3	SnCl ₄ (3.0)	54(97:3)
4	AlCl ₃ (3.0)	16(96:4)
5	SbCl ₅ (3.0)	4(97:3)
6	BF ₃ ·Et ₂ O(3.0)	1(91:9)

a) The selectivity was determined by 400 MHz ¹H nmr.

Next, several 4-*t*-butyldimethylsiloxy-2-trichloromethyl-1,3-dioxan-4-acetates (**1** and **2**) were reduced with Et₃SiH by use of TiCl₄ as a promoter to afford *cis*-2-trichloromethyl-1,3-dioxan-4-acetates (**3**) (Table 2).



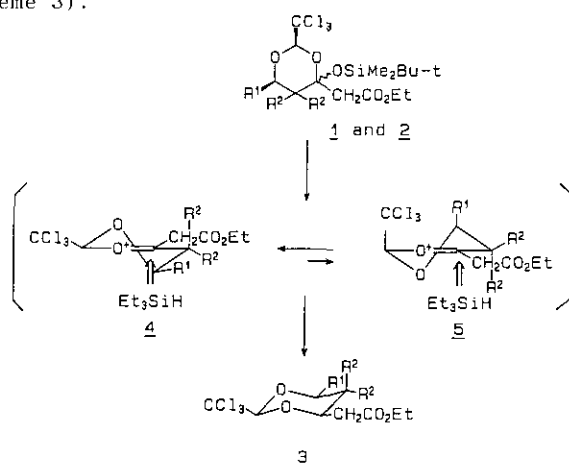
Scheme 2

Table 2. Reduction of Siloxy Group

Entry	1. or 2	R ¹	R ²	Yield / %(2,4-cis/trans) ^{a)}
1	2a	Me	H	92(>99:1)
2	1a	Me	H	91(98:2)
3	2b	Ph	H	67(97:3)
4	1b	Ph	H	65(98:2)
5	1c	<i>n</i> -C ₇ H ₁₅	Me	94(>99:1)
6	1d	Ph	Me	97(>99:1)
7	1e	PhCH ₂ CH ₂	Me	98(>99:1)

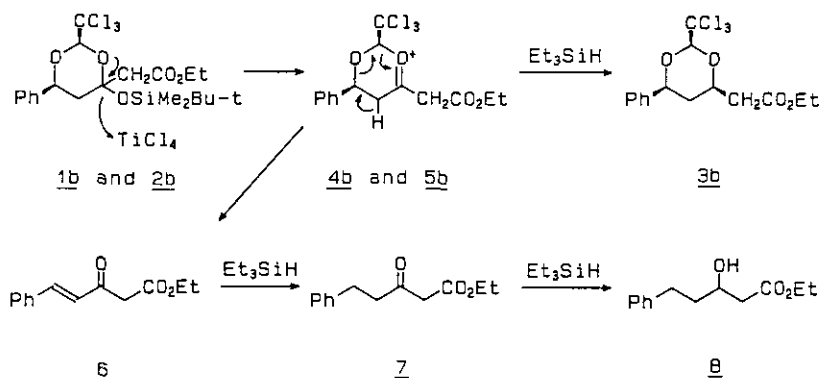
a) The selectivity was determined by 400 MHz ¹H nmr.

2,4-*cis*-isomers (**3**) were stereoselectively prepared irrespective of the stereochemistry of the siloxy group. The results suggest that the reaction proceeds via the oxonium intermediate, that is, Et_3SiH attacked the oxonium intermediate (**4**), major conformer, from α -side due to torsional strain and the oxonium intermediate (**5**), minor conformer from α -side, as well due to 1,3-diaxial interaction. (Scheme 3).



Scheme 3

When **1b** was reduced using 5 equivalents of Et_3SiH , ethyl 6 α -phenyl-2 α -trichloromethyl-1,3-dioxan-4 α -acetate (**3b**) was obtained in 71% yield along with ethyl 3-hydroxy-5-phenylvalerate (**8**) in 23% yield. Therefore, we supposed that in the cases of **1b** and **2b**, alternative pathway became significant because phenyl group at 6-position and hydrogens at 5-position contributed to produce ethyl 3-oxo-5-phenyl-4-pentenoate (**6**) (Scheme 4).



Scheme 4

The stereochemistry of **3** was determined by the NOE analysis (400 MHz ^1H nmr spectrum) for the ring methine protons.

A typical procedure is described for preparation of ethyl 5,5-dimethyl-6 α -phenyl-2 α -trichloromethyl-1,3-dioxan-4 α -acetate (**3d**): Under argon atmosphere, a solution of 4 α -t-butyldimethylsiloxy-5,5-dimethyl-6 α -phenyl-2 α -trichloromethyl-1,3-dioxan-4 β -acetate (**1d**) (2.63 g, 5.0 mmol) and Et_3SiH (871 mg, 7.5 mmol) in CH_2Cl_2 (30 ml) was added dropwise to a 1.0 molar solution of TiCl_4 in CH_2Cl_2 (15 ml, 15 mmol) at -23°C , and then the reaction mixture was stirred for 30 min. Then, the reaction was quenched with aqueous saturated NaHCO_3 . The organic materials were washed with brine, dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (10:1 hexane-ethyl acetate as an eluent) to give **3d** (1.92 g, 97%). For the purpose of preparation of syn-1,3-diols, the remove of trichloroethylidene acetal of **3** prepared by the present procedure is now under investigation.

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