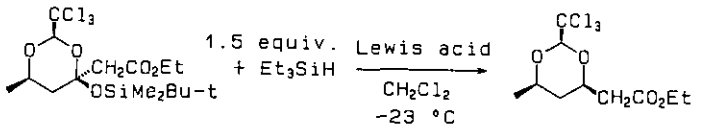
STEREOSELECTIVE REDUCTION OF t-BUTYLDIMETHYLSILOXY GROUP OF ETHYL 2-TRICHLOROMETHYL-4-t-BUTYLDIMETHYLSILOXY-1,3-DIOXAN-4-ACETATES

Koichi Homma and Teruaki Mukaiyama*

Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162, Japan

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 papar, 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 $TrSbSl_6$ 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 electroncgative trichloromethyl group at 2-position. Thus, several Lewis acids were screened for the reduction of the siloxy group of ethyl 4α-t-butyldimethylsiloxy-6α-methyl-2α-trichloromethyl-4β-acetate (**1a**) (Table 1). Titanium tetrachloride was superior to the other Lewis acids in terms of yield and selectivity.



1a 3a

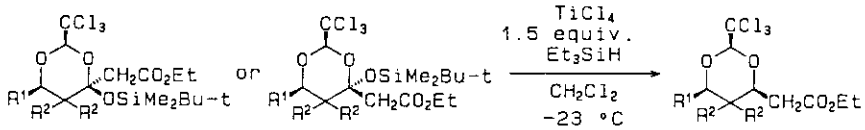
Scheme 1

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	$BF_3 \cdot Et_2O$(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 Et_3SiH by use of $TiCl_4$ as a promoter to afford cis-2-trichloromethyl-1,3-dioxan-4-acetates (**3**) (Table 2).



1 **2** **3**

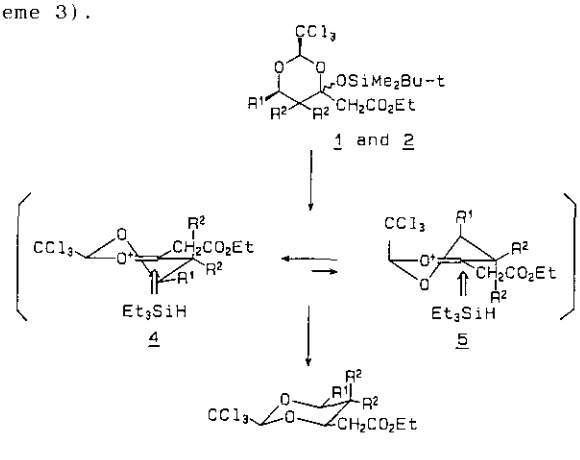
Scheme 2

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**	n-C_7H_{15}	Me	94(>99:1)
6	**1d**	Ph	Me	97(>99:1)
7	**1e**	$PhCH_2CH_2$	Me	98(>99:1)

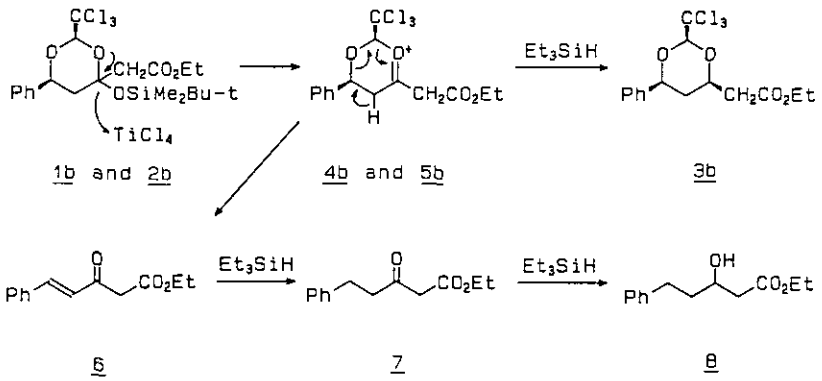
a) The selectivity was determined by 400 MHz ^1H nmr.

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 6α-phenyl-2α-trichloromethyl-1,3-dioxan-4α-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 ^{1}H nmr spectrum) for the ring methine protons.

A typical procedure is described for preparation of ethyl 5,5-dimethyl-6α-phenyl-2α-trichloromethyl-1,3-dioxan-4α-acetate (**3d**): Under argon atmosphere, a solution of 4α-t-butyldimethylsiloxy-5,5-dimethyl-6α-phenyl-2α-trichloromethyl-1,3-dioxan-4β-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 ℃, 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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REFERENCES

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