CHEMISTRY LETTERS, pp. 161-164, 1990.

Stereoselective Addition of t-Butyldimethylsiloxy-1-ethoxyethene to 2-Trichloromethyl-1,3-dioxan-4-ones

Koichi HOMMA and Teruaki MUKAIYAMA
Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

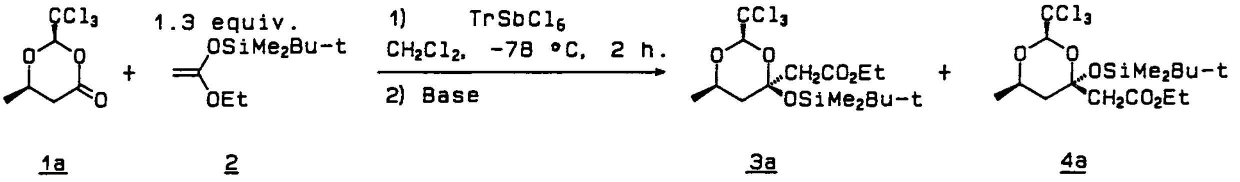
In the presence of a catalytic amount of trityl hexachloroantimonate, 2-trichloromethyl-1,3-dioxan-4-ones (1), easily prepared from β-hydroxycarboxylic acids,[1)] are stereoselectively attacked by t-butyldimethylsiloxy-1-ethoxyethene to afford 1,3-dioxan-4-acetic acid derivatives. The stereoselectivity is dependent on both the substituent at the 5-position of 1 and the amount of the catalyst.

In previous papers,[2)] we have reported that, in the presence of a catalytic amount of $TrSbCl_6$ or $SbCl_5$, lactones smoothly reacted with t-butyldimethylsiloxy-1-ethoxyethene (**2**) to form in situ silylated cyclic hemiketals, which were in turn converted to cyclic ethers on treatment with triethylsilane.

Seebach and co-workers have reported that silyl nucleophiles such as allyltrimethylsilane, trimethylsilyl cyanide and **2** attack the acetal carbon of 1,3-dioxan-4-ones in the presence of $TiCl_4$ or i-$PrOTiCl_3$ in a highly stereoselective manner to afford β-alkoxycarboxylic acids.[1)]

Now we wish to report that in the presence of a catalytic amount of $TrSbCl_6$, 2-trichloromethyl-1,3-dioxan-4-ones (1) are stereoselectively attacked by **2** to afford 1,3-dioxan-4-acetic acid derivatives and that the stereoselectivity is dependent on both the substituent at the 5-position of 1 and the amount of the catalyst.[3,4)]

First, we examined the effect of the amount of $TrSbCl_6$ and the kind of bases used for quenching (Table 1). It was found there that the amount of catalyst employed had a significant effect on the stereochemical outcome of the reaction. When 5 mol% of $TrSbCl_6$ was employed, the 2,4-cis isomer (**3a**) was obtained exclusively. The 2,4-cis isomer (**3a**)/2,4-trans isomer (**4a**) ratio decreases with an increase in the amount of $TrSbCl_6$, and **4a** became predominant with 20 mol% of $TrSbCl_6$. The base used for quenching had only a marginal effect on the



Scheme 1.

Table 1. The Effect of the Amount of $TrSbCl_6$ and the Base for Quenching

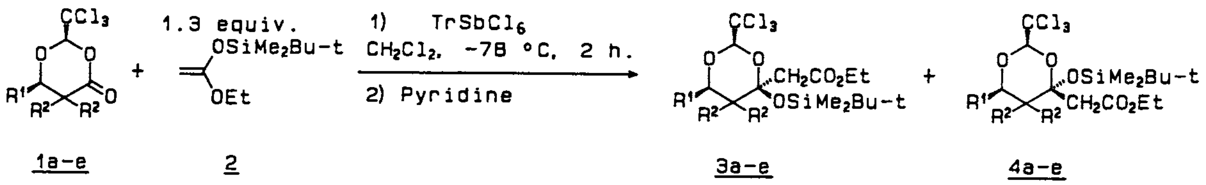
Entry	$TrSbCl_6$ (mol%)	Base	Yield / %		**3a/4a**
			3a	**4a**	
1	20	Pyridine	7.1	80	8:92
2	10	Pyridine	19	71	21:79
3	5	Pyridine	93	-	100:0
4	5	CsF	92	-	100:0
5	5	Aqueous $NaHCO_3$	88	4.7	95:5
6	5	Phosphate buffer	84	5.1	94:6

diastereomer ratio. Pyridine and cesium fluoride gave the highest stereoselectivity when 5 mol% of $TrSbCl_6$ is used as the catalyst.

Next, we examined the stereoselectivity of the addition of **2** to several 2-trichloromethyl-1,3-dioxan-4-ones (**1a**-**e**) (Table 2).

2,4-cis Isomers (**3c**-**e**) are preferentially produced in the case of 5,5-disubstituted 1,3-dioxan-4-ones (**1c**-**e**) irrespective of the amount of $TrSbCl_6$ (entries 5 - 9). While in the case of 5-unsubstituted 1,3-dioxan-4-ones (**1a** and **1b**), the stereoselectivity is dependent on the amount of $TrSbCl_6$: 2,4-trans isomers (**4a** and **4b**) are mainly produced in the presence of 20 mol% of $TrSbCl_6$ (entries 1 and 3); 2,4-cis isomers (**3a** and **3b**) are exclusively produced by using 5 mol% of $TrSbCl_6$ (entries 2 and 4).

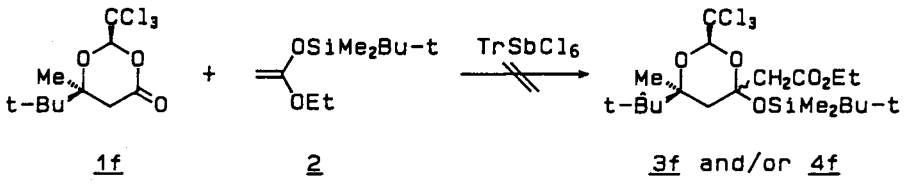
When cis-6-t-butyl-6-methyl-2-trichloromethyl-1,3-dioxan-4-one (**1f**) is used, the addition of **2** does not proceed under the equivalent conditions (Scheme 3), therefore we assumed that the nucleophile (**2**) attacks from the axial side due to torsional strain to afford the adduct anion (**5**) (Scheme 4). When 5 mol% of $TrSbCl_6$ is used, **5** is trapped very rapidly with t-butyldimethylsilyl cation. On the other hand, when more than 10 mol% of $TrSbCl_6$ is used, the oxo anion of **5** is blocked by trityl cations, and thereby under these reaction conditions, the adduct anions (**5** and **7**) are in equilibrium via keto anion (**6**) similar to the tautomeric equilibrium between lactol and hydroxyketone.$^{5)}$ As the adduct anion (**7**) may be thermodynamically more stable than the other anion (**5**) in the case of 5-unsubstituted 1,3-dioxan-4-ones, 2,4-trans isomers are mainly produced. On the other hand, in the case of 5,5-disubstituted 1,3-dioxan-4-ones, **5** is more stable than **7** probably due to steric repulsion between the geminal methyl groups at 5-position and the acetate group at 4-position leading to the preferential formation of the 2,4-cis isomers.



Scheme 2.

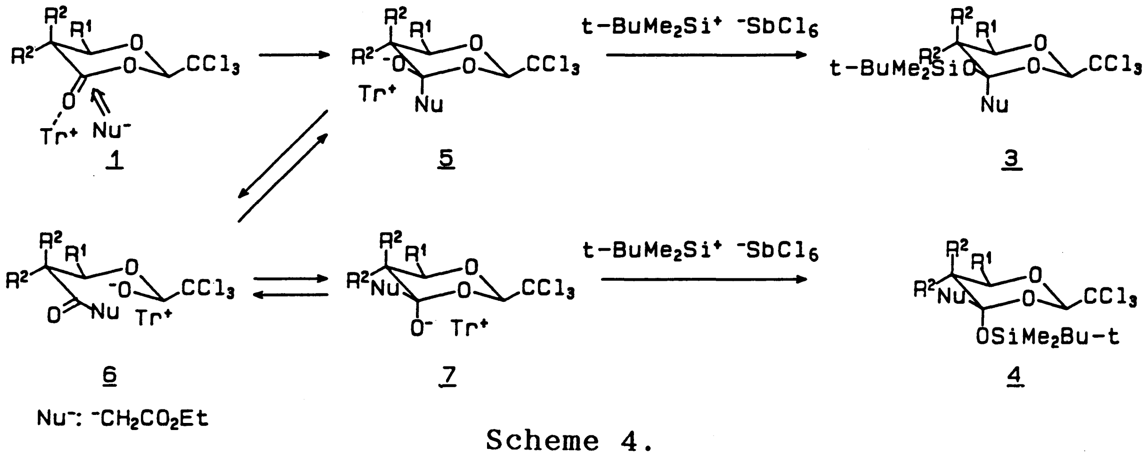
Table 2. The Reaction of 2-Trichloromethyl-1,3-dioxan-4-ones and t-Butyldimethylsiloxy-1-ethoxyethene

Entry	1	R^1	R^2	$TrSbCl_6$ (mol%)	Yield / %		3/4
					3	4	
1	**1a**	Me	H	20	7.1	80	8:92
2	**1a**	Me	H	5	93	-	100:0
3	**1b**	Ph	H	20	6.6	77	8:92
4	**1b**	Ph	H	5	91	-	100:0
5	**1c**	$n\text{-}C_7H_{15}$	Me	20	98	-	100:0
6	**1c**	$n\text{-}C_7H_{15}$	Me	5	100	-	100:0
7	**1d**	Ph	Me	20	92	0.8	99:1
8	**1d**	Ph	Me	5	96	-	100:0
9	**1e**	$PhCH_2CH_2$	Me	5	99	-	100:0



Scheme 3.

A typical procedure is described for the preparation of ethyl 4α-t-butyldimethylsiloxy-6α-methyl-2α-trichloromethyl-1,3-dioxan-4β-acetate (**3a**): Under argon atmosphere, $TrSbCl_6$ (14.6 mg, 0.025 mmol) was added to a solution of cis-6-methyl-2-trichloromethyl-1,3-dioxan-4-one (116.6 mg, 0.5 mmol) and t-butyldimethylsiloxy-1-ethoxyethene (133.3 mg, 0.66 mmol) in CH_2Cl_2 (2.5 ml) at -78 °C,



Scheme 4.

and then the reaction mixture was stirred for 2 h. at the same temperature. The reaction was quenched with a solution of pyridine (21.1 mg, 0.27 mmol) in CH_2Cl_2 (1 ml). The reaction mixture was washed with brine, dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by flash column chromatography on silica gel (30:1 hexane-ethyl acetate as an eluent) to give **3a** (201.8 mg, 93%).

References

1) D. Seebach, R. Imwinkelried, and G. Stucky, Angew. Chem., Int. Ed. Engl., 25, 178(1986); D. Seebach, R. Imwinkelried, and G. Stucky, Helv. Chim. Acta, 70, 448(1987).
2) T. Mukaiyama, K. Homma, and H. Takenoshita, Chem. Lett., 1988, 1725; K. Homma and T. Mukaiyama, Chem. Lett., 1989, 893.
3) In the case of 6-methyl-1,3-dioxan-4-one and cis-2-t-butyl-6-phenyl-1,3-dioxan-4-one, the corresponding adducts of t-butyldimethylsiloxy-1-ethoxyethene were not detected under similar conditions.
4) The stereochemistry was determined by NOE analysis (400-MHz NMR spectrum).
5) For review, see: P. R. Jones, Chem. Rev., 63, 461(1963).

(Received November 7, 1989)