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A Highly Stereoselective Synthesis of α-Glucosides from 1-O-Acetyl Glucose by Use of Tin(IV) Chloride - Silver Perchlorate Catalyst System

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In the presence of a catalytic amount of tin(IV) species generated from tin(IV) chloride and silver perchlorate, 1-O-acetyl-D-glucose stereoselectively reacts with silyl alkoxides to give the corresponding α-glucosides in high yields.

Stereoselective glycosylation reaction is one of the most important problems in carbohydrate chemistry and many glycosylation methods have been developed since the classical Königs-Knorr synthesis.1) While 1,2-trans glycosides have been relatively easily prepared by the assist of the neighbouring effect of acetyl or benzoyl group at C-2 position, stereoselective synthesis of 1,2-cis glycosides2) is rather difficult because of the absence of such effect. The glycopyranosyl fluoride method3) using the fluoride together with $SnCl_2$-$AgClO_4$ reported from our laboratory is one of the most convenient and effective tools for the preparation of 1,2-cis glycosides and frequently employed using a variety of activators such as SiF_4,4) Me_3SiOTf,4) Cp_2MCl_2-$AgClO_4$ (M=Ti, Zr, Hf),5) and Me_2GaX (X=Cl, OTf).6)

Increasing importance of glycosylation reaction prompted us to challenge new possibility to develop a simple and efficient method starting from easily available 1-O-acetyl sugars.7) In this communication, we would like to describe a highly stereoselective synthesis of α-glucosides from 1-O-acetyl glucose and silyl alkoxides by using a novel catalyst system, tin(IV) chloride and silver perchlorate.

In the first place, O-glycosylation reaction of 1-O-acetyl-2,3,4,6-tetra- O-benzyl-D-glucopyranose (**1**) with 3β-cholestanyl trimethylsilyl ether was tried by using several suitable Lewis acids. We have already reported that the synthesis of 1,2-cis-ribofuranosides from 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose and silylated nucleophiles is effectively achieved by use of a catalytic amount of tin(IV) chloride and tin(II) triflate together with a stoichiometric amount of lithium perchlorate.8) It was found there that, by using the above catalyst system, the corresponding α-glucoside was predominantly obtained in 73% yield (α/β=81/19), however, diastereomeric ratio was not improved even after examining detailed reaction conditions. It was postulated then that the cationic anomeric center, generated from 1-O-acetyl sugar with the elimination of acetoxyl group by the promotion of Lewis acid, should be stabilized by such a stable counter anion as perchlorate ion and that this bulky counter anion blocks β-side of the anomeric center to make the preferential attack of silyl alkoxides from α-side.9) Based on the consideration, some attempts to generate a strong Lewis acid with perchlorate group was tried by choosing the suitable combination of a Lewis acid and silver perchlorate. After screening several Lewis acids by taking the above mentioned model reaction (Table 1, Entries 2 - 5), high yield and stereoselectivity were attained when tin(IV) species generated in situ from tin(IV) chloride and silver perchlorate was employed as a catalyst.

Concerning the effect of solvents, the best result was obtained when the reaction was carried out in diethyl ether (See Table 2).

Several examples of the present glycosylation reaction are demonstrated in Table 3. In every case including sterically hindered silyl alkoxides, α-glucosides are prepared in good yields with high stereoselectivity. It is noted that methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-α-D-glucopyranoside (2) was obtained in 95% yield (α / β=97/3) when methyl 2,3,4-tri-O-benzyl-6-O-(trimethylsilyl)-α-D-glucopyranoside (3) was employed as a silyl alkoxide. In a similar manner, when tert-butyl trimethylsilyl ether was used, the corresponding α-glucoside was obtained in 68% yield (α / β=86/14).

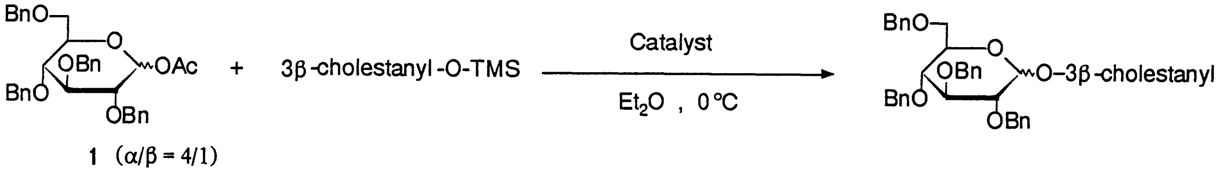


Table 1. Effect of Catalyst

Entry	Catalyst	Yield / %	α/β
1	$SnCl_4 + Sn(OTf)_2$ (20 mol%) + $LiClO_4$ (100 mol%)	73	81 / 19
2	$SnCl_4 + AgClO_4$ (20 mol%)	91	94 / 6
3	$FeCl_3 + AgClO_4$ (20 mol%)	61	92 / 8
4	$TiCl_4 + AgClO_4$ (20 mol%)	45	93 / 7
5	$SbCl_5 + AgClO_4$ (20 mol%)	21	92 / 8

Table 2. Effect of Solvent a)

Entry	Solvent	Yield / %	α/β
1	CH_2Cl_2	86	77 / 23
2	Toluene	39	74 / 26
3	THF	49	66 / 34
4	Et_2O	91	94 / 6

a) Catalyst : $SnCl_4 + AgClO_4$ (20 mol%).

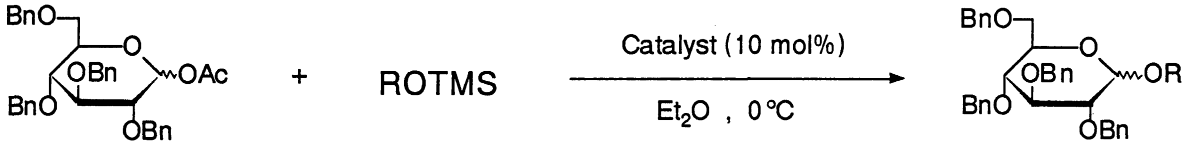
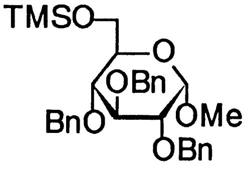


Table 3. Synthesis of α-glucopyranosides a)

Entry	ROTMS (1.2 equiv.)	Yield / %	α / β
1	3β-cholestanyl-O-TMS	94	95 / 5
2	c-C_6H_{11}-O-TMS	87	92 / 8
3 b)	3	95	97 / 3
4	4	86	90 / 10
5	5	95	92 / 8

a) Catalyst : $SnCl_4 + AgClO_4$.
b) Catalyst (5 mol%).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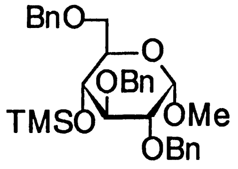
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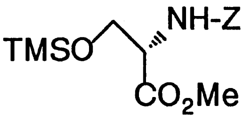
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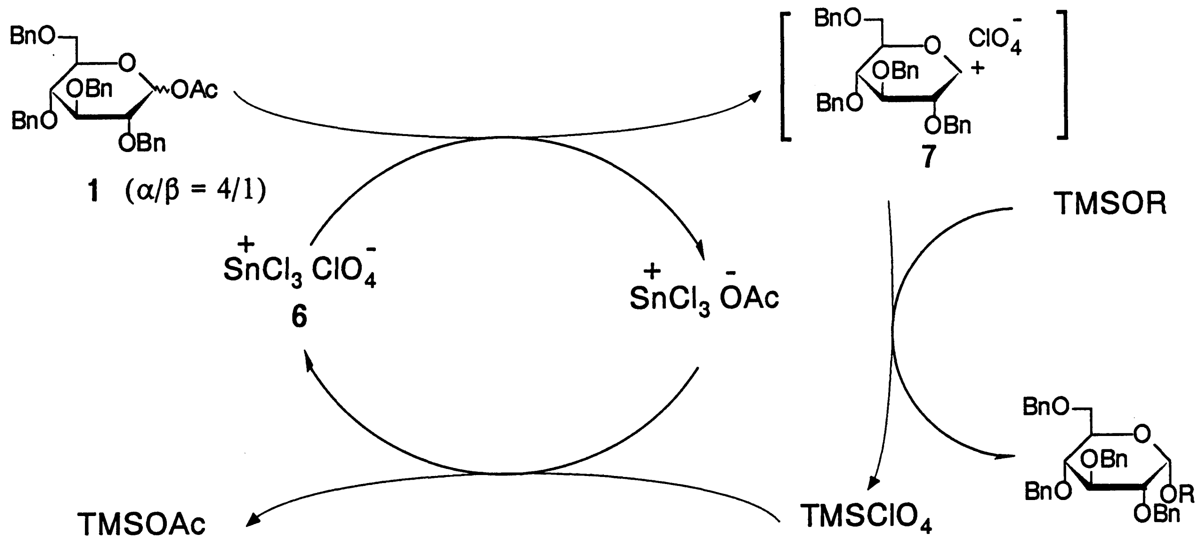
A typical experimental procedure is as follows; a toluene solution of 0.5 M tin(IV) chloride (0.03 ml) was added to silver perchlorate (0.015 mmol) suspended in ether (3 ml) at room temperature, and the mixture was shielded from a light and stirred for 1 h. To this mixture was added an ethereal solution (3 ml) of 1 (0.3 mmol) and 3 (0.36 mmol) at 0 °C. After stirring the mixture for 24 h, aqueous sodium hydrogen carbonate was added. Usual work up and separation by TLC afforded 2 (92.2%) and β-anomer (2.9%).

The present reaction is assumed to proceed via the S_N1 type intermediate (7) as shown in the following catalytic cycle. Tin(IV) species (6), generated from tin(IV) chloride and silver perchlorate, activates the anomeric acetoxy group of 1-O-acetyl glucose to form the intermediate salt (7) stabilized by perchlorate ion. This bulky counter anion blocks β-side of the anomeric center and silyl alkoxides attack from α-side predominantly. The produced trichlorotin acetate and trimethylsilyl perchlorate formed along with the desired α-glucoside regenerated the catalyst.

Thus, the catalytic amount of tin(IV) species, easily prepared in situ from tin(IV) chloride and silver perchlorate, realizes the highly stereoselective glycosylation reaction between a simple glycosyl donner, 1-O-acetyl glucose, and silyl alkoxides. Further investigations to develop glycosylation of other sugars by using this tin(IV) chloride-silver perchlorate catalyst system are now in progress.



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