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Stereoselective 1,2-cis Glycosylation Reaction of 1-O-Acetylribose with Silylated Nucleophiles by the Promotion of a New Catalyst System

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1,2-cis-Ribofuranosides are stereoselectively prepared in high yields by the reaction of 1-O-acetyl-β-D-ribose with silylated nucleophiles by the promotion of a new catalyst system, the combined use of a catalytic amount of tin(IV) chloride and tin(II) triflate with a stoichiometric amount of lithium perchlorate.

Development of stereoselective glycosylation reaction is one of the most important tasks in carbohydrate chemistry.$^{1)}$ Though Königs-Knorr method and its modifications are well established, requirement of more than a stoichiometric amonut of heavy metals and unstability of starting halo sugars still remain as severe problems.$^{2)}$ We have already reported that, in the presence of trityl perchlorate, 1-O-bromoacetyl-β-D-glucose or 1-O-acetyl-β-D-ribose reacts with alcohols to afford the corresponding α-glycosides preferentially.$^{3)}$ In this reaction, α-glucosides are obtained with high diastereoselectivities, however, α-selectivities of ribosides are moderate as frequently observed in the treatment of furanoside series. In order to develop more convenient method for the preparation of 1,2-cis-ribosides, continued efforts have been made to find a new catalyst system which effectively promotes 1,2-cis glycosylation reaction by the catalytic use.

Recently we have found that combined use of a neutral molecule (trityl chloride or trimethylsilyl chloride)$^{4)}$ or a Lewis acid$^{5)}$ and tin(II) compound realizes high efficiency in several reactions, such as aldol reaction of acetals or aldehydes with silyl enol ethers, or the Michael reaction of α,β-unsaturated ketones with silyl enol ethers, etc. From this point of view, we expected to apply this catalyst system to the stereoselective glycosylation reaction. In this communication, we would like to describe a convenient method for the preparation of 1,2-cis-ribofuranosides by the use of a new catalyst system, the combined use of a catalytic amount of tin(IV) chloride and tin(II) triflate with a stoichiometric amount of lithium perchlorate.

In the first place, O-glycosylation reaction of 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose with 3β-cholestanyl trimethylsilyl ether was chosen as a model, and several reaction parameters such as combination of Lewis acids, amounts of the catalyst, solvents, and temperature, etc. were examined. Though neither tin(IV) chloride,[6] tin(II) triflate, nor lithium perchlorate was effective in this reaction, remarkable improvement of yield was observed when the reaction was carried out in the coexistence of a catalytic amount of tin(IV) chloride, tin(II) triflate, and a stoichiometric amount of lithium perchlorate (Table 1). The effect of various solvents on yields and stereoselectivity was shown in Table 2. When the reaction was carried out in dichloromethane, dichloroethane, or toluene, the diastereomer ratios were dramatically improved, and α-anomer was stereoselectively obtained. Concerning the reaction temperature, the best stereoselectivity was obtained at -23 °C. The reaction underwent with lower stereoselectivity at 0 °C, whereas both of the reaction rate and stereoselectivity were decreased at -45 °C.

Several examples of the present glycosylation reaction are demonstrated in Table 3. In every case, α-ribofuranosides are prepared in good yields with high -selectivities. When silyl enol ethers or allyltrimethylsilane are employed as nucleophile, α-C-ribofuranosides are obtained with excellent diastereoselectivities. α-Selectivity decreases when trimethylsilyl cyanide is used, while

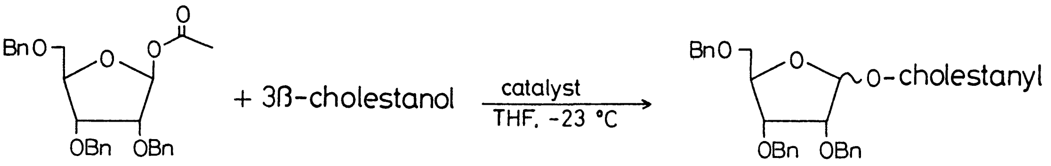


Table 1. Effect of catalyst

Catalyst	Yield/%	α / β
$SnCl_4$(30 mol%)	0	-
$Sn(OTf)_2$(30 mol%)	0	-
$SnCl_4$(30 mol%)+$LiClO_4$(100 mol%)	0	-
$Sn(OTf)_2$(30 mol%)+$LiClO_4$(100 mol%)	trace	-
$SnCl_4$+$Sn(OTf)_2$(30 mol%)	6	38/64
$SnCl_4$+$Sn(OTf)_2$(20 mol%)+$LiClO_4$(100 mol%)	95	35/65

Table 2. Effect of solvent

Solvent	Yield/%	α / β
THF	95	35/65
DME	69	41/59
Toluene	69	88/12
CH_2Cl_2	74	90/10
CH_2ClCH_2Cl	66	90/10

Catalyst: $SnCl_4$+$Sn(OTf)_2$(30 mol%)+$LiClO_4$(100 mol%)

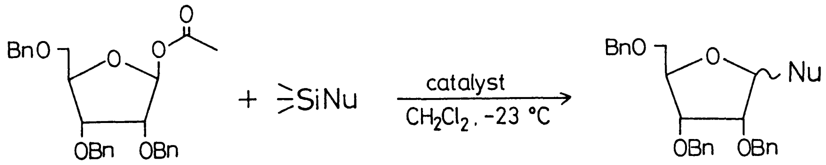
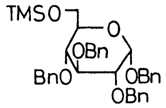
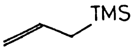
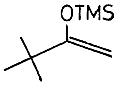
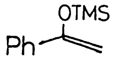


Table 3. Synthesis of α-ribofuranosides

TMSNu (equiv.)	Catalyst	Time/h	Yield/%	α / β
3β-cholestanol(1.2)	A	5	86	90/10
n-$C_{18}H_{38}$OTMS (1.2)	A	5	71	92/8
 (1.2)	B	21	66	100/ 0
 (3.0)	A	3	62	100/ 0
	B	3	86	100/ 0
	C	3	64	100/ 0
 (3.0)	A	2	81	100/ 0
 (3.0)	B	3	91	100/ 0
TMSCN (3.0)	B	4	75	70/30
$TMSN_3$ (3.0)	B	5	89	88/12

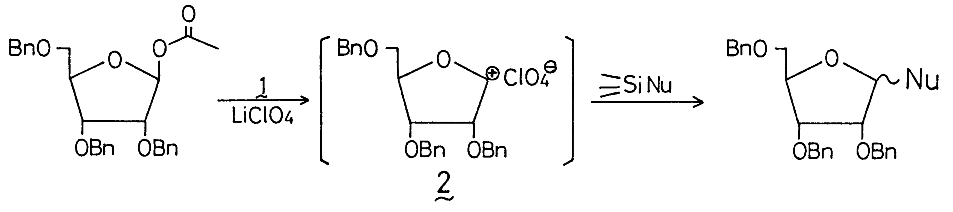
Catalyst A: $SnCl_4$+Sn(OTf)$_2$(20 mol%)+$LiClO_4$(100 mol%)
B: $SnCl_4$+Sn(OTf)$_2$(10 mol%)+$LiClO_4$(100 mol%)+$NaIO_4$(10 mol%)
C: $SnCl_4$+Sn(OTf)$_2$(10 mol%)+$LiClO_4$(100 mol%)

α-anomer is obtained with good diastereoselectivities by the reaction with trimethylsilyl azide.

A typical experimental procedure is as follows; a 0.5 M tin(IV) chloride solution of dichloromethane (0.09 ml) was added to tin(II) triflate (0.05 mmol) and lithium perchlorate (0.23 mmol) suspended in dichloromethane (2 ml) at room temperature, and the mixture was stirred for 1 h. To this mixture was added a dichloromethane solution (2 ml) of 1-O-acetyl-2,3,5-tri-O-benzyl-β-D-ribofuranose (0.23 mmol) and 3β-cholestanyl trimethylsilyl ether (0.28 mmol) at -23 °C. After the mixture was allowed to stand for 21 h, aqueous sodium hydrogen carbonate was added. Usual work up and separation by TLC afforded 3β-cholestanyl 2,3,5-tri-O-benzyl-α-D-ribofuranoside (77.4%) and β-anomer (8.6%).

At present, we postulate the following active catalyst(1) generated from the catalyst system, plays an important role on the present reaction. This cationic tin species activates the anomeric acetoxy group of ribose derivative to form an

$Cl_3\overset{\oplus}{Sn}\ Cl\overset{\ominus}{Sn}(OTf)_2$ **1**



intermediate salt(2), which would be stabilized by the coexisted stannate anion. This large counter anion blocks β-side of the anomeric center to make the attack of silylated nucleophiles from α-side. In some cases, addition of a catalytic amount of sodium periodate improves yield. It is a quite interestring observation that additional sodium periodate accelerates the reaction, however, the behavior of the periodate is not clear at this stage. Further investigations concerning clarification of the structure of this new catalyst and utilization to the new synthetic reactions are now in progress.

References

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