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Stereoselective Synthesis of 2-Amino-2-deoxy-β-D-glucopyranosides and Galactopyranosides by Using a Catalytic Amount of Tin(II) Trifluoromethanesulfonate

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In the presence of a catalytic amount of tin(II) trifluoromethanesulfonate, various 2-amino-2-deoxy-β-D-glucopyranosides or galactopyranosides are stereoselectively synthesized in good yields from 1,3,4,6-tetra-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxy carbonylamino)-β-D-glucopyranose or galactopyranose and alkyl trimethylsilyl ethers, respectively.

2-Acetamido-2-deoxy-β-D-glycosides widely exist as important fragments of peptidoglycans, glycoproteins, mucopolysaccharides, and blood group determinants. For the preparation of these compounds, it is especially important to obtain the desired aminoglycosides in high yields with high stereoselectivities. To achieve this goal, a number of glycosylation reactions using D-glucosamine derivatives have been reported.[1] However, there are some problems such as instability of the glycosyl donners, poor yields of the glycosides, difficulty of deprotection of the amino function, toxic character of the promoters, and necessity of several steps to obtain the desired glycosides. In addition, more than stoichiometric amounts of promoters are required for the completion of the desired glycosylations, and there are few examples to obtain the β-aminoglycosides by using a catalytic amount of promoter. Based on the above results, the development of a useful method for the preparation of β-aminoglycosides by a catalytic process under mild conditions was studied.

Recently, Shiba *et al.* have reported an efficient method for the preparation of β(1→6) glucosamine disaccharides by employing 2,2,2-trichloroethoxycarbonyl (Troc) group[2] for the protection of amino functional group.[1e] The Troc group has several advantageous points as follows; (1) the formation of β-glycosides with the neighboring effect (2) the prevention of the undesired by-products caused by an oxazoline formation (3) the easiness of removal, compared with the other protective groups.[3] These informations led us to study on the catalytic glycosylation reaction starting from 2-Troc-amino sugars and alkyl trimethylsilyl ethers using an active acidic promoter.

In the first place, glycosylation reaction of 1,3,4,6-tetra-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose (**1**)[4] with cyclohexyl trimethylsilyl ether was tried by using several acidic catalysts. We have already reported a useful glycosylation reaction starting from 1-O-acetyl-2,3,4,6-tetra-O-benzyl-D-glucopyranose and alkyl trimethylsilyl ethers using a catalytic amount of active acidic species generated from $SnCl_4$ and $AgClO_4$.[5] When this catalyst was employed in the present glycosylation reaction of **1**, the corresponding β-glucoside (**2**) was predominantly obtained in 88% yield, however, a small amount of undesired α-glucoside was also isolated (8%). It may probably be caused by rapid anomerization of the initially

formed β-anomer to α-anomer under the reaction conditions.

Based on the above results, several other weak Lewis acids were screened by taking the above mentioned reaction of 1 and cyclohexyl trimethylsilyl ether as a model (see Table 1).

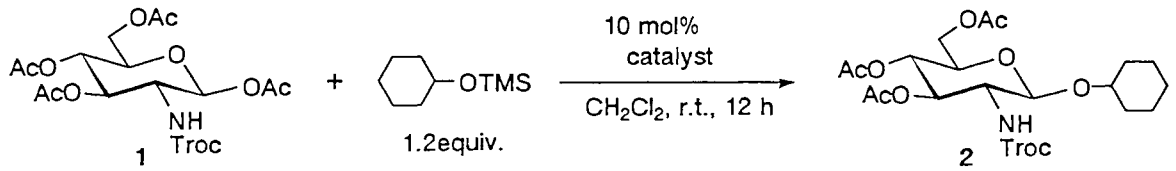


Table 1. Effect of catalysts

Entry	Catalyst (10 mol%)	Yield / % [a]
1 [b]	$SnCl_3(ClO_4)$	88
2	$SnCl_3(OTf)$	97
3	$Sn(OTf)_2$	97
4	$Zn(OTf)_2$	N.R.
5	TrOTf	94

a) Isolated yield. b) Reaction time: 20 min.

It was found that the desired glucoside was obtained in high yield when tin(II) trifluoromethanesulfonate ($Sn(OTf)_2$) or trichlorotin trifluoromethanesulfonate ($SnCl_3(OTf)$), generated in situ from tin(IV) chloride ($SnCl_4$) and silver trifluoromethanesulfonate, was employed as a catalyst.[6] Of the above two catalysts, $Sn(OTf)_2$ has advantages over $SnCl_3(OTf)$ in its preparation,[7] handling, and keeping. Furthermore, after screening various solvents, the use of dichloromethane as a solvent gave the best result (see Table 2).

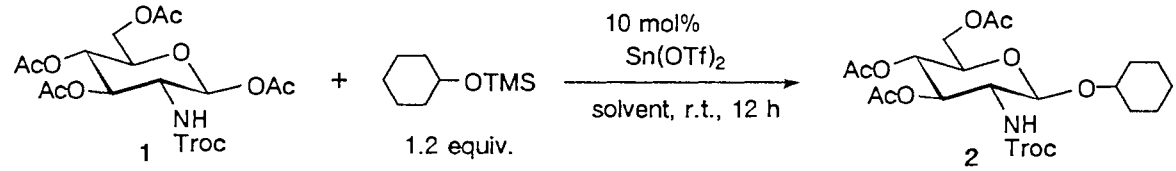


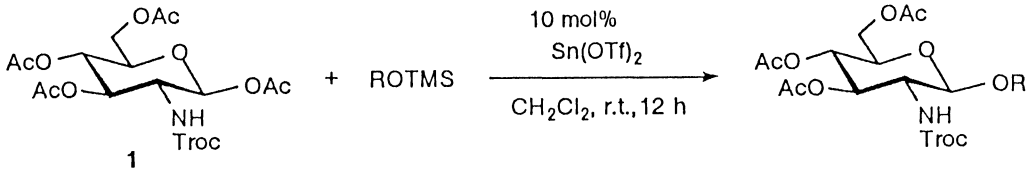
Table 2. Effect of solvents

Entry	Solvents	Yield / % [a]
1	CH_2Cl_2	97
2	Toluene	96
3	CH_3CN	64
4	CH_3NO_2	85

a) Isolated yield.

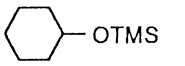
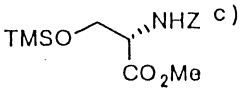
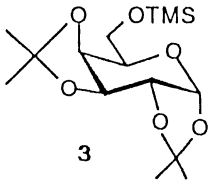
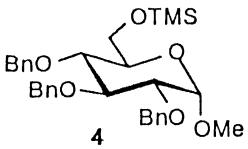
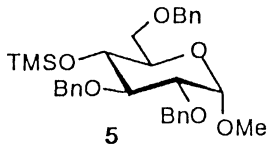
Several examples of the present glycosylation reaction are demonstrated in Table 3. In every case including sterically hindered alkyl trimethylsilyl ethers such as methyl 2,3,6-tri-O-benzyl-4-O-trimethylsilyl-α-D-glucopyranoside (5), the desired β-glucosides are prepared in high yields.[8] The reaction with alkyl trimethylsilyl ethers proceeded very sluggishly under the present reaction conditions when the α-anomer of 1 was used.

Next, the above procedure was further applied to the glycosylation reaction of 1,3,4,6-tetra-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-galactopyranose (**6**) with cyclohexyl trimethylsilyl ether. As a result, the corresponding β-galactoside was also obtained in high yield. Several examples of the present glycosylation reaction of **6** with alkyl trimethylsilyl ethers including 1,2,3,4-di-O-isopropylidene-α-D-galactopyranose (**3**), methyl 2,3,4-tri-O-benzyl-6-O-trimethylsilyl-α-D-glucopyranoside (**4**), and methyl 2,3,6-tri-O-benzyl-4-O-trimethylsilyl-α-D-glucopyranoside (**5**) are summarized in Table 4.



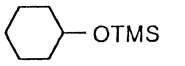
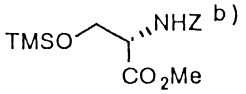
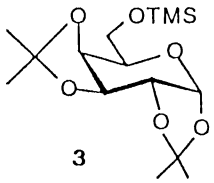
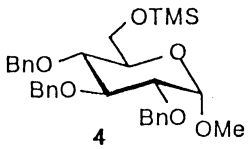
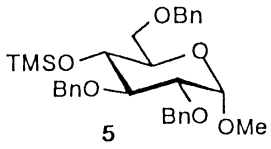
Troc = 2,2,2-trichloroethoxycarbonyl

Table 3. Synthesis of β-aminoglucosides

Entry	ROTMS (1.2 equiv.)	Yield / % [a]
1		97
2 [b]		92
3		96
4	3β-CholestanylOTMS	97
5		93
6		95
7 [d]		82

a) Isolated yield. b) 5 mol% of catalyst was used. c) Z = benzyloxycarbonyl. d) MS 5A was added.

Table 4. Synthesis of β-aminogalactosides

Entry	ROTMS (1.2 equiv.)	Yield / % [a]
1		97
2		98
3	3β-CholestanylOTMS	98
4		94
5		>99
6		80

a) Isolated yield. b) Z = benzyloxycarbonyl.

A typical experimental procedure for the preparation of cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranoside is as follows; $Sn(OTf)_2$ was dried at 100 °C under reduced pressure for 1 h prior to use. To a stirred suspension of $Sn(OTf)_2$ (0.015 mmol) in dichloromethane (3 ml) was added a solution of 1,3,4,6-tetra-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbonylamino)-β-D-glucopyranose (**1**; 0.15 mmol) and cyclohexyl trimethylsilyl ether (0.18 mmol) at room temperature. After stirring the mixture for 12 h, aqueous sodium hydrogen carbonate was added. Usual work up and separation by column chromatography on silica gel (eluent: ethyl acetate/hexane = 1/3) afforded the desired β-glucoside (97%) along with a trace amount of α-glucoside.

Thus, a convenient $Sn(OTf)_2$ catalyzed glycosylation method for the preparation of 2-amino-2-deoxy-β-D-glucopyranosides and galactopyranosides was established.

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References

1) a) M. Kiso and L. Anderson, *Carbohydr. Res.*, **136**, 309 (1985); b) H. Paulsen, D. Hadamczyk, W. Kutschker, and A. Bunsh, *Justus Liebigs Ann. Chem.*, **1985**, 129; c) Y. Ito, M. Sugimoto, S. Sato, and T. Ogawa, *Tetrahedron Lett.*, **27**, 4753 (1986); d) P. Boullanger, J. Banoub, and G. Descotes, *Can. J. Chem.*, **65**, 1343 (1987); e) M. Imoto, H. Yoshimura, T. Shimamoto, N. Sakaguchi, S. Kusumoto, and T. Shiba, *Bull. Chem. Soc. Jpn.*, **60**, 2205 (1987); f) T. Inazu and T. Yamanoi, *Chem. Lett.*, **1989**, 69; g) D. R. Mootoo and B. Fraser-Reid, *Tetrahedron Lett.*, **30**, 2363 (1989); h) K. Higashi, K. Nakayama, T. Soga, E. Shioya, K. Uoto, and T. Kusama, *Chem. Pharm. Bull.*, **38**, 3280 (1990); i) G. H. Veeneman and S. H. van Boom, *Tetrahedron Lett.*, **31**, 1331 (1990).

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3) H.-P. Wessel, T. Inversen, and D. R. Bundle, *Carbohydr. Res.*, **130**, 5 (1984).

4) Glucopyranose **1** was prepared in the similar manner to that reported by ref. 1d).

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6) Various β-aminoglycosides are synthesized in moderate yields starting from 3,4,6-tri-O-actyl-2-acetamide-2-deoxy-α-D-glucopyranosyl chloride and alcohols by the use of stoichiometric amounts of $Sn(OTf)_2$ and 1,1,3,3-tetramethyl urea. A. Lubineau, J. Le Gallic, and A. Malleron, *Tetrahedron Lett.*, **28**, 5041 (1987).

7) R. J. Batchelor, J. N. R. Ruddick, J. R. Sams, and F. Aubke, *Inorg. Chem.*, **16**, 1414 (1977); T. Mukaiyama, N. Iwasawa, R. W. Stevens, and T. Haga, *Tetrahedron*, **40**, 1381 (1984).

8) In every case, the corresponding α-glucosides were obtained only in less than 2 %.

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