CHEMISTRY LETTERS, pp. 2105-2108, 1992. © 1992 The Chemical Society of Japan

A Highly Stereoselective Synthesis of β-Glucosides from Pentaacylglucopyranose and Alkyl Silyl Ether by the Use of a Catalytic Amount of Active Species Generated from Methyltrichlorosilane and Silver Perchlorate

Teruaki MUKAIYAMA, Manabu KATSURADA, and Yousuke IIDA
Department of Applied Chemistry, Faculty of Science,
Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo 162

An efficient catalytic β-glycosylation reaction starting from pentaacylglucopyranose and alkyl silyl ether was performed using an active species generated from $MeSiCl_3$ and $AgClO_4$. 1-O-Acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose stereoselectively reacted with alkyl silyl ethers with the assistance of neighboring effect to give the corresponding β-glucosides in high yields.

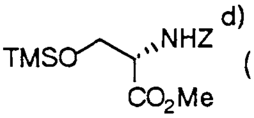
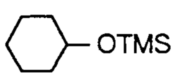
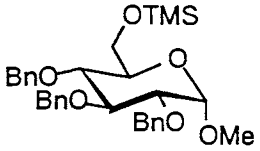
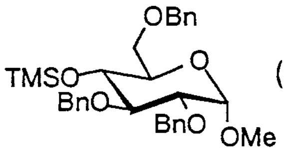
β-Glycosylation reaction of glucose was well-established by the Königs-Knorr reaction[1)] forming the desired β-glucosides in satisfactory yield and stereoselectivity. However, there still remain the following important problems; i.e. 1) a starting material, glycosyl bromide or glycosyl chloride, is often unstable and difficult to handle, 2) more than one equimolar amount of heavy metal activators, such as silver salts or mercury salts, are required, 3) because of the formation of orthoesters, the yields of glucosides are sometimes low.

Recently, a useful α-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 species generated from $SnCl_4$ and $AgClO_4$ was reported from our laboratory.[2)] The method gave the desired α-glucosides in high yields (86%-95%) and good stereoselectivities (α/β=90/10-97/3) by a simple experimental procedure. Now, we would like to describe an efficient method for the catalytic β-glycosylation reaction starting from easily available pentaacylglucopyranose with the assistance of neighboring effect.

Different from the above mentioned α-glycosylation reaction, the yield was up to 40% when pentaacetyl-β-D-glucopyranose was treated with cyclohexyl trimethylsilyl ether in the presence of 20 mol% of the catalyst generated from $SnCl_4$ and $AgClO_4$. After screening several combinations of Lewis acid and $AgClO_4$, the combination of $SiCl_4$ and $AgClO_4$ gave the β-glucoside in moderate yields ($SiCl_4$ + $AgClO_4$: 47%, $SiCl_4$ + $2AgClO_4$: 67%) and the combination of $MeSiCl_3$ and $AgClO_4$ (1 : 2) gave the β-glucoside in 74% yield. Low yielding of the desired β-glucosides in the above experiments may depend on the following reasons. 1) The deactivation of the catalyst is caused by coordination to 6-O-acetyl group and ring oxygen atom. 2) Decomposition and anomerization of the starting material, pentaacetyl-β-D-glucopyranose, take place during the reaction as shown in the following experiments. When pentaacetyl-β-D-glucopyranose was stirred for 40 h in the absence of a nucleophile under the reaction conditions, only 41% of pentaacetyl glucopyranose was isolated with α-configuration. Further, when the produced β-glucoside, cyclohexyl β-D-glucopyranoside, was kept stirring for 48 h under the reaction conditions, 74% of cyclohexyl D-glucopyranoside was recovered with anomeric ratio (α/β) of 87/13. 3) Of two isomeric starting materials, pentaacetyl-α-D-glucopyranose did not smoothly react under the present reaction conditions, while both α- and β-anomers reacted smoothly in the previously reported α-glycosylation reaction of 1-O-acetyl-2,3,4,6-tetra-O-benzyl-D-glucopyranose. These results indicated that pentaacetylglucopyranose is much less reactive compared with 1-O-acetyl-tetra-O-benzyl-D-glucopyranose and only pentaacetyl-β-D-glucopyranose could react with alkyl silyl ether under the reaction conditions owing to its neighboring effect. Thus 1,2-trans configulation of the starting pentaacylated glucose is crucial for the present β-glycosylation reaction.

Based on the above observations, the use of pivaloyl derivative3) with β-configulation instead of pentaacetylglucopyranose was tried. It was expected then that the unfavorable coordination may be prevented by O-pivaloyl group and eventually to enhance the activation of 1-O acetyl group. Actually 1-O-acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose4) gave the desired glucosylated product in high yield with high stereoselectivity as shown in Table 1. For example, disaccharide such as methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-pivaloyl-

Table 1. Synthesis of β-Glucosides a)

Entry	ROTMS		Time/h	Yield/%	α/β
1	MeOTMS	(1.2 equiv.)	15.5	93	2/98 b)
2		(1.2 equiv.)	36	85	>1/99 b)
3 e)		(1.2 equiv.)	20	89	>1/99 b)
4		(1.5 equiv.)	4	91	2/98 c)
5 f)		(1.5 equiv.)	20	69	10/90 c)

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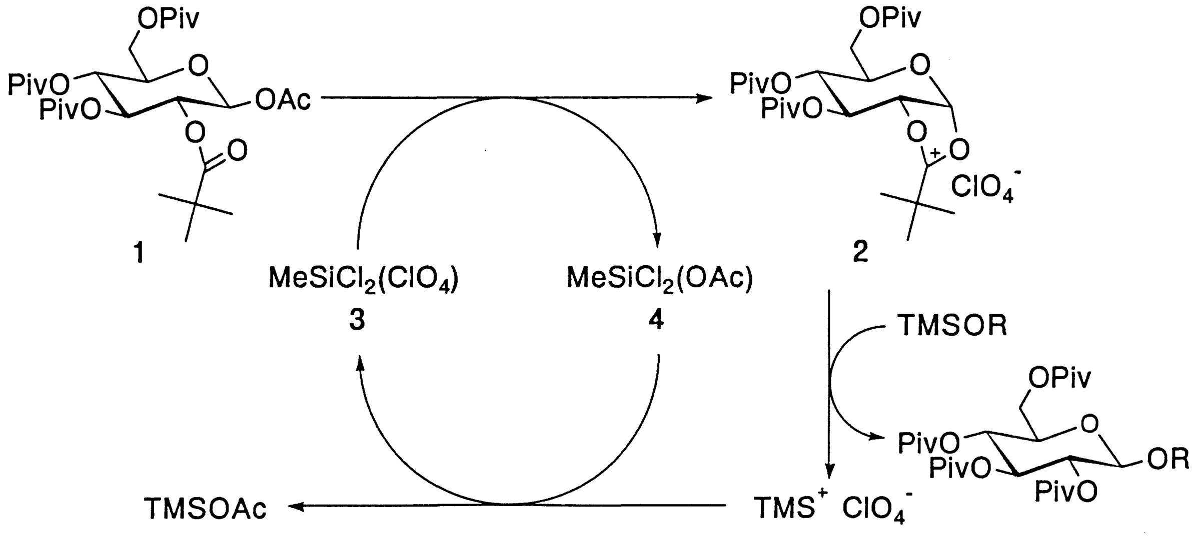
a) The reaction was carried out at 0 °C in CH_2Cl_2 using 10 mol% of catalyst generated from $MeSiCl_3$ and $AgClO_4$. b) Determined by ^1H NMR (270 MHz). c) Determined by HPLC analysis.5) d) Z=benzyloxycarbonyl. e) The reaction was carried out at room temperature in CH_3CN. In this case, the yield and selectivity were better in CH_3CN than those in CH_2Cl_2. f) 2.5 mol% of catalyst was used.

β-D-glucopyranosyl)-α-D-glucopyranoside was obtained in 91% yield (α/β=2/98) when methyl 2,3,4-tri-O-benzyl-6-O-(trimethylsilyl)-α-D-glucopyranoside was employed as an alkyl silyl ether. On the other hand, sterically hindered alkyl silyl ether, such as methyl 2,3,6-tri-O-benzyl-4-O-(trimethylsilyl)-α-D-glucopyranoside, reacted slowly, and the yields of glucoside were relatively low (60-70%) since the desilylation of the silylated nucleophile took place at the same time. In the case of tert-butyl trimethylsilyl ether, no glucoside was obtained at all.

A typical experimental procedure is as follows; 0.5 mol dm^{-3} solution of $MeSiCl_3$ in toluene (0.03 ml) was added to $AgClO_4$ (0.015 mmol) suspended in CH_2Cl_2 (2.5 ml) at room temperature and stirred for 1 h in the dark. To this mixture was added a solution of 1-O-acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose (0.15 mmol) and methyl 2,3,4-tri-O-benzyl-6-O-trimethylsilyl-α-D-glucopyranoside (0.225 mmol) in CH_2Cl_2 (2.5 ml) at 0 °C. After stirring for 4 h, to the mixture was added aqueous sodium hydrogencarbonate. Usual work up and isolation by TLC afforded the corresponding disaccharide in 91% yield (α/β=2/98, determined by HPLC analysis[5]).

The present reaction is assumed to proceed via dioxocarbenium ion intermediate **2** as shown in the following catalytic cycle (Scheme 1). Silicon species **3**, generated from $MeSiCl_3$ and $AgClO_4$, activates the anomeric acetoxy group of 1-O-acetyl-2,3,4,6-tetra-O-pivaloylglucopyranose **1** with the assistance of the neighboring effect of 2-O-pivaloyl group to form the intermediate **2** stabilized by perchlorate anion, which in turn reacts smoothly with alkyl silyl ethers to afford the desired β-glucosides. A small amount of α-anomer was also isolated, which might have been produced by an anomerization of initially formed β-anomer under the present reaction conditions.



Scheme 1.

Thus, the highly stereoselctive β-glycosylation reaction between simple glycosyl donor, 1-O-acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose, and alkyl silyl ethers is effectively promoted by using the catalytic amount of active silicon species, easily prepared in situ from $MeSiCl_3$ and $AgClO_4$.

References

1) Reviews: G. Wuff and G. Rohle, *Angew. Chem., Int. Ed. Engl.*, **13**, 157 (1974); H. Paulsen, *ibid.*, **21**, 155 (1982); R. R. Schmidt, *ibid.*, **25**, 212 (1986); H. Kunz, *ibid.*, **26**, 294 (1987).

2) T. Mukaiyama, T. Takashima, M. Katsurada, and H. Aizawa, *Chem. Lett.*, **1991**, 533; T. Mukaiyama, M. Katsurada, and T. Takashima, *ibid.*, **1991**, 985.

3) H. Kunz and A. Harreus, *Liebigs Ann. Chem.*, **1982**, 41; H. Kunz and A. Harreus, *ibid.*, **1986**, 717.

4) Preparation of 1-O-acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose was as follows; pentapivaloyl-D-glucopyranose, obtained by treatment of D-(+)-glucose with pivaloyl chloride in pyridine at room temperature, was treated with HBr (30% in AcOH) in CH_2Cl_2 at room temperature to afford 2,3,4,6-tetra-O-pivaloyl-D-glucopyranosyl bromide. Successive treatment of the product with $Hg(OAc)_2$ in AcOH at room temperature formed 1-O-acetyl-2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranose in 90% yield (2 steps). ^{1}H NMR (270 MHz, $CDCl_3$) δ=5.74 (1H, d, $J_{1\text{-}2}$=8.6 Hz, H-1), 5.36 (1H, dd, $J_{2\text{-}3}$=9.6 Hz, $J_{3\text{-}4}$=9.2 Hz, H-3), 5.17 (1H, dd, $J_{3\text{-}4}$=9.2 Hz, $J_{4\text{-}5}$=9.9 Hz, H-4), 5.16 (1H, dd, $J_{1\text{-}2}$=8.6 Hz, $J_{2\text{-}3}$=9.6 Hz, H-2), 4.19 (1H, dd, $J_{6\text{-}6'}$=13 Hz, $J_{5\text{-}6}$=2.0 Hz, H-6), 4.11 (1H, dd, $J_{6\text{-}6'}$=13 Hz, $J_{5\text{-}6'}$=5.0 Hz, H-6'), 3.87 (1H, ddd, $J_{4\text{-}5}$=9.9 Hz, $J_{5\text{-}6}$=2.0 Hz, $J_{5\text{-}6'}$=5.0 Hz, H-5), 2.08 (3H, s, acetyl), 1.22 (9H, s, pivaloyl), 1.15 (9H, s, pivaloyl), 1.13 (9H, s, pivaloyl), 1.12 (9H, s, pivaloyl); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ=178.0, 177.0, 176.5, 176.4, 168.8, 91.88, 73.20, 72.09, 70.02, 67.37, 61.42, 38.87, 38.76, 38.72, 27.12, 27.06, 27.03, 26.95, 26.70, 26.52, 20.65; IR (KBr, cm^{-1}) 1739; MS (CI, NH_3) 576 (M^++18, +NH_4^+); Mp 157.0-157.2 °C; $[\alpha]_D^{26}$ +13.1° (c 1.00, $CHCl_3$). Found: C, 59.9; H, 8.3%. Calcd for $C_{28}H_{46}O_{11}$: C, 60.2; H, 8.3%.

5) HPLC was carried out with Hitachi intelligent pump L-6200 and UV detector L-4000 with a Shodex SIL-5B column [4.6 mm x 250 mm; solvent: hexane/ethyl acetate=4/1; flow rate: 0.8 ml min^{-1}; detection: UV at 254 nm].

(Received July 2, 1992)