CHEMISTRY LETTERS, pp. 587-588, 1975. Published by the Chemical Society of Japan

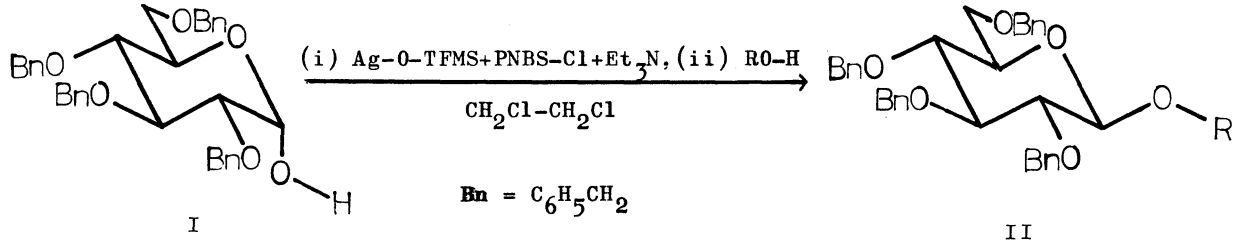
DIRECT GLUCOSIDATION OF 2,3,4,6-TETRA-O-BENZYL-α-D-GLUCOPYRANOSE

Shinkiti KOTO, Yoshio HAMADA, and Shonosuke ZEN
School of Pharmaceutical Sciences, Kitasato University
Shirokane, Minato-ku, Tokyo 108

2,3,4,6-Tetra-O-benzyl-α-D-glucopyranose was condensed with methanol, cyclohexanol, and methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside to give corresponding β-glucosides via activation by a system of silver trifluoromethanesulfonate - p-nitrobenzenesulfonyl chloride - triethylamine.

Research for new methods for the efficient glycosidation is still one of stimulating problems in the synthetic carbohydrate chemistry[1]. Recent efforts for systematic syntheses of some fairly large oligosaccharides[2,3,4] (megalosaccharide[5]) has been prompting us to develop a new facile method for glycosidation employing a blocked 1-O-hydroxyl sugar[6] such as 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (I). The procedure consists of a couple of successive reactions all in a single batch, i.e., (i) activation[7] of the anomeric hydroxyl group and (ii) condensation with an alcohol.

An equimolar mixture (0.3 mmol scale) of I, silver trifluoromethanesulfonate (Ag-O-TFMS), and p-nitrobenzenesulfonyl chloride (PNBS-Cl) in 1,2-dichloroethane was treated by an equimolar triethylamine at -10°C for 30 min. and then a suitable alcohol (1.0 ∿ 1.5 eq.) was added to the resulting mixture, which was further stirred at 0°C for appropriate durations. After removal of silver chloride, treatment by anionic resin, and chromatography over silica gel, benzylated glucosides (II) were obtained in reasonable yields[8].



I (TBG) II

Fig. 1

Of pilot experiments partly shown in Table 1 using methanol as an alcohol, the run with Ag-O-TFMS and PNBS-Cl was best. The activated form of I in the runs 1 ∿ 5 is to be p-nitrobenzenesulfonate, because methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside gave corresponding 6-O-p-nitrobenzenesulfonate[9] by the same reagent in the reaction (i) in Fig. 1. In this sence, the method presented here is regarded as a variation of the method from the glycosyl sulfonate[10,11] but it saves a couple of steps, p-nitrobenzoylation and successive bromination. Although no good evidence has yet been available, it could not be said as simply as the activating compound in the case of Ag-O-TFMS was the mixed anhydride[12,13] or the type of complex with amine[14], because

the reaction (i) without I formed a quasi-homogeneous brownish mixture instead of white precipitations and then the addition of I to this mixture at -10°C brought about precipitations instantly to form the active compound which underwent the reaction (ii) with alcohol.

The use of a system of methanesulfonic anhydride - triethylamine - dichloroethane at 0°C was less efficient (55% by total, α : β ≃ 1 : 1) than that of the system mentioned above. It is to be noted, however, that the ratio of anomers formed depended upon what the anomeric leaving group is.

Table 1 Results of Experiments

Run	Silver salts	Sulfonyl chlorides	(i) Activation Temp. °C	Dur. hr	(ii) Condensation Alcohol	(eq.)	Temp. °C	Dur. hr	Yields %
1	Ag-O-TFMS	PNBS-Cl	-10	0.5	M	(1.5)	0	3	67[1,3]
2	Ag-O-TFMS	PNBS-Cl	-10	0.5	C	(1.5)	0	6	51[1,4]
3	Ag-O-TFMS	PNBS-Cl	-10	0.5	MTBG	(1.0)	0	4	44[1,5]
4	$AgClO_4$	PNBS-Cl	-50	0.5	M	(1.5)	-10	3	49[1]
5	$AgBF_4$	PNBS-Cl	-10	1.5	M	(1.5)	0	3	36[1]
6	Ag-O-Ms	Ms-Cl	-5	1.5	M	(1.5)	0	3	30[2]
7	Ag-O-Ts	Ts-Cl	5	1.0	M	(1.5)	5	3	poor[2]

TFMS- = $-SO_2CF_3$, PNBS- = $-SO_2C_6H_4NO_2(p)$, Ms- = $-SO_2CH_3$, Ts- = $-SO_2C_6H_4CH_3(p)$
M = Methanol, C = Cyclohexanol, MTBG = Methyl 2,3,4-tri-O-benzyl-α-D-glucoside

[1]Yields were measured gravimetrically for crystalline β-anomers. All's have adequate results of elemental analysis and their structure were confirmed by derivations into the corresponding de-O-benzylated compounds. [2]Yields were given by total (α : β ≃ 1 : 1). [3]Mp 74 ∿ 75 °C, $[\alpha]_D^{20}$ +11.1 (c 5.6 $CHCl_3$). [4]Mp 105 ∿ 106 °C, $[\alpha]_D^{20}$ +8.2 (c 1.6, $CHCl_3$). [5]Mp 137 ∿ 138 °C, $[\alpha]_D^{20}$ +19.2 (c 2.9, $CHCl_3$).

References and Notes

1) G.Wulff and G.Röhle, Angew. Chem., 86, 173 (1974)
2) Y.Takiura, S.Honda, T.Endo, and K.Kakehi, Chem. Pharm. Bull., 20, 438 (1972)
3) S.Koto, T.Uchida, and S.Zen, Bull. Chem. Soc. Japan, 46, 2520 (1973)
4) R.Eby and C.Schuerch, Macromol., 7, 397 (1974)
5) E.A.Kabat, 'Carbohydrate in Solution', ed. by H.S.Isbell, Amer. Chem. Soc. 1973, p.309
6) M.Kuhn and A.von Wartburg, Helv. Chim. Acta, 51, 1631 (1968)
7) G.Schuramm, H.Grötch, and W.Pollman, Angew. Chem, 74, 54 (1962)
8) The β-anomer were obtained almost exclusively.
9) Checked by isolation of the sulfonate and determination of its PMR in $CDCl_3$.
10) R.Eby and C.Schuerch, Carbohydrate Res., 34, 79 (1974)
11) T.Machinami and T.Suami, Chem. Lett., 1177 (1974)
12) F.Klages and F.E.Maleki, Ann., 691, 15 (1966)
13) F.Klages, K.Hoheisel, E.Mühlbauer, and F.E.Maleki, Chem. Ber., 96, 2057 (1963)
14) T.Oishi, K.Kamata, S.Kosugi, and Y.Ban, Chem. Comm., 1148 (1972)

(Received March 13, 1975)