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A NOVEL PROCEDURE FOR THE PREPARATION OF 1-OH SUGAR DERIVATIVES USING 2-METHOXYETHYL GLYCOSIDES

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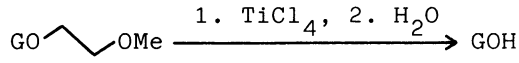
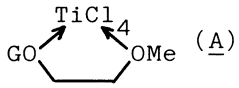
Treatment of benzyl-protected 2-methoxyethyl glycopyranosides with titanium tetrachloride followed by hydrolysis provides a new method for the preparation of the corresponding 1-OH sugar derivatives. The present method is shown to be useful for the preparation of mono-O-acetyl- and mono-O-allyl-tri-O-benzyl-D-glucopyranoses.

Systematic synthesis of oligosaccharides using dehydrative glycosylation[1] requires the preparation of glycosyl donors having a free hydroxyl group at C-1 such as 2,3,4,6-tetra-O-benzyl-D-glucopyranose(1). They are usually prepared via acid-hydrolysis of benzyl-protected methyl glycosides,[2-8] and isomerization of similar derivatives of allyl glycosides and subsequent hydrolysis.[9] We now wish to communicate a novel method for the preparation of 1-OH sugar derivatives, which consists of the treatments of protected 2-methoxyethyl glycopyranosides with $TiCl_4$ in CH_2Cl_2 and subsequently with aq $NaHCO_3$ and a column chromatography on silica gel. $TiCl_4$ seems to coodinate efficiently with 2-methoxyethoxyl group[10] as A



(G denotes the totally protected glycosyl moiety)



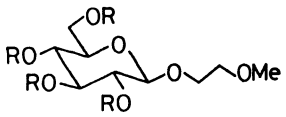
(A)

to produce the glycosyl chloride. Using this method, 1, 2,3,4,6-tetra-O-benzyl-D-galactopyranose(2), -D-mannopyranose(3), 2,3,4-tri-O-benzyl-L-fucopyranose(4), -L-rhamnopyranose(5), -D-xylopyranose(6), and -L-arabinopyranose(7) were prepared.

The present method is especially suitable for the preparation of glycosyl donors protected by an acetyl group and benzyl ones,[1c,11] because it has been difficult to obtain such compounds via acid-hydrolysis of protected methyl glycosides. Using this mild processing, four positional isomers of mono-O-acetyl- and those of mono-O-allyl-tri-O-benzyl-D-glucopyranoses(8-11 and 12-15) were prepared in good yields(Table 1).

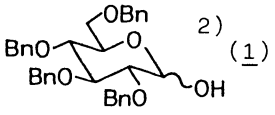
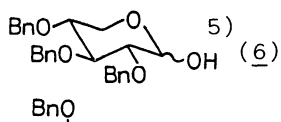
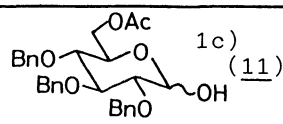
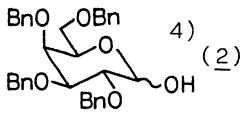
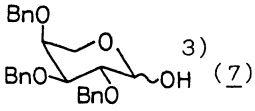
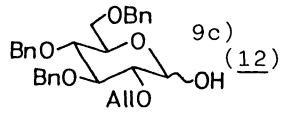
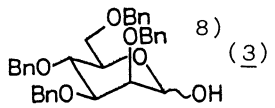
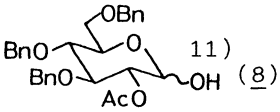
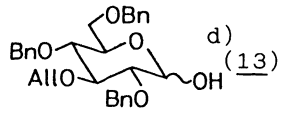
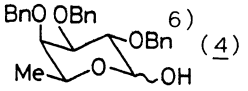
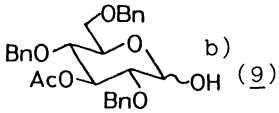
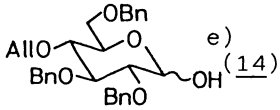
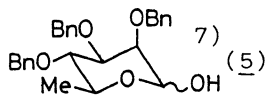
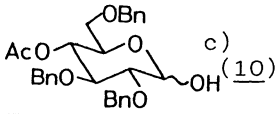
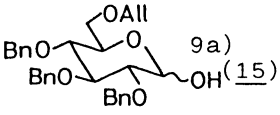
The procedure to remove the 2-methoxyethyl group is as follows: A solution of a totally protected 2-methoxyethyl glycopyranoside(0.1-0.3 mmol) and $TiCl_4$(0.7 equiv.) in CH_2Cl_2(10 ml/mmol-glycoside) was stirred for 5 min at room temperature, vigorously stirred with iced aq $NaHCO_3$, and then extracted with toluene. After evaporation, the residue was adsorbed on a column of silica gel with toluene and kept standing overnight for the complete hydrolysis of the glycosyl chloride initially formed. Elution by toluene-2-butanone system afforded the corresponding 1-OH derivative as the main product.

2-Methoxyethyl 2,3,4,6-tetra-O-benzyl-ß-D-glucopyranoside (16, the precursor of 1) was prepared through the benzylation of the acetate 17[12] with benzyl chloride and KOH. Similarly, 2-methoxyethyl per-O-benzyl-ß-D-galacto-, -ß-L-fuco-, -ß-D-xylo-, and -α-L-arabinopyranosides were prepared. 2-Methoxyethyl per-O-benzyl-α-D-manno- and -α-L-rhamnopyranosides were prepared through acid-catalyzed glycosylation and benzylation. 2-Methoxyethyl 3,4,6-tri-O-benzyl-ß-D-glucopyranoside was obtained by the partial benzylation of the 3,4-dibenzyl ether prepared through benzylation and subsequent detritylation of the 2,6-dityrityl ether of 18. The 2,4,6-tribenzyl ether was obtained in a 42% yield via regioselective benzylation of 17 with benzyl chloride and NaOH at 100°C. The 2,3,6- and the 2,3,4-isomers were derived from 18 via the 4,6-O-benzylidene acetal and the 6-O-trityl ether, respectively. Acetylation and allylation of these tribenzyl ethers afforded the precursors of 8-15.



16 R=$PhCH_2$
17 R=Ac
18 R=H

Table 1. Yields of 1-OH Derivatives from Protected 2-Methoxyethyl Glycosides[a)]

1-OH Derivative	Yield(%)	1-OH Derivative	Yield(%)	1-OH Derivative	Yield(%)
 2) (1)	66	 5) (6)	80	 1c) (11)	76
 4) (2)	74	 3) (7)	71	 9c) (12)	70
 8) (3)	66	 11) (8)	77	 d) (13)	62
 6) (4)	63	 b) (9)	60	 e) (14)	62
 7) (5)	78	 c) (10)	63	 9a) (15)	66

a) All compounds prepared gave correct analyses. b) Mp 124.5-126°C, $[\alpha]_D^{20}$ +42° (c 1.4, $CHCl_3$). c) Mp 118-119°C, $[\alpha]_D^{20}$ +13°(c 0.6, $CHCl_3$). d) Mp 115-116°C, $[\alpha]_D^{20}$ +30°(c 1.0, $CHCl_3$). e) Mp 108-110°C, $[\alpha]_D^{20}$ +35°(c 2.0, $CHCl_3$).

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