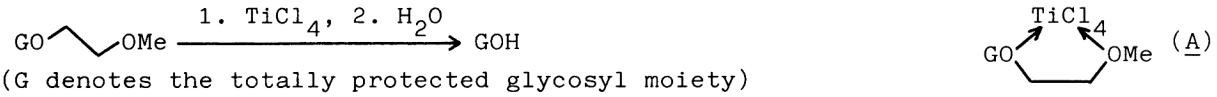
CHEMISTRY LETTERS, pp. 1189-1190, 1983.

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

Naohiko MORISHIMA, Shinkiti KOTO*, Kumi KANEMITSU, and Shonosuke ZEN
School of Pharmaceutical Sciences, Kitasato University,
Shirokane, Minato-ku, Tokyo 108

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 efficienly with 2-methoxyethoxyl group[10] as A



(A)

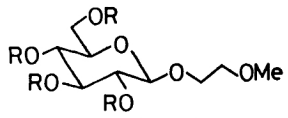
(G denotes the totally protected glycosyl moiety)

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).

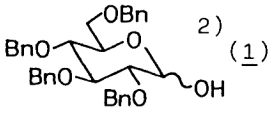
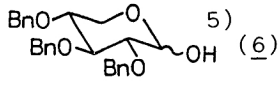
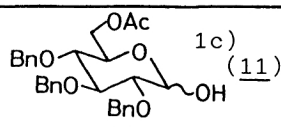
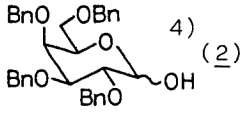
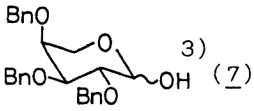
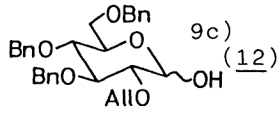
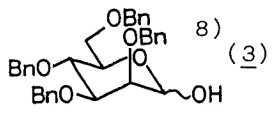
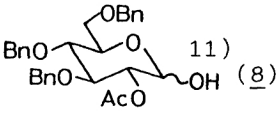
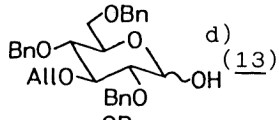
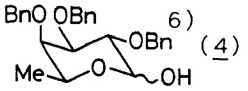
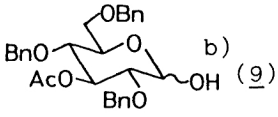
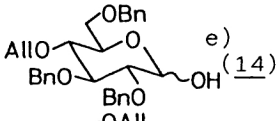
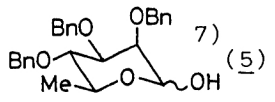
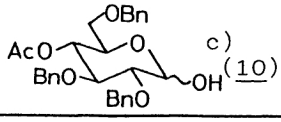
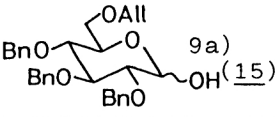
The procedure to remove the 2-methoxyethyl group is as follows: A solution of a totally protected 2-methoxyethyl glycopyranoside(0.1-0.3 mmol) and $TiCl_4$(0.7 equiv.) in CH_2Cl_2(10 ml/mmol-glycoside) was stirred for 5 min at room temperature, vigorously stirred with iced aq $NaHCO_3$, and then extracted 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-ditrityl 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, $CHCl_3$).

References

1) a) N.Morishima, S.Koto, and S.Zen, Chem. Lett., 1982, 1039; b) N.Morishima, S.Koto, M.Uchino, and S.Zen, ibid., 1982, 1183; c) S.Koto, N.Morishima, Y. Kihara, H.Suzuki, S.Kosugi, and S.Zen, Bull. Chem. Soc. Jpn., 56, 188 (1983), and foregoing papers cited therein.
2) O.T.Schumidt, T.Auer, and H.Schmadel, Chem. Ber., 93, 556 (1960).
3) S.Tejima and H.G.Fletcher,Jr., J. Org. Chem., 28, 2999 (1963).
4) P.W.Austin, F.E.Hardy, J.G.Buchanan, and J.Baddiley, J. Chem. Soc., 1964, 1419.
5) S.Tejima, R.K.Ness, R.L.Kaufman, and H.G.Fletcher,Jr., Carbohydr. Res., 7, 485 (1968).
6) M.Dejter-Juszynski and H.M.Flowers, Carbohydr. Res., 18, 219 (1971).
7) J.M.J.Flechet and H.H.Bear, Carbohydr. Res., 42, 369 (1975).
8) S.Koto, N.Morishima, Y.Miyata, and S.Zen, Bull. Chem. Soc. Jpn., 49, 2639 (1976).
9) a) P.A.Gent and R.Gigg, J. Chem. Soc., Perkin Trans. 1, 1974, 1835; b) ibid., 1975, 361; c) Carbohydr. Res., 49, 325 (1976).
10) S.Koto, N.Morishima, R.Kawahara, K.Ishikawa, and S.Zen, Bull. Chem. Soc. Jpn., 55, 1092 (1982).
11) M.A.E.Shaban and R.W.Jeanloz, Carbohydr. Res., 52, 103 (1976).
12) B.Helferich and R.Hiltmann, Justus Liebigs Ann. Chem., 531, 160 (1937).

(Received May 12, 1983)