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DEHYDRATIVE α-GLUCOSYLATION USING A MIXTURE OF p-NITROBENZENESULFONYL CHLORIDE, SILVER TRIFLUOROMETHANESULFONATE, N,N-DIMETHYLACETAMIDE, AND TRIETHYLAMINE

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Stereoselective synthesis of α-linked di- and trisaccharides is performed by the one-stage glucosylation using 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose and a mixture of p-nitrobenzenesulfonyl chloride, silver trifluoromethanesulfonate, N,N-dimethylacetamide, and triethylamine in dichloromethane.

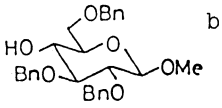
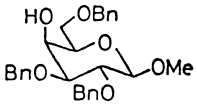
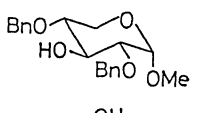
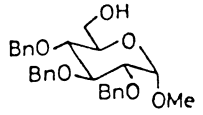
Simplification of glycosylation procedure can be attained by the use of a condensing reagent or reagent mixture which selectively activates the anomeric center of a glycosyl doner such as 2,3,4,6-tetra-O-benzyl-α-D-glucopyranose (1) in the presence of a glycosyl acceptor.[1] Among a number of studies[2] on selective α-glucosylation, the one-stage procedure[1c,d] has rarely been presented. We now wish to communicate a convenient procedure for the α-glucosylation using 1 and a mixture of p-nitrobenzenesulfonyl chloride (NsCl), silver trifluoromethanesulfonate (AgOTf), N,N-dimethylacetamide (DMA), and triethylamine (Et_3N) in dichloromethane.

The general procedure for the glucosylation of the secondary hydroxyl group, denoted as Condition A in Table 1, is as follows: To a mixture of a glycosyl acceptor (0.33 mmol scale), 1 (1.3 equiv.), NsCl (2.5 equiv.), AgOTf (2.5 equiv.), and DMA (2.5 equiv.) in CH_2Cl_2 (1.8 ml), Et_3N (2.5 equiv.) was added at -40°C, at which temperature the mixture was stirred overnight. The mixture was processed[1b] and then chromatographed on silica gel. For the glucosylation of the primary hydroxyl group, an excess amount of DMA (5.0 equiv.) is necessary to result in a sufficient α-selectivity (Condition B in Table 1).

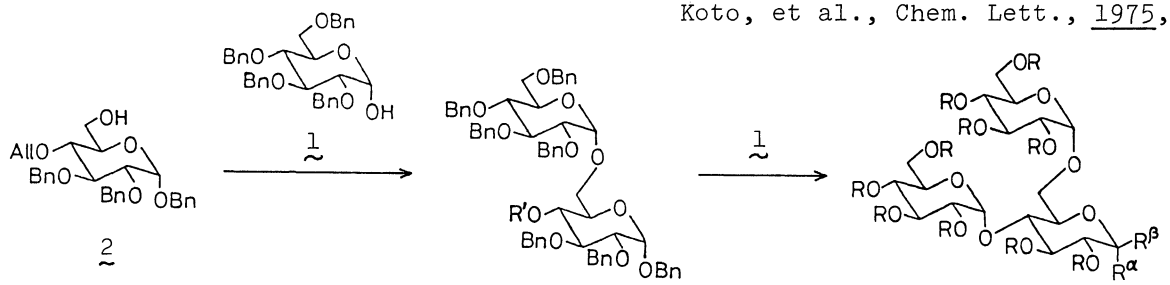
Using this procedure, a new synthesis of a branched trisaccharide, 4,6-di-O-(α-D-glucopyranosyl)-D-glucopyranose (6)[3], was carried out in the following manner: The glucosylation of benzyl 4-O-allyl-2,3-di-O-benzyl-α-D-glucopyranose (2)[4] (0.7 mmol scale) with Condition B gave the isomaltose derivative 3a (51%, $[\alpha]_D^{20}$ +77°(c 1.6, $CHCl_3$), δ($CDCl_3$): 95.2(C-1), 97.8(C-1')) and the gentiobiose one 3b (31%, $[\alpha]_D^{20}$+45°(c 1.0, $CHCl_3$), δ($CDCl_3$): 95.5(C-1), 104.1(C-1')). Deallylation[5] of 3a afforded benzyl 2,3,2',3',4',6'-hexa-O-benzyl-α-D-isomaltoside (4) (90%, $[\alpha]_D^{20}$+64°(c 1.6, $CHCl_3$)). Compound 4 was then glucosylated with Condition A to furnish the totally protected trisaccharide 5 (62%, $[\alpha]_D^{20}$+82°(c 1.7, $CHCl_3$),

δ($CDCl_3$): 94.4(C-1), 96.8(C-1'→4), 97.5(C-1"→6)). Hydrogenolysis of 5 gave 6 (64%, $[\alpha]_D^{20}$+139°(c 0.3, H_2O) [lit.[3] $[\alpha]_D^{22}$+125°(c 0.9, H_2O)], δ(D_2O): 93.2(C-1α), 97.1(C-1β), 101.1(C-1'→4), 99.9(C-1"→6)). All of the compounds thus synthesized gave correct analyses.

Table 1 Results of Disaccharide Syntheses

Glycosyl Acceptor	Condition	Yield[a] %	α:β
 b)	A	86	93:7[e]
 c)	A	87	90:10[f]
 d)	A	87	88:12[g]
	B	88	73:27[h]

a) Based on the glycosyl acceptor charged. b) Mp 72-73°C, $[\alpha]_D^{20}$-17° (c 1.8, $CHCl_3$). c) H.B.Borén, et al. Acta Chem. Scand., 27, 2740 (1973). d) N.Morishima, et al., Bull. Chem. Soc. Jpn., 55, 631 (1982). e) The α-anomer, $[\alpha]_D^{20}$+35°(c 0.8, $CHCl_3$); the β-anomer, mp 99-100°C, $[\alpha]_D^{20}$+22° (c 1.0, $CHCl_3$). f) The α-anomer, $[\alpha]_D^{20}$+61°(c 1.2, $CHCl_3$); the β-anomer, $[\alpha]_D^{20}$+26°(c 1.0, $CHCl_3$). g) The glucosides were identified with those reported before (S.Koto, et al., Bull. Chem. Soc. Jpn., in submission). h) The α-anomer was identified with that reported in Ref. 2d and the β-anomer with that prepared before (S. Koto, et al., Chem. Lett., 1975, 587).



All=allyl, Bn=benzyl

3a: R'=All
4: R'=H

5: R=Bn, R^{α}=OBn, R^{β}=H
6: R=H, R^{α},R^{β}=OH,H

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