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Note

Utilisation of the D-glucopyranosyl group as a non-participating group in stereoselective glycosylation: synthesis of *O*-α-D-glucopyranosyl-(1→2)-*O*-α-D-glucopyranosyl-(1→6)-D-glucose

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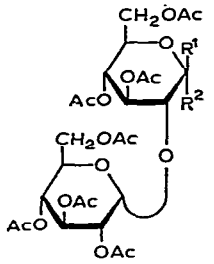
Dextrans[1] are bacterial polysaccharides consisting mainly of (1→6)- in addition to (1→2)-, (1→3)-, and (1→4)-α-D-glucosidic linkages. Several oligosaccharides have been isolated after degradation of dextrans by chemical and enzymic hydrolysis, usually in very small quantities. The chemical synthesis of such oligosaccharides will facilitate their identification and also provide model compounds for enzymic, immunochemical, and spectroscopic studies. However, few syntheses have been accomplished[2,3].

We now report the synthesis of, and ^{13}C-n.m.r. data for, the title trisaccharide (**6**), which has been isolated[4] after degradation of dextran NRRL B1397, and in admixture with *O*-α-D-glucopyranosyl-(1→2)-[*O*-α-D-glucopyranosyl-(1→6)]-D-glucose[5] after degradation of dextran NRRL B1298.

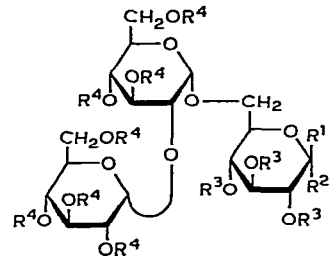
Various methods[6] are available for the stereoselective formation of glycosides having the substituents at positions 1 and 2 in *cis* relationship (1,2-*cis*-glycosides), which utilise glycosylating agents having non-participating groups at position 2. For the synthesis of **6**, the D-glucopyranosyl group was used as a non-participating group[7], since it is also a part of the target compound.

Condensation of hepta-*O*-acetyl-α-kojibiosyl bromide[8] (**1**), under halide ion-catalysed conditions[9], with benzyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (**2**) in dichloromethane gave only low yields[10] of the protected trisaccharide **3**, which is not surprising because of the stabilising effect of the acyl groups upon the C-1–Br bond[11]. When dichloromethane–*N*,*N*-dimethylformamide was used as solvent, formylation of **2** at HO-6 occurred[8].

The β-glycosyl chloride (Helferich[12]) method gave much higher yields of **3**. Thus, **1** was converted into the β-chloride **4** by treatment with tetraethylammonium chloride, and condensed immediately with **2** in a $AgClO_4$–Ag_2CO_3-catalysed reaction



1 R^1 = H, R^2 = Br
4 R^1 = Cl, R^2 = H



3 R^1 = OBzl, R^2 = H, R^3 = Bzl, R^4 = Ac
6α R^1 = R^3 = R^4 = H, R^2 = OH
6β R^1 = OH, R^2 = R^3 = R^4 = H

TABLE I

^{13}C-N.M.R. DATA FOR **3**, **6**, AND MODEL COMPOUNDS[a]

Atom	*Chemical shift (p.p.m.) (CDCl₃, internal Me₄Si)*				*Chemical shift (p.p.m.) (D₂O)*				
	A	**3**	*B*	*C*	**6**[b]		*Isomaltose*[20]		*D*[b]
					α	β	α	β	
C-1	102.9[c]	102.4			92.9	96.8	93.8	97.7	
C-2	82.5	82.5			72.7	75.0	73.3	75.9	
C-3	84.7	84.9			73.7	76.7	75.0	77.7	
C-4	77.8	75.6			70.4	70.4	71.3	71.3	
C-5	75.5	74.9			70.8	75.1	71.3	75.9	
C-6	61.8	67.1			67.1	67.1	67.4	67.4	
1:CH_2	71.4	71.3							
2:CH_2	74.8	74.8							
3:CH_2	75.5	74.6							
4:CH_2	74.8	74.4							
C-1′		94.3[d]	97.7[e]			97.0			
C-2′		78.3	79.3			76.5			
C-3′		71.0	72.2			72.7			
C-4′		69.1	69.4			70.4			
C-5′		67.7	67.5			73.2			
C-6′		61.9	62.5			61.5			
C-1″		95.4[f]		95.2[g]		96.3			98.6
C-2″		70.3		70.4		72.5			72.8
C-3″		71.0		71.0		73.8			74.1
C-4″		68.6		68.9		70.6			70.6
C-5″		68.4		67.8		72.3			72.3
C-6″		62.1		62.1		61.5			61.5

[a]A, benzyl 2,3,4-tri-*O*-benzyl-β-D-glucopyranoside; B, methyl 2,3,4-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranoside; C, benzyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside; D, benzyl α-D-glucopyranoside. [b]Internal 1,4-dioxane (67.3 p.p.m.). [c]$J_{C-1,H-1}$ 158 Hz. [d]$J_{C-1',H-1'}$ 172 Hz. [e]$J_{C-1',H-1'}$ 170 Hz. [f]$J_{C-1'',H-1''}$ 175 Hz. [g]$J_{C-1'',H-1''}$ 173 Hz.

in dichloromethane to give **3** together with $<10\%$ of the corresponding β isomer. Pure **3** was isolated by column chromatography, and subjected to hydrogenolysis and Zemplén deacetylation to give **6**.

The ^{13}C-n.m.r. signals of the "reducing" and "non-reducing" residues in **3** were unambiguously assigned (see Table I) by comparison with those of **2** and benzyl 2,3,4,5-tetra-*O*-acetyl-α-D-glucopyranoside. The assignments of C-1′, C-2′, and C-6′ of the middle D-glucosyl residue are unequivocal, whereas those of C-3′, C-4′, and C-5′ were assisted by the spectrum of methyl 3,4,6-tri-*O*-acetyl-2-*O*-methyl-α-D-glucopyranoside, kindly provided by Dr. A. Lipták. The anomeric configuration of the interglycosidic linkages is proved by the values (172 and 175 Hz, respectively) for $J_{C\text{-}1,H\text{-}1}$. The ^{13}C resonances of **6** were assigned on the basis of published data for α- and β-isomaltose[20], and on that for benzyl α-D-glucopyranoside. The spectrum of **6** indicates an αβ-ratio of ~1:2.2 for the reducing residue.

EXPERIMENTAL

For general methods, see Ref. 8. T.l.c. of **6** was performed on pre-coated cellulose layers (Merck) with detection by aniline hydrogen phthalate[13] at 105°. Natural-abundance, ^{1}H noise-decoupled, ^{13}C Fourier-transform n.m.r. spectra were recorded with a Varian XL-100-FT NMR spectrometer at 25.16 MHz, using 5-mm spinning tubes. Chemical shifts are given relative to that of internal Me_4Si for solutions in $CDCl_3$, and to internal 1,4-dioxane (67.3 p.p.m.) for solutions in D_2O. All measurements were performed at 33°, and $^1J_{C,H}$ coupling constants were determined by the usual gated-decoupling technique.

Benzyl 2,3,4-tri-O-benzyl-6-O-[3,4,6-tri-O-acetyl-2-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-α-D-glucopyranosyl]-β-D-glucopyranoside (**3**). — A solution of hepta-*O*-acetyl-α-kojibiosyl bromide[8] (2.8 g) in MeCN (40 ml) was treated with tetraethylammonium chloride (1.18 g) at room temperature until the optical rotation reached a minimum (~20 min). The mixture was then poured into benzene (200 ml), which was washed with water (5 × 20 ml), dried (Na_2SO_4), and concentrated. The residual syrup crystallised from dry ether to give **4** (2.3 g); the ^{1}H-n.m.r. spectrum of **4**, recorded immediately after isolation, indicated the presence of a small amount of **1**.

Compound **4** (2.15 g) was added immediately to a mixture of **2**[14] (1.763 g), Ag_2CO_3 (0.5 g), $AgClO_4$ (86 mg)[15], Drierite (8 g), and CH_2Cl_2 (40 ml) at 0°. The mixture was then stirred for 2 h at 0°, filtered (Hyflo Supercel), diluted with CH_2Cl_2 (200 ml), washed with water (3 × 30 ml), dried (Na_2SO_4), and concentrated. The residual syrup was eluted from Kieselgel G (200 g) by using benzene–ether (1:3)[16,17], to give **3** as a colourless glass (1.4 g, 37%), R_F 0.46 (Kieselgel; benzene–ether, 1:3), $[\alpha]_D$ +86.5° (*c* 1.5, chloroform).

Anal. Calc. for $C_{60}H_{70}O_{23}$: C, 62.1; H, 6.1. Found: C, 62.3; H, 6.0.

O-α-D-*Glucopyranosyl-(1→2)-O-α-D-glucopyranosyl-(1→6)-D-glucose* (**6**). — A solution of **3** (1.1 g) in EtOH (40 ml) was hydrogenolysed over 10% Pd–C (Fluka, 200 mg) for 24 h at atmospheric pressure and room temperature. The mixture was

diluted with acetone (100 ml), filtered, and concentrated, and the residual, colourless syrup (720 mg, 95%) was triturated with benzene–methanol (3:1), to give 6-*O*-[3,4,6-tri-*O*-acetyl-2-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl)-α-D-glucopyranosyl]-D-glucose (**5**) as an amorphous solid, R_F 0.40 (Kieselgel, benzene–methanol, 3:1).

To a solution of **5** (0.4 g) in MeOH (30 ml) were added catalytic amounts of NaOMe. The solution was left overnight at room temperature, and then treated successively with Amberlite IR-120(H^+) and IR-4B(HO^-) resins, filtered, and concentrated. The resulting, colourless syrup (230 mg, 91%) was eluted[18] from charcoal–Celite 535 (1:1, 5 g) by using a water–ethanol gradient (up to 15% ethanol) to give **6** as a white, amorphous powder, R_F 0.1 (t.l.c., cellulose; acetic acid–ethyl acetate–pyridine–water, 1:7:5:3)[19], $[\alpha]_D$ +150.5° (*c* 0.8, water); lit.[4] $[\alpha]_D$ +144° (water).

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