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Preliminary communication

Synthesis of 2-*O*-α- and -β-L-fucopyranosyl-D-galactose

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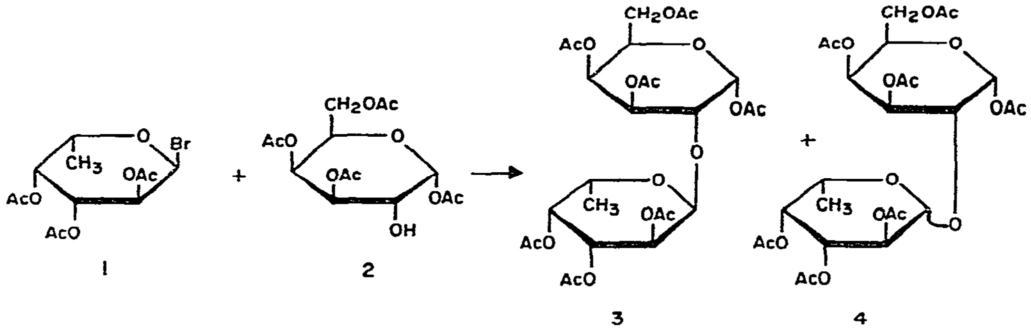
Syntheses of some of the disaccharides containing an α-(1→2)-linkage have been accomplished by the reaction of *O*-acylglycosyl halides with appropriately protected aglycons[1–4]. Such reactions have generally been conducted in the presence of mercuric cyanide in nitromethane[1] or nitromethane–benzene[2,3], or in the presence of mercuric cyanide and mercuric bromide in absolute acetonitrile[4]. However, Koeppen[5] has shown that, under the latter conditions, the condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with 1,3,4,6-tetra-*O*-acetyl-α-D-glucose results in the formation of both the α-D- and β-D-(1→2)-linkages in the approximate ratio of 1:1. In the present studies, the reaction of 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (**1**) with 1,3,4,6-tetra-*O*-acetyl-α-D-galactose[4] (**2**) has been investigated under these



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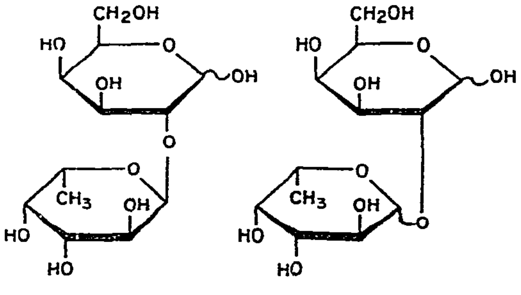

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different conditions, and both the α-L- (3) and β-L-fucopyranosyl (4) anomers have been sucessfully isolated; these were deacetylated to give the corresponding disaccharides **5** and **6**.

A solution of **2** (3.36 g, 9.6 mmoles), mercuric cyanide (1.22 g, 4.8 mmoles) and mercuric bromide (1.73 g, 4.8 mmoles) in acetonitrile (30 ml) was stirred with bromide **1** (3.53 g, 10 mmoles) for 3.5 h at room temperature. After being processed in the usual way, it gave a syrup which crystallized from absolute ethanol. The crystals were filtered off, and recrystallized from ethanol to give pure β-L-fucoside **4** (1.2 g, 20%), m.p. 222–224°, $[\alpha]_D^{23}$ +54.7° (*c* 1, chloroform); n.m.r. data ($CDCl_3$): τ 3.7 (d, *J* 3.5 Hz, 1 H, attributed to H-1 of α-D-galactopyranose residue), 5.52 (d, *J* 6.5 Hz, H-1, β-L-fucopyranosyl group), 7.84–8.03 (21 H, 7 OAc) 8.8 (d, *J* 6.5 Hz, 3 H, CH–Me); t.l.c. in (*a*) 3:2 benzene–ethyl acetate, R_2 1.33, (*b*) 9:1 benzene–methanol, R_2 1.46.

The mother liquor obtained after the removal of **4** was kept for 3–4 days at room temperature. When some crystals appeared, it was stored for 48 h at 0°. The crystals were filtered off and recrystallized from ethanol–petroleum ether, to give the α-L-fucoside **3** (1.1 g, 18.4%), m.p. 172–174°, $[\alpha]_D^{23}$ −28.3° (*c* 1, chloroform); n.m.r. data ($CDCl_3$): τ 3.62 (d, *J* 3.5 Hz, H-1, as present in **2**), 4.95 (d, *J* 3.5 Hz, H-1, α-L-fucopyranosyl group), 7.77–8.03 (21 H, 7 OAc), 8.84 (d, *J* 6.5 Hz, 3 H, CH–Me); t.l.c. in solvent (*a*) R_2 1.55, and in (*b*), R_2 1.54.

The mother liquor was found by t.l.c. to contain more of the α-L anomer. It was evaporated to a syrup; a solution thereof in benzene was chromatographed on a column of silica gel. The disaccharide fractions eluted with 5:1 benzene–ether were combined, and evaporated to give a solid which was recrystallized as before, to give **3** (0.6 g, 10%; total yield of **3**, 28.4%).

In another experiment, a stirred solution of **2** (3.36 g; 9.6 mmoles) in 1:1 nitromethane–benzene (180 ml) was evaporated until ~40 ml of the solvent had distilled, and was then cooled to room temperature. Mercuric cyanide (2.06 g; 8 mmoles) and bromide **1** (2.84 g; 8 mmoles) were added, and the mixture was stirred for 2 days at room temperature. The same amounts of mercuric cyanide and bromide **1** were introduced, and the reaction was allowed to proceed for 2 more days at room temperature. After the usual processing, the syrup crystallized from ethanol–petroleum ether when nucleated with crystals of the β-L anomer (**4**) to give **4** (0.65 g, recrystallized, 7.5%). When nucleated with **3**, the mother liquor gave the α-L anomer **3** (0.9 g, 15%). Additional amounts of **3** were isolated by column chromatography of the mother liquor, as already described, giving a further 1.1 g (18.4%; total yield, 33.4%).

On treatment with a catalytic amount of sodium methoxide in methanol by the usual method, disaccharide derivative **3** gave 2-*O*-α-L-fucopyranosyl-D-galactose (**5**) (86.5% yield); $[\alpha]_D^{23}$ −58.0° (*c* 1, water): lit.[3] $[\alpha]_D^{25}$ −56.7°, −56.5°. The heptaacetate **4** similarly afforded 2-*O*-β-L-fucopyranosyl-D-galactose (**6**) (83% yield); $[\alpha]_D^{23}$ +48.3° (*c* 1, water). Both disaccharides were obtained as amorphous materials.

The mobilities of the free disaccharides were found to be identical in t.l.c. and paper chromatography. The two disaccharides **5** and **6** were separately reduced with sodium borohydride, and the alditols converted into the per-*O*-(trimethylsilyl) derivatives. Clear separation was observed in g.l.c., which showed a single peak for the product from each disaccharide, having T_S 1.08 and 1.15 sec for the derivatives of **5** and **6**, respectively*.

The 2-*O*-α-L-fucopyranosyl-D-galactose thus synthesized was used as a substrate for the purification of 1,2-α-L-fucosidase[6]. In the previous investigation[6], no attempt was made to isolate the β-L anomer. In the present study, the anomers were successfully separated. It has been observed that the formation of 2-*O*-β-L-fucopyranosyl-D-galactose is enhanced by use of the method of Helferich and Zirner[4], whereas use of mercuric cyanide gives the β-L anomer in low yield. It is quite possible that the structure of the aglycon employed for the synthesis of such disaccharides having a (1→2)-linkage may affect the anomeric linkage of the reaction products. Levy *et al.*[3] employed benzyl 6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranoside for the synthesis of the α-L-fucopyranoside **5** by using mercuric cyanide as the catalyst.

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*For general methods, see ref. 7. T_S refers to the retention time of a compound relative to that of the per-*O*-(trimethylsilyl) derivative of sucrose.