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PREPARATION AND STRUCTURE OF 1,2,6,2′,3′,4′,6′-HEPTA-*O*-BENZOYL-β-CELLOBIOSE AND 6-*O*-BENZOYLCELLOBIOSE

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ABSTRACT

1,2,6,2′,3′,4′,6′-Hepta-*O*-benzoyl-β-cellobiose (**1**) was prepared and its structure ascertained. Ammonolysis of **1** gave 6-*O*-benzoylcellobiose and cellobiose.

INTRODUCTION

In former papers, we described the preparation of 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-maltose[1] and 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose[2]. Here, we describe the preparation and demonstration of structure of 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose (**1**).

Benzoylation of cellobiose in 20% sodium hydroxide solution with benzoyl chloride gave a mixture of partially benzoylated products, from which compound **1** could be separated, by extraction and crystallization, in 21.4% yield.

Nuclear magnetic resonance (n.m.r.) spectral data[3], and the fact that benzoylation of **1** gave octa-*O*-benzoyl-β-cellobiose[4], showed that compound **1** has the β anomeric configuration.

To determine the position of the free hydroxyl group, compound **1** was methylated seven times with diazomethane–boron trifluoride etherate[1,2,5,6] to give a hepta-*O*-benzoyl-*O*-methylcellobiose (**2**). Debenzoylation of **2** gave a methylcellobiose (**3**), and reduction of compound **3** with sodium borohydride afforded a methylcellobiitol which, on hydrolysis, gave 3-*O*-methyl-D-glucitol and D-glucose. These results showed that compound **1** is 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-cellobiose.

Treatment of **1** with methanolic ammonia gave both cellobiose (39.5%) and 6-*O*-benzoylcellobiose (59%), and no nitrogenated compounds could be detected.

Similar results had been observed with 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-maltose[1] and with 1,2,6,2′,3′,4′,6′-hepta-*O*-benzoyl-β-lactose[2]; this constitutes additional proof that a benzoyl group at O-3 is required for the migration reaction that leads to formation of nitrogenated disaccharide compounds.

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Partially acylated disaccharides with known structures may be of interest in further synthetic reactions, and benzoylation under the conditions described is an easy way to obtain some hepta-*O*-benzoylated disaccharides having free 3-hydroxyl groups.

EXPERIMENTAL

General procedures. — Chromatography was performed on Whatman No. 1 and 3MM papers, and on cellulose columns, with 5:2:2 butyl alcohol–ethanol–water as the developing solvent. The spray reagents used were (*a*) silver nitrate–sodium methoxide[7], (*b*) aniline hydrogen phthalate[8], and (*c*) permanganate–periodate[9]. Thin-layer chromatography was performed on plates of Silica Gel G (Merck) with 4:1 benzene–ethyl acetate as eluant, and iodine vapor for detection. Melting points are not corrected. The optical rotations were determined with a Rudolph (Model 70) polarimeter. The n.m.r. spectra were recorded at 60 MHz with a Varian A-60 spectrometer, in chloroform-*d* solution and with tetramethylsilane as the internal standard.

1,2,6,2',3',4',6'-Hepta-O-benzoyl-β-cellobiose (**1**). — Cellobiose (10 g) was dissolved in ice-cold, 20% sodium hydroxide solution (480 ml), and benzoyl chloride (55 ml) was added portionwise with vigorous shaking. The mixture was stirred for 20 min, whereupon the whole mass solidified. It was kept for 1 h at room temperature, water was added, and the solid was filtered off and washed with water until the washings were neutral. The solid was extracted with boiling methanol (700 ml). The residual syrup crystallized from 1:1 chloroform–methanol; after three recrystallizations from the same solvent, 6.5 g (21.4%) of **1** was obtained as needles, m.p. 201–204°, $[\alpha]_D^{20}$ −7.4° (*c* 0.75, chloroform); the n.m.r. spectrum showed no signals[3] at τ 3.00–3.50.

Anal. Calc. for $C_{61}H_{50}O_{18}$: C, 68.31; H, 4.71. Found: C, 68.55; H, 4.59.

1,2,6,2',3',4',6'-Hepta-O-benzoyl-3-O-methyl-β-cellobiose (**2**). — Compound **1** (2.5 g) was methylated seven times with diazomethane (prepared each time from 16 g of 1-methyl-1-nitrosourea)[10] and boron trifluoride etherate in dichloromethane, to give **2** in chromatographically pure form. Crystallization from 4:1 chloroform–methanol gave 2.86 g (94%) of **2** as needles, m.p. 121–123°; $[\alpha]_D^{20}$ −71.2° (*c* 0.8, chloroform).

Anal. Calc. for $C_{62}H_{52}O_{18}$: C, 68.63; H, 4.79; OCH_3, 2.9. Found: C, 68.87; H, 4.94; OCH_3, 2.64.

3-O-Methylcellobiose (**3**). — Compound **2** (250 mg) was debenzoylated with sodium methoxide in methanol. After 4 days, the solution was made neutral with Amberlite IR-120 (H^+) resin, and evaporated to dryness. The residual syrup was fractionated by chromatography on Whatman 3MM paper to give **3** as a syrup (94 mg, 45%) in a chromatographically pure form; $[\alpha]_D^{20}$ +40.1° (*c* 0.85, water).

Anal. Calc. for $C_{13}H_{24}O_{11}$: C, 43.82; H, 6.74. Found: C, 43.21; H, 6.79.

Reduction of 3-O-methylcellobiose, and hydrolysis of the resulting 3-O-methylcellobiitol. — Compound **3** (94 mg) was dissolved in water (1.5 ml) and reduced with

sodium borohydride (15 mg) in water (1 ml) for 2.5 h. Amberlite IR-120 (H^+) resin was added to decompose the excess of reagent and to remove the sodium ions. The suspension was filtered, and the filtrate evaporated. The residue was dried by several additions and evaporations of methanol, to give a chromatographically pure syrup (93 mg, 98.1%), $[\alpha]_D^{20}$ +19.9° (*c* 1.15, water), R_F 0.20. This compound was hydrolyzed with 0.25M hydrochloric acid (3.5 ml) during 4 h at 100°. The solution was made neutral with De-acidite G resin, evaporated, and chromatographed on Whatman 3MM paper. D-Glucose (35 mg), $[\alpha]_D^{20}$ +53.4° (equil., *c* 0.97, water) {lit.[11] $[\alpha]_D$ +52.2° (equil., water)} and 3-*O*-methyl-D-glucitol (55 mg), $[\alpha]_D^{20}$ +17.2° (*c* 1.1, water) {lit.[12] $[\alpha]_D$ +16.1° (*c* 6.5, water)} were obtained.

*Ammonolysis of 1,2,6,2',3',4',6'-hepta-*O*-benzoyl-β-cellobiose* (**1**). — Compound **1** was dissolved by agitation in 16% methanolic ammonia (24 ml). The solution was kept for 21 h at room temperature, and evaporated to dryness, and benzamide was sublimed off in high vacuum at 60°. The residual syrup was fractionated by chromatography on Whatman 3MM paper, to give cellobiose (13 mg, 39.5%), R_F 0.5, $[\alpha]_D^{20}$ +34.7° (equil., *c* 1.2, water) {lit.[11] $[\alpha]_D$ +35° (equil., water)} and 6-*O*-benzoylcellobiose (24.6 mg, 59%), R_F 0.58, $[\alpha]_D^{20}$ +31.3→+43.7° (equil., *c* 1, water) {lit.[4] $[\alpha]_D$ +34→+44° (equil., *c* 1, water)}.

*Octa-O-benzoyl-β-cellobiose by benzoylation of 1,2,6,2',3',4',6'-hepta-*O*-benzoyl-β-cellobiose* (**1**). — Compound **1** (0.53 g) was dissolved in 2.5 ml of pyridine, and 1 ml of benzoyl chloride was added with shaking. After 24 h at room temperature, the mixture was heated for 3 h at 60° and 30 min at 100°, and then cooled and dissolved in chloroform. The solution was successively washed with cold 0.25M sulfuric acid, saturated sodium hydrogen carbonate solution, and water, dried (anhydrous sodium sulfate), and evaporated to dryness. The residual syrup was dissolved in 3:7 acetone–methanol, and 0.49 g (83%) of octa-*O*-benzoyl-β-cellobiose crystallized as needles of m.p. 147–149°, $[\alpha]_D^{20}$ +36.5° (*c* 0.72, chloroform), R_F 0.52.

Anal. Calc. for $C_{68}H_{54}O_{19}$: C, 69.48; H, 4.64. Found: C, 69.34; H, 4.51.

From the mother liquors, octa-*O*-benzoyl-β-cellobiose of m.p. 188–191° crystallized {lit.[4] m.p. 188–191°, $[\alpha]_D$ +37° (*c* 1.14, chloroform)}. Recrystallization and seeding of the octabenzoate of m.p. 147–149° did not give the high-melting compound, but recrystallization and seeding of the octabenzoate of m.p. 188–191° gave the low-melting compound **5**. The n.m.r. spectra of both dimorphous forms showed no signals[3] at τ 3.00–3.50.

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