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Action of Strong Acids on Acetylated Glycosides

V.* Synthesis of β-Isomaltose Octaacetate

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From the investigations on halogen and oxygen substituted alkyl glucosides reported in Part IV of this series [1], the possibility of transglycosidation of certain disaccharides has been elucidated. There should be a great difference between disaccharides of the gentiobiose type and those of the cellobiose type. In the former there is only one carbon atom with an electron attracting substituent in β-position in the agluconic part of the molecule, while in the latter there are two. These electron attracting groups reduce the velocity of transglycosidation considerably, and consequently the glycosidic bond in cellobiose is very stable towards reagents that normally catalyze transglycosidation. The glycosidic bond in gentiobiose should be much more sensitive. This is indicated by the experiments of Pascu [2], who treated gentiobiose octaacetate with titanium tetrachloride in order to obtain gentiobiose chloride heptaacetate. He obtained a product which had a higher specific rotation and a lower melting point than that reported by other authors for the substance. Pascu's value for the optical rotation was also not in agreement with that calculated by the application of Hudson's rules of *iso*-rotation. One must therefore conclude that his product contained considerable amounts of isomaltose chloride heptaacetate.

The difference between gentiobiose and cellobiose is further demonstrated by the following experiment. α-Gentiobiose octaacetate and α-cellobiose octaacetate were dissolved in 2 C sulfuric acid in acetic anhydride-acetic acid, 10 : 3, and the optical rotation was measured at appropriate intervals. The reaction is very complex, involving α/β-transformation of the acetates, transglycosidation, acetolysis, and finally α/β-transformation of the glucose penta-

* A preliminary communication on this subject has been published in *Nature* **164** (1949) 706.

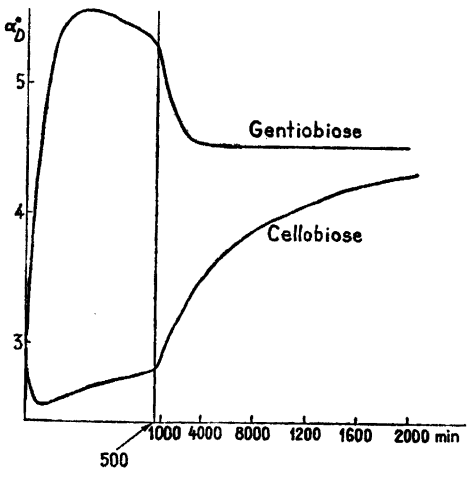

Fig. 1. Transglycosidation and acetolysis of the octaacetates Hof α-gentiobiose and α-cellobiose.

acetate formed by the acetolysis. The results are given in Fig. 1. The results may be interpreted by assuming that the gentiobiose derivative is transformed rather quickly, but that no transglycosidation can be observed with the cellobiose derivative.

Finally, the octaacetate of isomaltose, 6-α-D-glucopyranosyl-D-glucose, has been prepared from the gentiobiose derivative by transglycosidation. Crystalline derivatives of isomaltose have been prepared recently by hydrolysis of dextran [3] and by hydrolysis of starch [4], but the present paper reports the first total synthesis of this sugar and also one of the first syntheses of a disaccharide with an α-glycosidic bond. The substance was prepared in the following manner. Gentiobiose octaacetate (α- or β-) was treated with a large excess of titanium tetrachloride in absolute chloroform. The resulting mixture of isomaltose and gentiobiose chloride heptaacetate was treated with mercuric acetate in acetic acid. By this reaction the β-octaacetates were obtained, and they were then separated by recrystallization.

EXPERIMENTAL

α-Gentiobiose octaacetate

α-Gentiobiose octaacetate was prepared from amygdalin heptaacetate by hydrogenolysis, according to Bergmann and Freudenberg [5], but the method was improved to give better yields. Amygdalin heptaacetate (10 g) was dissolved in hot acetic acid (60 ml) and palladium black (1 g) was added. This mixture was shaken mechanically in an atmosphere of hydrogen and the temperature maintained at 40° by illumination with an infrared lamp. In about 15 minutes the optimum amount of hydrogen (740 ml) had been consumed. The palladium was removed by filtration and the solution was concentrated to a thick sirup under reduced pressure. Instead of isolating the gentiobiose heptaacetate formed, the sirup was dissolved in a solution of anhydrous zinc chloride (6 g) in acetic anhydride (60 ml) and kept at room temperature for 24 hours. The solution was then poured into ice water (1000 ml) and the precipitate was collected and recrystallized from methanol (75 ml). Two recrystallizations yielded the pure substance. M. p. 186—186.5°. $[\alpha]_D^{20}$ + 51°*. The average yield of several runs was 4.4 ± 0.4 g.

β-Gentiobiose octaacetate was prepared according to Reynolds and Evans [6].

The treatment of gentiobiose and cellobiose octaacetate with sulfuric acid was made

* All melting points uncorrected. All rotations in chloroform, $c = 2$.

by the method described in Part IV[7] of this series. The only difference was that the concentration of cellobiose octaacetate was much smaller than that of the other glucosides, owing to its low solubility. In order to obtain greater accuracy, the rotation was measured in a 4 dm tube.

β-Isomaltose octaacetate

Gentiobiose octaacetate (5 g, α- and β- are equally suitable) was dissolved in absolute chloroform (70 ml) and mixed with a solution of titanium tetrachloride (6 g) in the same solvent (70 ml). A yellow precipitate was formed immediately. The mixture was boiled on a water bath (65—70°) for five hours. (When the mixture was heated on a steam bath, some decomposition occurred and the yield was smaller.) After cooling, the mixture was poured into ice water (500 ml). The precipitate dissolved and the chloroform phase became almost colorless. It was separated, washed with water, dried over calcium chloride, and concentrated to a sirup under reduced pressure. This sirup, consisting of the chloride heptaacetates of isomaltose and gentiobiose, was dissolved in a solution of mercuric acetate (4 g) in acetic acid (40 ml). By this treatment the chloride heptaacetates were transformed into the β-octaacetates. (In a control experiment, glucose chloride tetraacetate was transformed into the β-pentaacetate in a quantitative yield by this method.) After two hours the solution was poured into water (500 ml) and extracted with chloroform (2 × 50 ml). The chloroform was washed with dilute sodium carbonate and water, dried over calcium chloride, and concentrated under reduced pressure. The residue was recrystallized from ethanol (25 ml). β-Gentiobiose octaacetate (1.0 g) of m. p. 188—189° separated. The mother liquor was concentrated under reduced pressure and the residue dissolved in methanol (7 ml) and seeded with pure β-isomaltose octaacetate *. The substance crystallized very slowly, complete separation requiring about one week in the refrigerator. Yield 1.85 g (46 %). M. p. 129—130°. $[\alpha]_D^{20}$ + 95°. Two further recrystallizations from methanol yielded the pure substance. M. p. 142—143°. $[\alpha]_D^{20}$ + 98°. The melting point was not depressed when mixed with the β-isomaltose octaacetate prepared by Wolfrom, Georges and Miller [3].

SUMMARY

β-Isomaltose octaacetate has been prepared from gentiobiose octaacetate in a series of reactions, involving a transglycosidation.

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