SYNTHESIS OF DISACCHARIDES VIA THE tert-BUTYL ETHERS OF MONOSACCHARIDES

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Previously it was shown that in glycosylation [1] and the esterification of carboxylic acids [2] the tert-butyl ethers of alcohols behave like the alcohols and, in some cases, give the glycosides and esters in higher yields than do the corresponding alcohols. These reactions can be interpreted as being a direct substitution of the tert-butyl group, in which connection the nucleophilicity of the ether oxygen is increased due to the +I effect of the tert-butyl group. The direct substitution of the O-tert-butyl group in the glycosylation reaction uncovers interesting possibilities for synthesis in the carbohydrate series, and was used by us previously to synthesize the O-glycosides of hydroxyamino acids [1] and the nonreducing disaccharides of the trehalose type [3].

In a search for approaches to the synthesis of polysaccharides we tried the tert-butyl ethers of monosaccharides for the synthesis of disaccharides of the reducing type. It proved that the (1 → 6)-bonded disaccharides are formed in good yields by the glycosylation of the 6-O-tert-butyl derivatives of monosaccharides, as follows from the glycosylation of 1,2;3,4-diisopropylidene-6-O-tert-butyl-α-D-galactopyranose (I) and 1,2,3,4-tetra-O-acetyl-6-O-tert-butyl-β-D-glucopyranose (II). The tert-butyl derivatives (I) and (II) were obtained in 60% yield by the reaction of 1,2;3,4-diisopropylidene-α-D-galactopyranose and 1,2,3,4-tetra-O-acetyl-β-D-glucopyranose with excess isobutylene in acetone solution, in the presence of catalytic amounts of H_2SO_4, and were isolated by chromatography on SiO_2. The structure of (I) was confirmed by the mass spectrum, which proved to resemble the spectrum of the starting 1,2;3,4-diisopropylidenegalactose; the principal peaks in the spectrum are shifted by m/e 56 (mass of tert-butyl group [4]). The reaction of (I) with acetobromoglucose in refluxing $MeNO_2$, in the presence of $Hg(CN)_2$, gave the β-glycopyranosyl-(1 → 6)-galactose derivative (III) in 56% yield, the structure of which was confirmed by direct comparison with an authentic specimen.

The reaction of (II) with acetobromoglucose under analogous conditions gave β-gentiobiose octaacetate in 67% yield, the structure of which was confirmed by direct comparison with an authentic specimen.

EXPERIMENTAL METHOD

The melting points were measured on a Kofler block. The optical rotation was measured on a Perkin—Elmer-141 M polarimeter. The solutions were evaporated in vacuo below 40°C.

The TLC was run in a bound layer of KSK silica gel. The solvent system was: chloroform—acetone, 95:5 (system A).

1,2;3,4-Diisopropylidene-6-O-tert-butyl-α-D-galactopyranose (I). To a solution of 1 g of 1,2;3,4-di-O-isopropylidene-α-D-galactopyranose [5] ($[\alpha]_D^{20}$ − 50° ($CHCl_3$), bp 150° (2 mm) in abs. acetone contained in a glass ampul were added 0.1 ml of conc. H_2SO_4 and a 10-fold excess of liquid isobutylene (20 ml), and the ampul was sealed and let stand overnight at ~20°. The ampul was cooled, opened, and after removing the excess isobutylene the reaction mixture was neutralized with satd. $NaHCO_3$ solution, extracted with $CHCl_3$, the extract was washed with water, dried over Na_2SO_4, the solvent was distilled off, and

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the obtained yellowish sirup was vacuum distilled. The yield of (I) was 0.75 g (60%), bp 120° (12 mm); $[\alpha]_D^{20}$ − 5.8° (C 2.5, acetone). Found: C 61.29; H 8.99%. $C_{16}H_{28}O_6$. Calculated: C 60.74; H 8.98%. The mass spectrum contains the peaks of the ions with m/e 316 (10); 301 (60); 245 (15); 187 (15); 185 (20); 169 (25); 127 (50); 43 (100).

6-O-tert-Butyl Ether of 1,2,3,4-Tetra-O-acetyl-β-D-glycopyranose (II). To a solution of 1.05 g of 1,2,3,4-tetra-O-acetyl-β-D-glucopyranose [6] [mp 127°, $[\alpha]_D^{20}$ + 12° (C 1.5, $CHCl_3$)] in 15 ml of CH_2Cl_2 were added 0.1 ml of conc. H_2SO_4 and 10 ml of liquid isobutylene, and the ampul was sealed and let stand overnight at ~20°. The ampul was cooled, opened, and after removing the excess isobutylene the reaction mixture was washed in succession with water, satd. $NaHCO_3$ soln., and water, and dried over Na_2SO_4. The residue from the evaporation was recrystallized from ethanol to give 0.8 g (60%) of product with mp 134°, $[\alpha]_D^{20}$ + 20° (C 1.5, $CHCl_3$); cf. [7].

1,2:3,4-Di-O-isopropylidene-6-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-α-D-galactopyranose (III). A mixture of 150 mg of (I), 200 mg of acetobromoglucose, 120 ml of $Hg(CN)_2$, and 10 ml of abs. CH_3NO_2 was refluxed for 15 min, cooled, washed in succession with satd. $NaHCO_3$ soln. and water, and dried over Na_2SO_4. The product with R_f 0.5 in system A was isolated by column chromatography on SiO_2 (elution with the gradient $C_6H_6 \rightarrow$ MeOH). We isolated 40 mg of (I) and 100 mg (56%) of (III), mp 138°, $[\alpha]_D^{20}$ − 5.65° (C 2, $CHCl_3$); cf. [8].

β-Gentiobiose Octaacetate. To a solution of 0.81 g of (II) in 20 ml of CH_3NO_2 were added 1.25 g of acetobromoglucose and 0.7 g of $Hg(CN)_2$. The mixture was refluxed for 30 min, cooled, washed in succession with satd. $NaHCO_3$ soln. and water, and dried over Na_2SO_4. The substance with R_f 0.4 in system A was isolated by column chromatography on SiO_2 using gradient elution ($C_6H_6 \rightarrow CHCl_3$); the yield was 0.91 g (67%), mp 190-192° (from MeOH), $[\alpha]_D^{20}$ − 5.2° (C 3, $CHCl_3$). The mixed melting point with an authentic specimen was not depressed.

CONCLUSIONS

The 6-O-tert-butyl ether derivatives of gluco- and galactopyranose were synthesized. It was shown that the tert-butyl ethers of monosaccharides can be used to synthesize disaccharides.

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