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SUGAR ACETATES AS GLYCOSYLATING AGENTS IN OLIGOSACCHARIDE SYNTHESIS

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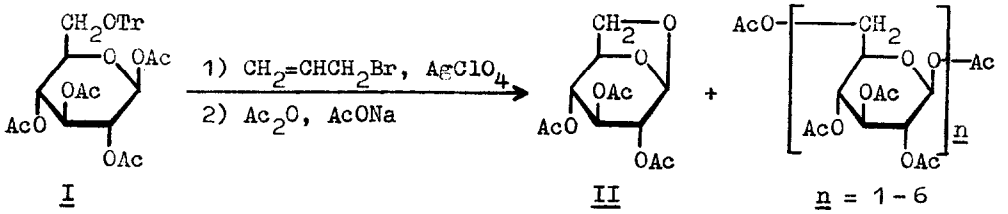
Fully acetylated sugars have been used as glycosylating agents in the synthesis of aryl glycosides in the presence of acidic catalysts or Lewis acids[1]. We now show that sugar acetates can also be used for this purpose in oligosaccharide synthesis.

Treatment of 1,2,3,4-tetra-O-acetyl-6-O-trityl-β-D-glucopyranose (I) with allyl bromide and silver perchlorate gave rise to 2,3,4-tri-O-acetyl-1,6-anhydro-β-D-glucopyranose (II). In addition, analysis of the deacetylated reaction mixture showed the presence of glucose, gentiobiose, and oligosaccharides up to hexamer.



I II n = 1 - 6

Compound I (0.57 g) and $AgClO_4$ (0.21 g) were dissolved in dry benzene (4 ml) and treated with allyl bromide (0.09 ml). The solution was stirred for 24 h at room temperature. Several drops of sym.-collidine were added, and silver bromide was filtered off. After evaporation of the filtrate,

the sirupy residue was acetylated (Ac_2O/AcONa), and the products were chromatographed on silica gel. Gradient elution with benzene-butanone gave II[2] (in 29% yield), m.p. 110° (from ether-hexane), $[\alpha]_D$ -47° (c 1, EtOH); β-D-glucose pentaacetate[3] (in 13% yield), m.p. 132-133° (from ether-hexane), $[\alpha]_D$ +4° (c 1, $CHCl_3$); β-gentiobiose octaacetate[4] (in 15% yield), m.p. 194-196° (from ethanol), $[\alpha]_D$ -6° (c 1, $CHCl_3$); and β-gentiotriose undecaacetate[5] (in 12% yield), m.p. 215-216° (from ethanol), $[\alpha]_D$ -7° (c 0.64, $CHCl_3$).

A portion of the reaction mixture was deacetylated (Zemplén) and analyzed by paper chromatography. A plot of log $(\frac{1}{R_F} - 1)$ against n, where n is degree of polymerization, yielded a straight line (Fig. 1), showing the products to be a homologous series of oligosaccharides with β-(1→6)-glucoside bonds.

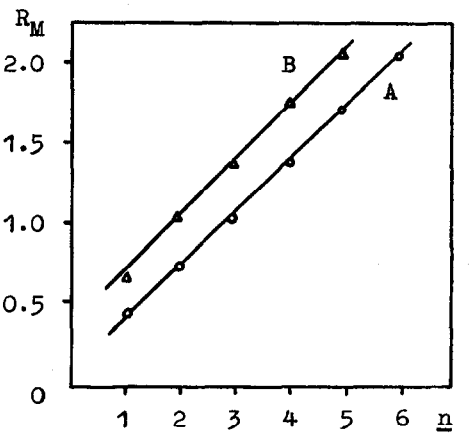


Fig. 1.

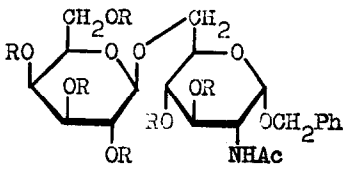
Relation between $R_M = \log (\frac{1}{R_F} - 1)$ and n: A - isoamyl alcohol-pyridine-water (5:5:4); B - butanol-ethanol-water (4:1:2).

Thus, the reaction led to „selfglycosylation" of I both intramolecularly to II and intermolecularly to a mixture of oligosaccharides. Haq and Whelan[6] obtained similar results with 2,3,4-tri-O-acetyl-α-D-glucopyranosyl bromide under the conditions of the Koenigs-Knorr reaction.

In order to test our proposal we examined the reaction when the possibility of intramolecular glycosylation was excluded. The interaction of β-D-galactose pentaacetate (III) with benzyl 2-acetamido-3,4-di-O-acetyl-

2-deoxy-6-O-trityl-α-D-glucopyranoside[7] (IV) in benzene gave benzyl 2-acetamido-3,4-di-O-acetyl-6-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2-deoxy-α-D-glucopyranoside (V) in low yield; the yield increasing considerably on passing over to nitromethane.

Allyl bromide (0.20 ml) was added to a solution of $AgClO_4$ (0.42 g), III (0.78 g), and IV (1.25 g) in dry nitromethane (5 ml). The mixture was kept for 1.5 h at 50° (periodical shaking) and neutralized with sym.-collidine. After separation of AgBr and evaporation of the filtrate, the residue was acetylated with Ac_2O in pyridine. The product V was isolated by column chromatography on silica gel (gradient elution with ether-methanol). De-O-acetylation of V yielded 0.25 g (27%) of benzyl 2-acetamido-2-deoxy-6-O-(β-D-galactopyranosyl)-α-D-glucopyranoside (VI), m. p. 232-234° (from ethanol), $[\alpha]_D$ +119° (c 1, MeOH); anal. for $C_{21}H_{31}NO_{11}$. Besides V,

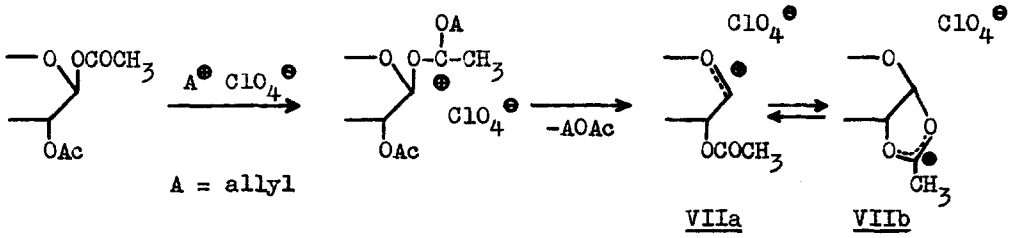


V R = Ac
VI R = H

about 50% of the starting materials (III and IV) and a small amount of benzyl 2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-α-D-glucopyranoside were isolated from the reaction mixture.

A solution of VI in a mixture of methanol and acetic acid was hydrogenolyzed in the presence of palladium-on-charcoal. The known disaccharide[8,9] 2-acetamido-2-deoxy-6-O-(β-D-galactopyranosyl)-D-glucose, $[\alpha]_D$ +27° (c 0.5, water), R_{Gal} 0.63 (solvent A), was obtained. The structure of the product was proved also by its complete enzymic hydrolysis with β-glucosidase from sweet almond.

The mechanism proposed for the reaction involves attack of allyl cation on the sugar acetate leading to the sugar perchlorate (VIIa or VIIb). The latter is able to glycosylate trityl ethers (cf.[4]).



VIIa VIIb

The above results thus show for the first time that sugar acetates can be used as glycosylating agents in oligosaccharide synthesis.

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