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Note

A novel, stereospecific synthesis of β-D-glucopyranosyl phosphate

L. V. VOLKOVA, L. L. DANILOV, AND R. P. EVSTIGNEEVA
M. V. Lomonosov Fine Chemical Technology Institute, Moscow (U. S. S. R.)
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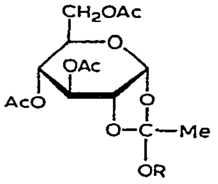
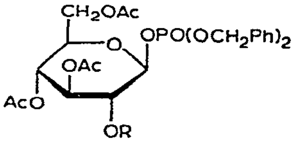
The preparation of β-D-glycopyranosyl phosphates is usually based upon the reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromides with silver dibenzyl phosphate[1] or "monosilver phosphate"[2], followed by the removal of protecting groups, phosphorylation of the anomeric hydroxyl group by *o*-phenylene phosphorochloridate[3], or treatment of the Brigl anhydride with dibenzyl hydrogen phosphate[4].

A novel method for the preparation of β-D-glycopyranosyl phosphates involves the reaction of alkyl orthoacetates with dibenzyl hydrogen phosphate. The preparation of β-D-glucopyranosyl dihydrogen phosphate is cited to illustrate this method.



1 R= *tert*-Bu
2 R= Et



3 R = Ac
4 R = H

The reaction of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(*tert*-butyl orthoacetate)[5,6] (**1**) with dibenzyl hydrogen phosphate in dry benzene at 19–20° for 30 min gave 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl dibenzyl phosphate (**3**). Under similar reaction conditions, the ethyl orthoacetate **2** yielded a mixture of **3** and 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl dibenzyl phosphate[4] (**4**). The formation of 2-hydroxy compounds was noted in the ring opening of ortho esters by alcohols in the presence of acid catalysts[7]. Hydrogenation of **3**, using a palladium catalyst, followed by deacetylation[2], gave β-D-glucopyranosyl dihydrogen phosphate isolated as its di(cycohexylammonium) salt.

EXPERIMENTAL

General methods. — Thin-layer chromatography (t.l.c.) was performed on alumina (neutral, Brockmann III) with ether (*A*), on silicic acid with 1:1 ether–benzene (*B*), or on Silica Gel KSK with 7:1:2 propan-2-ol–25% ammonia–water (*C*).

The spots were revealed by a molybdate spray[8]. Column chromatography was performed on alumina (neutral, Brockmann III). Optical rotations were determined with an SPU-M polarimeter at 19–20°. The n.m.r. spectrum was recorded with a Varian XL-100 spectrometer for a solution in $CDCl_3$ with Me_4Si as internal standard. Chemical shift values are given on the δ scale.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl dibenzyl phosphate (**3**). — (*a*) Compound **1** (0.5 g) was added to a solution of dibenzyl hydrogen phosphate (0.4 g) in dry benzene (15 ml). After 30 min at 19–20°, no ortho ester remained in the reaction mixture (t.l.c., solvent *A*). The solution was passed through a small column of alumina (5 g) to remove non-reacted dibenzyl hydrogen phosphate, and the product was eluted with benzene. The effluent was evaporated to dryness under diminished pressure, and the residue was crystallised from ether–hexane to give **3** (0.7 g, 85%), m.p. 76.5–78°, $[\alpha]_D$ −8.4°, $[\alpha]_{397}$ −22° (*c* 3, chloroform), R_F 0.71 (solvent *A*), 0.60 (solvent *B*). N.m.r. data: δ 5.38 (*q*, $J_{1,2}$ 12.4, $J_{1,P}$ 7.5 Hz, H-1); lit.[2] m.p. 78–79°, $[\alpha]_D$ −9° (*c* 3, chloroform).

Anal. Calc. for $C_{28}H_{33}O_{13}P$: C, 55.26; H, 5.47; P, 5.09. Found: C, 55.41; H, 5.63; P, 5.40.

(*b*) Compound **2** (1.2 g) was added to a solution of dibenzyl hydrogen phosphate (1.05 g) in dry benzene (30 ml). After 2 h at 19–20°, no ortho ester remained in the reaction mixture (t.l.c.). The crude product was isolated as described in (*a*) and then eluted from a column of alumina (20 g) with 1:1 light petroleum–ether to give **3** (0.82 g, 42%), and with 1:2 light petroleum–ether to give **4** (0.61 g), m.p. 134–135°, $[\alpha]_D$ +29.5° (*c* 0.5, chloroform), R_F 0.48 (solvent *A*), 0.43 (solvent *B*); lit.[4] m.p. 135–136°, $[\alpha]_D$ +27° (*c* 2.96, chloroform).

β-D-Glucopyranosyl di(cyclohexylammonium) phosphate (**5**). — Compound **3** (3 g) was subjected to catalytic hydrogenation over a palladium catalyst, and the product was saponified with 0.1M methanolic sodium methoxide (10 ml). Cations were removed with Dowex-50W X8(H^+) resin, and the solution was then treated with Dowex-50W X8($C_6H_{11}NH_3^+$) to yield **5** (1.9 g, 86%), m.p. 175–176°, $[\alpha]_D$ +5.4°, $[\alpha]_{329}$ +19° (*c* 1, water), R_F 0.65 (solvent *C*); lit.[9] $[\alpha]_D$ +5.9° (*c* 2.5, water).

Anal. Calc. for $C_{18}H_{39}N_2O_9P \cdot H_2O$: C, 45.33; H, 8.60; N, 5.88; P, 6.51. Found: C, 44.96; H, 8.72; N, 5.61; P, 6.57.

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