Note

Synthesis of an acylated 2-hydroxyglycal from a 1,2-*trans*-polyacylglycosyl halide

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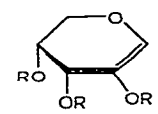
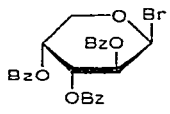
Acylated 2-hydroxyglycals are usually prepared[1] by the base-catalysed *trans*-elimination of hydrogen halide from polyacylglycosyl halides in which the halide and the 2-acyloxy group are *cis*-related. Recently, the strongly basic 1,5-diazabicyclo-[5.4.0]undec-5-ene (DBU) has been shown[2] to be an excellent base for this reaction, giving yields far superior to those obtained using bases such as diethylamine. This finding is now confirmed, and a modification of the method is reported, which allows the polyacylglycosyl halide to have the halide *trans* to the 2-acyloxy group.

3,4-Di-*O*-benzoyl-2-benzoyloxy-D-arabinal (1,5-anhydro-2,3,4-tri-*O*-benzoyl-D-*erythro*-pent-1-enitol, **1**) was required in connection with another investigation. *trans*-Elimination of hydrogen bromide from either 2,3,4-tri-*O*-benzoyl-β-D-arabinopyranosyl bromide (**2**) or 2,3,4-tri-*O*-benzoyl-α-D-ribopyranosyl bromide (**3**) should lead to this compound. The *arabino* compound **2** is readily prepared in high yield[3] from 1,2,3,4-tetra-*O*-benzoyl-D-arabinose, whereas the *ribo* compound **3** is only a minor product (*ca.* 5%) when 1,2,3,4-tetra-*O*-benzoyl-D-ribopyranose is treated with hydrogen bromide; the major product[4] is the β-anomer **4**. In keeping with the earlier findings[2], the olefin **1** resulted in high yield when either of the 1,2-*cis*-halides **2** or **3** was treated with DBU in *N,N*-dimethylformamide. The 90-MHz n.m.r. spectrum of **1** confirmed its structure. A low-field singlet at τ 3.10 was assigned to H-1, the H-3 signal appeared as a doublet ($J_{3,4}$ 4 Hz) at τ 3.82, and the H-4 signal as a quintet ($J_{4,5e}$ 5, $J_{4,5a}$ 9 Hz) at τ 4.39. The H-5e and H-5a signals appeared at τ 5.73 and 5.88 as a quartet and a triplet which partially overlapped. The large value of $J_{4,5a}$ suggests that **1** exists mainly in the half-chair conformation **5**. Similar n.m.r. spectral data were reported[5] recently for the corresponding triacetate **6**. The structure **1** was earlier assigned[6] to a compound* obtained from the action of phenylpolyphosphoric ester on 2,3,4-tri-*O*-benzoyl-D-ribopyranose (**7**), but the physical and n.m.r. spectral constants reported for this compound differ markedly from those given here.

*A Referee has suggested that this compound is 1,2,4-tri-*O*-benzoyl-3-deoxy-β-D-*glycero*-pent-2-enopyranose [R. J. Ferrier, N. Prasad, and G. H. Sankey, *J. Chem. Soc.* (*C*), (1968) 974; C. Bock and C. Pedersen, *Acta Chem. Scand.*, 24 (1970) 2465]; the physical constants are in excellent agreement.



1 R = Bz
6 R = Ac



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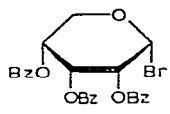

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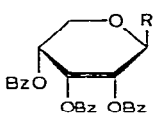
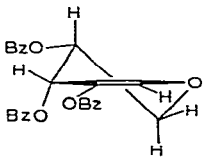
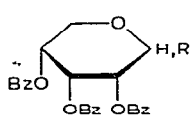


4 R = Br
9 R = BzO



5



7 R = OH
8 R = H

Catalytic hydrogenation of the olefin **1** gave 1,5-anhydro-2,3,4-tri-*O*-benzoyl-ribitol (**8**) as the major product, in agreement with the expectation that hydrogen transfer would occur to the less-hindered side of the molecule. Chromatographic examination of the mother liquors after debenzoylation revealed the presence of a small amount of 1,5-anhydroarabinitol (presumably the D form) as well as the *ribo* isomer.

When the β-bromide **4** was treated with DBU in *N*,*N*-dimethylformamide, extensive discolouration occurred. After work-up, small quantities of 2,3,4-tri-*O*-benzoyl-D-ribose (**7**) and 1,2,3,4-tetra-*O*-benzoyl-β-D-ribose (**9**) were obtained. The n.m.r. spectrum of the mother liquors suggested the presence of the olefin **1**, although none could be isolated. The formation of the tetrabenzoate **9** is unexpected, and it may have been formed from the tribenzoate **7** by trans-esterification.

The small amount of olefin **1** detected in the above reaction may have arisen from the α-bromide **3** formed by anomerization of the β-bromide **4** by bromide ion released in the reaction. If this were so, it seemed possible that the yield of olefin **1** might be enhanced by conducting the reaction in the presence of an excess of bromide ions. Recently, it has been shown[7] that lithium halide–hexamethylphosphoric triamide complexes are highly soluble sources of nucleophilic halide ion. When the reaction of the β-bromide **4** with DBU was repeated in the presence of an excess of the lithium bromide complex, a reasonable yield of the olefin **1** was obtained. No tetrabenzoate **9** was formed, and only a trace of tribenzoate **7** could be detected.

The preparation of the bromides **3** and **4** suggests[4] that the anomeric equilibrium between **3** and **4** strongly favours the β-anomer **4**. In view of this, the success of the above modification is encouraging and suggests that it should be generally applicable and make acylated 2-hydroxyglycals accessible even when the conventional starting material, a 1,2-*cis*-related polyacylglycosyl halide, is not available.

EXPERIMENTAL

General methods. — N.m.r. spectra were determined for carbon tetrachloride solutions using tetramethylsilane as internal standard on a Brucker Spectrospin 90-MHz n.m.r. spectrometer. Silica gel (Hopkin and Williams, M.F.C. grade) was

used for column chromatography. Whatman No. 1 paper in the system butyl alcohol–water (86:14, v/v) was used for paper chromatography.

3,4-Di-O-benzoyl-2-benzoyloxy-D-arabinal (**1**). — (*a*) A solution of 1,2,3,4-tetra-*O*-benzoyl-α-D-arabinopyranose (1.15 g) in dichloromethane (1 ml) was treated with a solution of hydrogen bromide in acetic acid (2 ml; 45% w/v). After 3 h at room temperature, more dichloromethane was added and the solution was washed successively with water, dilute aqueous potassium hydrogen carbonate, and water. Evaporation of the dried ($MgSO_4$) extract gave crude 2,3,4-tri-*O*-benzoyl-β-D-arabinopyranosyl bromide (**2**) which was immediately dissolved in *N,N*-dimethylformamide (2 ml). This solution was cooled to 0° and 1,5-diazabicyclo[5.4.0]undec-5-ene (0.35 ml) was added. After 1 h at room temperature, excess of water and ether were added. The ethereal extract was washed with dilute sulphuric acid, water, and dilute aqueous potassium hydrogen carbonate, and then dried ($MgSO_4$) and evaporated. The residue crystallized from methanol to give **1** (0.52 g, 59%), m.p. 93–94°, $[\alpha]_D$ +94° (*c* 0.8, dichloromethane); τ 2.0–2.8 (*m*, aromatic H), 3.10 (*s*, H-1), 3.82 (*d*, $J_{3,4}$ 4 Hz, H-3), 4.39 (*qi*, $J_{4,5e}$ 5, $J_{4,5a}$ 9 Hz, H-4), 5.73 (*q*, $J_{5e,5a}$ 11 Hz, H-5e), 5.88 (*t*, H-5a) (Found: C, 69.94; H, 4.62. $C_{26}H_{20}O_7$ calc.: C, 70.25; H, 4.55%).

(*b*) 1,5-Diazabicyclo[5.4.0]undec-5-ene (0.05 ml) was added to a solution of 2,3,4-tri-*O*-benzoyl-α-D-ribopyranosyl bromide (**3**) (90 mg) in *N,N*-dimethylformamide (0.2 ml). After 3 h at room temperature, the reaction mixture was worked up as in (*a*) to give **1** (47 mg, 67%), m.p. 90–92° (m.m.p. with previous sample, 92–93°), $[\alpha]_D$ +86° (*c* 0.6, dichloromethane).

Hydrogenation of olefin **1**. — Palladium oxide (60 mg) was added to a solution of the olefin **1** (112 mg) in glacial acetic acid (5 ml), and the mixture was hydrogenated at room temperature and pressure for 24 h. The catalyst was filtered off, and the filtrate was evaporated to an oil which crystallized from ether to give 1,5-anhydro-2,3,4-tri-*O*-benzoylribitol (**8**) (40 mg), m.p. 151–153° and m.m.p. 152–154° (lit.[8], m.p. 156–157°). The residue from the mother liquors was dissolved in 0.1M methanolic sodium methoxide and left overnight. Paper chromatography of the solution then showed the presence of 1,5-anhydroribitol (R_F 0.34) and a smaller quantity of 1,5-anhydroarabinitol (R_F 0.28).

Action of 1,5-diazabicyclo[5.4.0]undec-5-ene on *2,3,4-tri-O-benzoyl-β-D-ribopyranosyl bromide* (**4**). — 1,5-Diazabicyclo[5.4.0]undec-5-ene (0.95 ml) was added to a cooled solution of the bromide **4** (2.5 g) in *N,N*-dimethylformamide (4 ml). Considerable discolouration occurred after 3 h at room temperature. The reaction was worked up as in the previous experiment, but using dichloromethane in place of ether, to give a brown syrup (1.98 g). This was dissolved in benzene and chromatographed on silica (50 g). Elution with benzene–ether (19:1) gave a fraction (0.83 g) which, on crystallization from ethanol, gave 1,2,3,4-tetra-*O*-benzoyl-β-D-ribopyranose (**9**) (0.34 g, 12%), m.p. 128–130° and m.m.p. 128–130° (lit.[8], m.p. 129–131°). Elution with benzene–ether (3:1) gave a fraction (0.88 g) from which 2,3,4-tri-*O*-benzoyl-D-ribopyranose (**7**) (0.68 g, 29%), m.p. and m.m.p. 115–135° (lit.[9], 118–137° for a mixture of α and β anomers), was obtained from carbon tetrachloride.

Action of diazabicyclo[5.4.0]undec-5-ene on 2,3,4-tri-O-benzoyl-β-D-ribopyranosyl bromide (**4**) *in the presence of lithium bromide–hexamethylphosphoric triamide complex.* — Hexamethylphosphoric triamide (1 ml) was added to a suspension of lithium bromide (0.19 g; 2mmoles) in toluene (5 ml). The mixture was warmed and the resulting solution was evaporated. The residue was dissolved in *N,N*-dimethylformamide (1 ml), and the bromide **4** (0.27 g; 0.5 mmole) was added followed by diazabicyclo[5.4.0]undec-5-ene (0.10 ml). After 3 h at room temperature, very little discolouration had occurred and the mixture was worked up as before, using ether. Chromatography of the resulting syrup (0.22 g) on silica gel (10 g), with elution by benzene–ether (19:1), gave a fraction (0.18 g) which crystallized from methanol to give the olefin **1** (0.11 g, 50%), m.p. 88–90° (m.m.p. with previous material 90–92°). Elution with benzene–ether (3:1) gave a small quantity (25 mg) of material chromatographically indistinguishable from the tribenzoate **7**.

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