Acta Chemica Scandinavica B 30 (1976) 624—626

Reaction of Partially Benzoylated Sugars with Hydrogen Bromide. Preparation of Some Deoxyhexofuranoses

ANDERS FOGH, INGE LUNDT and CHRISTIAN PEDERSEN

Department of Organic Chemistry, Technical University of Denmark, DK-2800 Lyngby, Denmark

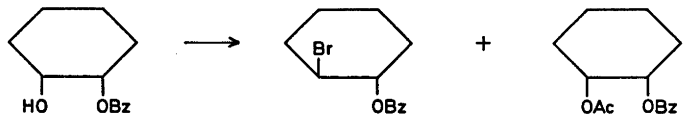
Treatment of methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside with hydrogen bromide in acetic acid followed by reaction with silver benzoate gave tetra-*O*-benzoyl-6-bromo-6-deoxy-β-D-galactofuranose. The latter was reduced to tetra-*O*-benzoyl-β-D-fucofuranose and to 5,6-dideoxy-α-L-*arabino*-hexofuranose derivatives.

Golding *et al.*[1] have found that *cis*-1,2-cyclohexanediol reacts rapidly with hydrogen bromide in acetic acid (HBA) to give *trans*-1-acetoxy-2-bromocyclohexane in high yield. Other 1,2-diols react similarly; the reaction proceeds *via* a monoacetate and a 1,3-dioxolanylium ion, which subsequently undergoes substitution with bromide ions to give the *trans*-acetoxy bromide.[1,2]

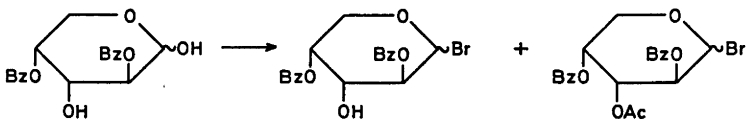
This reaction might be used for the preparation of bromo-deoxy carbohydrates by treatment of partially acylated carbohydrates with HBA. Since partially benzoylated sugars are often more readily prepared, and more stable, than their acetylated counterparts it was first investigated whether *cis*-2-benzoyloxycyclohexanol (*1*) would react with HBA analogous to the acetate. This was actually found to be the case; *trans*-1-benzoyloxy-2-bromocyclohexane (*2*) was formed in high yield together with the acetate (*3*) when *1* was treated with HBA for 2 h.

Attempts to apply this reaction to the preparation of bromo-deoxy sugars were in most cases unsuccessful. Treatment of 2,4-di-*O*-benzoyl-*D*-arabinopyranose (*4*) with HBA rapidly gave the corresponding glycosyl bromide (*5*). On further reaction the latter was slowly acetylated to give the 3-*O*-acetate (*6*). Bromine was not introduced at any position other than C1. Similar results were found when 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose was treated with HBA.

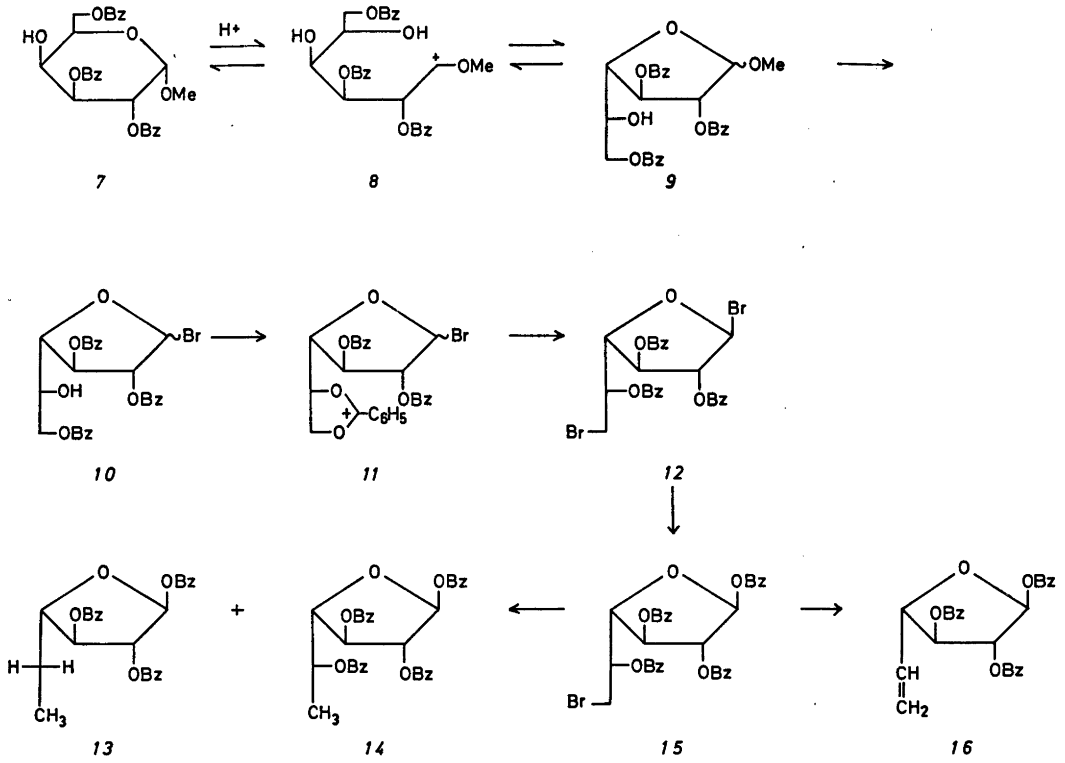
When, on the other hand, methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (*7*) was treated with HBA for 3 h at room temperature it was converted into tri-*O*-benzoyl-6-bromo-6-deoxy-β-D-galactofuranosyl bromide (*12*). Since *12*



1 *2* *3*



4 *5* *6*



is a rather unstable syrup it was not purified. Treatment of crude *12* with silver benzoate gave the crystalline 1-*O*-benzoate (*15*) in *ca.* 50 % yield based on *7*.

The first step in the reaction of *7* with HBA is probably a ring-contraction, giving the methyl furanoside (*9*) *via* the oxo-carbonium ion (*8*).[3,4] Reaction of *9* with HBr may then give the corresponding bromide (*10*) which yields the benzoxonium ion (*11*). Subsequent reaction of *11* with bromide ions finally gives *12*.

Hydrogenolysis of *15* with palladium on carbon gave tetra-*O*-benzoyl-β-D-fucofuranose (*14*) accompanied by a small amount of tri-*O*-benzoyl-5,6-dideoxy-α-L-*arabino*-hexofuranose (*13*). The latter is probably formed *via* the 5,6-unsaturated furanose (*16*). Reduction of *15* with zinc in acetic acid gave a good yield of *16* which on catalytic hydrogenation yielded *13* as the sole product. Some methyl 5,6-dideoxy-α-L-*arabino*-hexofuranosides have been prepared previously by Ball *et al.*[5]

The structure of *14* was proved through its ^{1}H NMR spectrum and by the fact that it gave crystalline D-fucose on debenzoylation. The structures of *12*, *13*, *15*, and *16* were derived from their NMR spectra only.

The reaction described above, although of limited general applicability, provides a convenient method for the preparation of D-fucofuranose derivatives.

EXPERIMENTAL

Melting points are uncorrected. Preparative thin layer chromatography (TLC) was performed on 20 × 40 cm plates using 1 mm layers of Merck silica gel PF_{254}. ^{1}H NMR spectra were measured at 100 or 90 MHz in deuteriochloroform using tetramethylsilane as internal reference.

trans-*2-Bromo-benzoyloxycyclohexane (2)*. To *cis*-2-benzoyloxycyclohexanol [6] (1.0 g) in dichloromethane (5 ml) was added 5 ml of a 30 % solution of hydrogen bromide in glacial acetic acid (HBA) and the mixture was kept at room temperature for 2 h. It was then diluted with dichloromethane, washed with water and aqueous sodium hydrogen carbonate, dried and evaporated. The residue (1.0 g) was separated into two fractions by column chromato-

graphy on silica gel using ether-pentane (1:3) as eluent. The fast moving fraction gave 765 mg (59 %) of *2*. An NMR spectrum was in agreement with the structure and showed no impurities. Crystallization from ethanol gave 500 mg of a product with m.p. 63 – 64 °C (reported [7] m.p. 64 °C).

The second fraction gave 105 mg (9 %) of *cis*-2-acetoxy-benzoyloxycyclohexane (*3*), which had its NMR spectrum identical with that of a previously described product.[6]

*Tetra-O-benzoyl-6-bromo-6-deoxy-β-*D*-galactofuranose (15).* Methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside [8] (*7*) (5.0 g) was dissolved in dichloromethane (5 ml) and HBA (25 ml) was added. The mixture was kept for 3 h at room temperature. Dichloromethane (50 ml) was added and the solution was washed with ice-water and with aqueous sodium hydrogen carbonate, dried and evaporated. The syrupy residue consisted largely of tri-*O*-benzoyl-6-bromo-6-deoxy-β-D-galactofuranosyl bromide (*12*), which could not be induced to crystallize. ^{1}H NMR: δ 6.64 (H1), 5.88 (H2), 5.59 (H3), 5.05 (H4), 5.98 (H5), *ca.* 3.7 (H6); $J_{12} \simeq 0$ Hz, $J_{23} \simeq 0$, $J_{34} = 4.2$, J_{45} *ca.* 4, J_{56} *ca.* 6.

The crude glycosyl bromide (*12*) was dissolved in acetonitrile (50 ml) and stirred for 3 h with silver benzoate (10 g). The mixture was diluted with dichloromethane, filtered through carbon and evaporated. The residue was dissolved in dichloromethane, filtered through carbon and evaporated. Crystallization from ether gave 3.2 g (49 %) of *15*, m.p. 158 – 162 °C. Recrystallization from ethyl acetate-pentane gave the pure product, 3.04 g (47 %), m.p. 163 – 165 °C, $[\alpha]_D^{20} - 37.0°$ (*c* 5.1, $CHCl_3$). Anal. $C_{34}H_{27}BrO_9$: C, H, Br. ^{1}H NMR: δ 6.81 (H1), 5.79 (H2), 5.70 (H3), 4.97 (H4), 5.94 (H5), 3.80 (H6); $J_{12} = 0.4$ Hz, $J_{23} = 1$, $J_{34} = 4.2$, $J_{45} = 3.5$, $J_{56} = 6.6$.

*Tetra-O-benzoyl-β-*D*-fucofuranose (14).* A solution of *15* (1.0 g) in ethyl acetate (15 ml) and triethylamine (1.2 ml) was hydrogenated overnight at room temperature and 1 atm. pressure in the presence of 400 mg 5 % palladium on carbon. The mixture was then filtered through carbon and the carbon was washed with dichloromethane. The filtrate was washed with 4 N hydrochloric acid and with aqueous sodium hydrogen carbonate and evaporated. The product (925 mg) was separated into two fractions by preparative TLC with ether-pentane as eluent. The fast-moving fraction gave 70 mg (10 %) of tri-*O*-benzoyl-5,6-dideoxy-α-L-*arabino*-hexofuranose (*13*), which was crystallized from methanol, m.p. 81 – 83 °C, $[\alpha]_D^{25} - 23.9°$ (*c* 1.5, $CHCl_3$). Anal. $C_{27}H_{24}O_7$: C, H. ^{1}H NMR: δ 6.24 (H1), 5.78 (H2), 5.44 (H3), 4.48 (H4), 1.99 (H5), 1.12 (H6); $J_{12} \simeq 0$ Hz, $J_{23} = 1.0$, $J_{34} = 3.8$, $J_{45} = 6.4$, $J_{56} = 7.3$.

The next fraction gave 687 mg (78 %) of the fucose derivative (*14*) as a syrup which was pure as seen from an NMR spectrum, $[\alpha]_D^{20} = 52.3°$ (*c* 3.5, $CHCl_3$). Anal. $C_{34}H_{28}O_9$: C, H. ^{1}H NMR: δ 6.78 (H1), 5.5 – 5.9 (H2, H3, and H5), 4.72 (H4), 1.58 (H6); $J_{12} = 0$ Hz, $J_{34} = J_{45} = 4.2$, $J_{56} = 6.6$.

The product could be crystallized with some difficulty from ethanol; m.p. 88 – 93 °C.

*Tri-*O*-benzoyl-5,6-dideoxy-α-*L*-arabino-hex-5-enofuranose (16).* A solution of *15* (3.0 g) in acetic acid (100 ml) and water (25 ml) was stirred at 90 °C. Zinc dust (9 g) was added in the course of 20 min and the mixture was then stirred for an additional 20 min. Dichloromethane was then added and the mixture was washed with water and aqueous sodium hydrogen carbonate, dried and evaporated. The syrupy residue (2.1 g) was crystallized from methanol to give 1.4 g (67 %) of *16*, m.p. 102 – 103 °C. Recrystallization from methanol gave the pure product, m.p. 104 – 106 °C, $[\alpha]_D^{25} - 23.1°$ (*c* 2.2, $CHCl_3$). Anal. $C_{27}H_{22}O_7$: C, H. ^{1}H NMR: δ 6.76 (H1), 5.81 (H2), 5.45 (H3), 5.00 (H4), 6.18 (H5), 5.60 (H6), 5.36 (H6′); $J_{12} \simeq 0$ Hz, $J_{23} = 1.3$, $J_{45} = 5.8$, $J_{46} = J_{46'} = 1.4$, $J_{56} = 17.2$, $J_{56'} = 10.3$, $J_{66'} = 1.4$.

*Tri-*O*-benzoyl-5,6-dideoxy-α-*L*-arabino-hexofuranose (13).* A solution of *16* (1.0 g) in ethyl acetate (10 ml) was hydrogenated with 200 mg of 5 % palladium on carbon. Filtration and evaporation from methanol gave 786 mg (78 %) of *13*, m.p. 78 – 82 °C. After recrystallization the product melted at 81 – 83 °C. A mixed melting point and an NMR spectrum proved the identity with that of the product described above.

Preparation of D*-fucose from 15.* The 6-bromo-derivative (*15*) (2.0 g) was hydrogenated as described above to give a mixture of *13* and *14*. The crude mixture was debenzoylated with sodium methoxide in methanol and the solution was neutralized with Amberlite IR-120 (H^+), filtered and evaporated. The residue was crystallized from ethanol-ethyl acetate to give 150 mg (32 %) of D-fucose, m.p. 134 – 141 °C. A mixed m.p. with authentic D-fucose gave no depression.

Microanalyses were carried out at Novo Microanalytical Laboratory.

REFERENCES

1. Golding, B.T., Hall, D. R. and Sakrikar, S. *J. Chem. Soc. Perkin 1* (1973) 1214.
2. Exner, J. H. *Tetrahedron Lett.* (1975) 1197.
3. Bock, K. and Pedersen, C. *Carbohydr. Res. 29* (1973) 331.
4. Bock, K. and Pedersen, C. *Acta Chem. Scand. B 28* (1974) 1041.
5. Ball, D. J., Flood, A. E., and Jones, J. K. N. *Can. J. Chem. 37* (1959) 1018.
6. Lundt, I. and Pedersen, C. *Acta Chem. Scand. 26* (1972) 1938.
7. Rieche, A., Schmitz, E., Schade, W., and Beyer, E. *Chem. Ber. 94* (1961) 2926.
8. Williams, J. M. and Richardson, A. C. *Tetrahedron 23* (1967) 1369.

Received December 15, 1975.