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Note

The anomers of *p*-nitrophenyl 2,3,5-tri-*O*-benzyl-D-arabinofuranoside

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p-Nitrophenyl α-L-arabinofuranoside has been prepared by Fielding and Hough[1] in low yield by interaction of peracetylated L-arabinose with *p*-nitrophenol and mercuric cyanide, followed by deacetylation. In 1956, the anomeric pair of *p*-aminophenyl arabinopyranosides, in both the D and the L series, was prepared by fusion of the corresponding acetates with *p*-nitrophenol in the presence of catalysts, followed by deacetylation, and hydrogenation of the products[2].

We wished to link *p*-aminophenyl β-D-arabinofuranoside to the tyrosine units of bovine serum albumin (BSA) by diazo coupling[3] to see if the resulting antigen would cross-react with antibodies* to fructofuranans[4]. In order to prepare this glycoside, we decided to study the reaction of 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl chloride (**3**) with *p*-nitrophenol. 2,3,5-Tri-*O*-benzyl-β-D-arabinofuranose[5] (**1**) was readily converted into the known chloride **3** (which is mostly the α anomer) *via* its 1-*p*-nitrobenzoate (**2**). Initially, the chloride **3** was treated with sodium *p*-nitrophenoxide in aqueous acetone by the method of Seidman and Link[6]. The resulting reaction-mixture consisted mostly of 2,3,5-tri-*O*-benzyl-D-arabinofuranose, undoubtedly resulting from hydrolysis of **3**. Thus, this approach to the preparation of the anomeric *p*-nitrophenyl 2,3,5-tri-*O*-benzyl-D-arabinofuranosides (**4α** and **4β**) seemed fruitless.

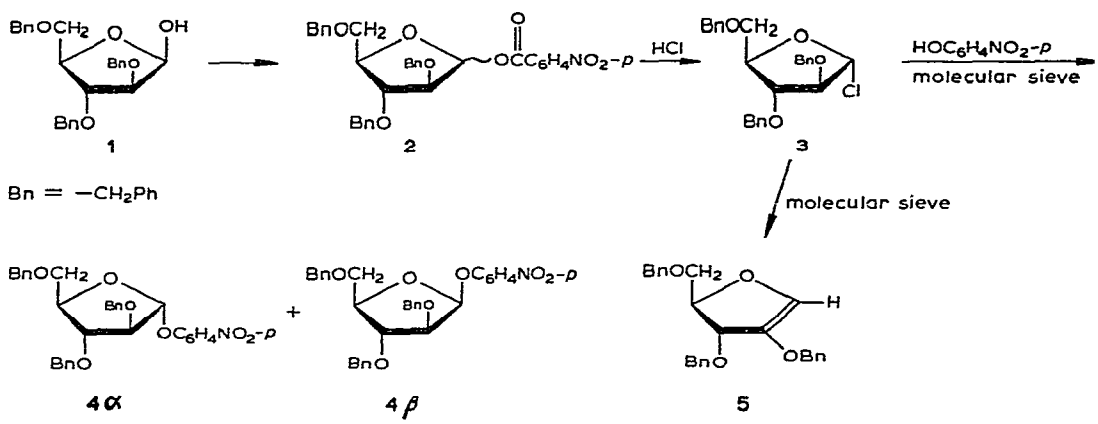
When the chloride **3** was treated with *p*-nitrophenol dissolved in dichloromethane in the presence of molecular sieve 4A as the acid acceptor[5], it yielded the two *p*-nitrophenyl glycosides, **4α** and **4β**, in the ratio of 7:1. Assignment of the anomeric configuration was based on the value of the optical rotation and on n.m.r. spectroscopy. Syrupy **4α** is highly dextrorotatory, and its anomeric proton appears as a singlet, indicating the *trans* orientation of H-1 and H-2. The glycoside **4β** was

*Hydrogenolysis, in the presence of palladium and hydrochloric acid, of **4β** (see later in this Note) in benzene–methanol, and subsequent coupling of the derived *p*-aminophenyl β-D-arabinofuranoside to BSA, yielded the expected product. This material, however, failed to precipitate with antibodies specific for fructofuranans.

crystallized; it is levorotatory, and shows, in its n.m.r. spectrum, a distinct doublet for H-1, indicating the *cis* relationship between H-1 and H-2.

In one experiment, the α-chloride **3** was stirred with molecular sieve for 15 min *prior* to addition of *p*-nitrophenol. From the mixture resulting, it was possible to isolate an unsaturated compound in 25% yield. Elemental analysis indicated this to be an anhydro-tribenzyl-pentenitol (presumably **5**). Chemical-ionization mass-spectrometry (c.i.m.s.) revealed a parent peak of 403, in agreement with the analysis. The n.m.r. spectrum of **5** showed no downfield anomeric proton, as expected. The vinylic proton could not be discerned separately in the spectrum, but it is believed to be hidden under the H-4 signal, as decoupling of this pattern revealed an otherwise unaccountable singlet.

From the fact that the reaction of the α anomer **3** with *p*-nitrophenol in dichloromethane mainly yields the α-glycoside (*i.e.*, with retention of configuration), it seems that the aglycon does not displace the halogen in **3** in the fashion of an SN2 displacement. It may be that, under the conditions here used, an ion-pair is formed at C-1 in **3**. The *p*-nitrophenol could then approach from that side which is *trans* to the benzyloxy group at C-2, thus producing mostly the α-D-glycoside.



EXPERIMENTAL

General. — The products were detected by t.l.c. on Silica Gel GF (250 μm; Analtech, Inc) by viewing under u.v. light, or by charring with 10% sulfuric acid. Separation of the products was achieved on precoated t.l.c. plates (20 × 20 cm) of Silica Gel 60 F-254 (2 mm; Merck, Darmstadt, Germany), and the bands were detected by viewing under u.v. light. Two solvent systems were used: *A*, 12:1 benzene–ethyl acetate, and *B*, 3:1 hexane (b.p. 65–68°)–ethyl acetate. Specific rotations were measured with a Perkin–Elmer 141 polarimeter, and n.m.r. spectra were recorded at 100 MHz with a Varian HA-100 spectrometer. 2,3,5-Tri-*O*-benzyl-β-D-arabino-furanose was purchased from Pfanstiehl Laboratories, Inc.

2,3,5-Tri-O-benzyl-D-arabinofuranosyl chloride (**3**). — 2,3,5-Tri-*O*-benzyl-1-*O*-(*p*-nitrobenzoyl)-D-arabinofuranose (**2**, 10 g), prepared from **1**, was treated with cold dichloromethane (210 ml) saturated with hydrogen chloride[5]. After 2 h at 0°, the precipitated *p*-nitrobenzoic acid was filtered off, and the filtrate evaporated *in vacuo* to a syrup (7.7 g, 97.8% yield) which remained stable indefinitely at −75°. The optical rotation and n.m.r. spectrum of the syrup indicated it to be mostly the α-D anomer; $[\alpha]_D^{20}$ +79.8° (*c* 1.3, chloroform); n.m.r. data (chloroform-*d*): δ 7.27 (d, 15 protons, Ph), 6.13 (s, 1 proton, H-1), 4.49, 4.52 (4-proton s, 2-proton s, PhCH_2), 4.34 (d, 1 proton, $J_{2,3}$ 2.0 Hz, H-2), 3.95 (dd, 1 proton, $J_{3,4}$ 6.6 Hz, H-3), and 3.62 (d, 2 protons, $J_{4,5}$ 4.4 Hz, H-5,5′).

p-Nitrophenyl 2,3,5-tri-O-benzyl-D-arabinofuranosides (**4α** *and* **4β**). — A solution of **3** (2 g) in dried dichloromethane (30 ml) containing molecular sieve (8.5 g; Type 4A, 1.59-mm pellets) and *p*-nitrophenol (1.3 g) was stirred overnight at room temperature. The molecular sieve was filtered off, and the filtrate was washed twice with 3% sodium hydroxide and twice with water, dried (sodium sulfate), and evaporated *in vacuo* to a syrup (1.9 g, 79.0% yield). The mixture of anomers could be resolved on t.l.c. plates (200 mg/plate) in system *A*. Based on several experiments, the ratio of α to β averaged ~7:1. Compound **4α**, isolated as a syrup, had $[\alpha]_D^{20}$ +119.5° (*c* 0.96, chloroform); n.m.r. data (chloroform-*d*): δ 8.18 (d, 2 protons, *J* 9.2 Hz, PhNO_2), 7.04 (d, 2 protons, *J* 9.2 Hz, PhNO_2), 7.30 (s, 15 protons, Ph), 5.73 (s, 1 proton, H-1), 4.57 (d, 6 protons, PhCH_2), 4.23–4.42 (m, 2 protons, H-2,4), 4.11 (dd, 1 proton, H-3), and 3.64 (d, 2 protons, $J_{4,5}$ 4.2 Hz, H-5,5′).

Anal. Calc. for $C_{32}H_{31}NO_7$: C, 70.96; H, 5.77; N, 2.59. Found: C, 71.17; H, 5.87; N, 2.58.

Compound **4β**, further resolved in system *B*, crystallized when triturated with a small amount of absolute ethanol. After recrystallization from ethanol–pentane, the prismatic needles had m.p. 58–60°, $[\alpha]_D^{20}$ −172.5° (*c* 0.7, chloroform); n.m.r. data (chloroform-*d*): δ 8.14 (d, 2 protons, *J* 9.0 Hz, PhNO_2), 7.04 (d, 2 protons, *J* 9.0 Hz, PhNO_2), 7.30 (15 protons, Ph), 5.49 (d, 1 proton, $J_{1,2}$ 3.2 Hz, H-1), 4.70, 4.65, 4.37 (2-proton d, 2-proton d, 2-proton s, PhCH_2), 4.14–4.33 (m, 3 protons, H-2,3,4), and 3.45 (d, 1 proton, $J_{4,5}$ 5.2 Hz, H-5,5′).

Anal. Calc. for $C_{32}H_{31}NO_7$: C, 70.96; H, 5.77; N, 2.59. Found: C, 70.96; H, 5.64; N, 2.44.

1,4-Anhydro-2,3,5-tri-O-benzyl-D-erythro-pent-1-enitol (**5**). — A solution of **3** (10.6 g) in dry dichloromethane (175 ml) was stirred with molecular sieve (40 g) for 15 min. *p*-Nitrophenol (6.9 g) was added, and the mixture was stirred overnight. Isolated as described in the previous experiment, a syrup (10.4 g) was obtained. A portion (0.4 g) of the syrup was resolved on two t.l.c. plates in system *A*. The lower band, a mixture of **4β** and **5**, was chromatographed (system *B*) a second time on one t.l.c. plate, yielding 0.1 g of **5**; $[\alpha]_D^{20}$ +6.8° (*c* 1.0, chloroform); n.m.r. data (chloroform-*d*): δ 7.32 (d, 15 protons, Ph), 4.57, 4,69, 4.78 (2-proton s, 2-proton s, 2-proton d, PhCH_2), 4.16–4.32 (m, 2 protons, H-1,4), 4.04 (d, 1 proton, $J_{3,4}$ 4.6 Hz,

H-3), and 3.65 (d, 2 protons, $J_{4,5}$ 5.4 Hz, H-5,5'). C.i.m.s. (methane) of **5** showed the presence of an M+1 peak of 403.

Anal. Calc. for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51. Found: C, 77.44; H, 6.74.

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