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Note

Ammonolysis reaction of octa-*O*-benzoylmelibiononitrile

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The reaction of ammonia with acetylated, benzoylated, and propanoylated aldononitriles has been extensively studied[1], but its extension to aldobiononitriles was limited to the acetylated derivatives. Octa-*O*-acetylcellobiononitrile[2], octa-*O*-acetyllactononitrile[3], and octa-*O*-acetylmelibiononitrile[4] gave the expected nitrogenated derivatives and the free hexapyranosylpentoses. Some hexapyranosylpentoses were prepared in high yield from the same aldobiononitriles, by reaction with sodium methoxide[5,6]. This reaction had been already described in the older literature[7], but it gave complex mixtures as it was applied to impure products.

We describe herein the reaction of octa-*O*-benzoylmelibiononitrile[8] (**1**) with methanolic ammonia, which gave a total yield of 51.3% of nitrogenated compounds. This is a yield much higher than that usually reported for such products from acetylated aldobiononitriles[2–4]. In every case, the main, nitrogenated product was the 1,1-bis(acylamido)-1-deoxyglycopyranosylpentitol. Yields of nitrogenated compounds formed by ammonolysis of octa-*O*-benzoyldisaccharides[9] were also higher than those obtained from the corresponding acetylated disaccharides[10]. This may be attributed to the higher resistance to ammonolysis of the benzoyl groups, leaving them available for migration, especially from O-3 and O-4 to the nitrogen atoms introduced at C-1 (ref. 11).

The relative proportion of 1,1-bis(acylamido)-1-deoxyaldobiitol to *N*-acylaldobiosylamines obtained in the previously studied ammonolysis of octa-*O*-acetylmelibiononitrile[4] was 3:1, and a similar ratio was obtained for the octabenzoate **1**. Thus 37.7% of 1,1-bis(benzamido)-1-deoxy-5-*O*-α-D-galactopyranosyl-D-arabinitol (**2**), 7.7% of *N*-benzoyl-5-*O*-α-D-galactopyranosyl-α-D-arabinofuranosylamine (**4**), and 5.9% of *N*-benzoyl-5-*O*-α-D-galactopyranosyl-β-D-arabinofuranosylamine (**5**) were isolated and characterized as their per-*O*-acetyl derivatives **3**, **6**, and **7**. In the ammonolysis of octa-*O*-acetylmelibiononitrile[4], only the *N*-acetyl analog of **3**, and not its β anomer was obtained. A preponderance of the α over the β anomer should

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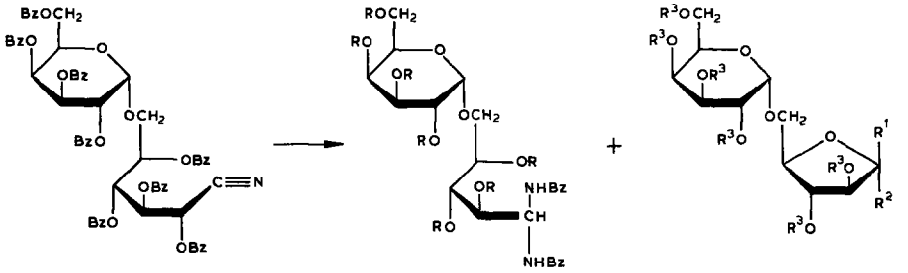
be expected for steric reasons, and it is noteworthy that a significant proportion of compound **5** was formed.

The free sugars 5-*O*-α-D-galactopyranosyl-α-D-arabinofuranose (**6**) (1.7%) and 5-*O*-α-D-galactopyranosyl-β-D-arabinofuranose (**7**) (1.4%) were formed in low yield, but they could be obtained in 86% yield, as a mixture, by degradation of **1** with sodium methoxide.



1

2 R = H
3 R = Ac

4 $R^1 = R^3 = H, R^2 = NHBz$
5 $R^1 = NHBz, R^2 = R^3 = H$
6 $R^2 = NHBz, R^3 = Ac, R^1 = H$
7 $R^1 = NHBz, R^2 = H, R^3 = Ac$
8 $R^1 = R^3 = H, R^2 = OH$
9 $R^1 = OH, R^2 = R^3 = H$

EXPERIMENTAL

General methods. — Melting points were determined with a Unimelt (Thomas–Hoover) instrument and are uncorrected. Optical rotations were measured at 20° with a Perkin–Elmer 141 polarimeter. T.l.c. was performed, on plates coated with Silica gel G (Merck, Darmstadt), with 17:3 (v/v) benzene–ethanol, and the spots were detected with I_2 vapor and the hydroxamic acid test[12]. Paper chromatography was performed on Whatman No. 1 paper by the descending technique using D-glucose as standard, and 5:2:2 (v/v) butanol–ethanol–water as solvent. Whatman CF 11 cellulose was used for column chromatography. For preparative paper chromatography, three developments on Whatman 3MM paper were performed with the same solvent. The reagents used were (*A*) $AgNO_3$–sodium methoxide[13] and (*B*) aniline hydrogen phthalate[14]. Solutions were evaporated under diminished pressure below 50°. Octa-*O*-benzoylmelibiononitrile was prepared as described[8].

*Ammonolysis of 2,3,4,5,2',3',4',6'-octa-*O*-benzoylmelibiononitrile* (**1**). — *Isolation of 1,1-bis(benzamido)-1-deoxy-5-*O*-α-D-galactopyranosyl-D-arabinitol* (**2**). Compound **1** (20 g) was dissolved in 16% methanolic ammonia (500 mL) by shaking for 0.5 h. The solution was kept for 24 h at room temp., evaporated to dryness, and

the residual syrup extracted with hot ethyl acetate (6 × 50 mL). The residue was dried in a vacuum desiccator and then dissolved in methanol (50 mL). After two crystallizations from methanol, **2** was obtained as needles (0.96 g), m.p. 231–232° (dec.), $[\alpha]_D^{20}$ +78.5° (*c* 0.7, pyridine); R_{Glc} 2.25 (reagent *A*), reagent *B* did not show a spot. The total amount of **2** obtained was 3.45 g (37.7%).

Anal. Calc. for $C_{25}H_{32}N_2O_{11}$: C, 55.97; H, 5.96; N, 5.22. Found: C, 55.85; H, 5.98; N, 5.35.

Chromatographic separation of **2, 4, 5, 8,** *and* **9**. The mother liquors from the crystallization of **2** were evaporated, and the residual syrup was chromatographed on a cellulose column (45 × 940 mm); 360 fractions of 15 mL each were collected. Fractions 10–69 gave benzamide, fractions 70–85 benzamide and **2** (0.08 g), and fractions 92–100 **2** (2.4 g).

1-N-*Benzoyl-5*-O-α-D-*galactopyranosyl*-α-D-*arabinofuranosylamine* (**4**). This compound was obtained from fractions 111–133 as a syrup (0.55 g, 7.7%); $[\alpha]_D^{20}$ +120.4° (*c* 1, methanol), R_{Glc} 1.15 (reagent *A*).

Anal. Calc. for $C_{18}H_{25}NO_{10}$: C, 52.04; H, 6.02; N, 3.37. Found: C, 51.72; H, 5.61; N, 3.24.

1-N-*Benzoyl-5*-O-α-D-*galactopyranosyl*-β-D-*arabinofuranosylamine* (**5**). This compound was obtained from fractions 135–168 as a syrup (0.42 g, 5.9%), $[\alpha]_D^{20}$ +100.2° (*c* 1.3, methanol), R_{Glc} 0.38 (reagent *A*).

Anal. Calc. for $C_{18}H_{25}NO_{10}$: C, 52.04; H, 6.02; N, 3.37. Found: C, 51.85; H, 5.72; N, 3.18.

5-O-α-D-*Galactopyranosyl*-α-D-*arabinofuranose* (**8**) *and 5*-O-α-D-*galactopyranosyl*-β-D-*arabinofuranose* (**9**). The evaporation of fractions 171–274 gave a mixture of **8** and **9** (0.14 g). It was separated by preparative paper chromatography to give **8** (0.09 g, 1.7%) and **9** (0.03 g, 0.6%). From fractions 275–340, **9** (0.04 g, 0.8%) was obtained as a syrup. Compound **8** gave R_{Glc} 0.44 (reagent *A* and *B*), $[\alpha]_D^{20}$ +98° (10 min)→ +82.1° (66 h; *c* 0.8, water); lit.[4] R_{Glc} 0.44, $[\alpha]_D$ +82° (equil.). Compound **9** gave R_{Glc} 0.18 (reagents *A* and *B*), $[\alpha]_D^{20}$ +76.1 (10 min)→ +82° (96 h; *c* 1, water); lit.[4] R_{Glc} 0.18, $[\alpha]_D$ +82.2° (equil.).

2,3,4-Tri-O-*acetyl-1,1-bis(benzamido)-1-deoxy-5*-O-*(2,3,4,6-tetra*-O-*acetyl*-α-D-*galactopyranosyl)*-D-*arabinitol* (**3**). — Compound **2** (90 mg) was dissolved in 1:1 pyridine–acetic anhydride (5 mL) by heating for 5 min in a boiling-water bath. The mixture was kept for 24 h at room temp. and evaporated to dryness in a vacuum desiccator. Crystallization from 1:2 methanol–water gave **3** (128 mg, 97%), needles, m.p. 111–114°, $[\alpha]_D^{20}$ +100.3° (*c* 0.7, chloroform), t.l.c. R_F 0.62.

Anal. Calc. for $C_{39}H_{46}N_2O_{18}$: C, 56.38; H, 5.54; N, 3.37. Found: C, 56.08; H, 5.95; N, 3.65.

2,3-Di-O-*acetyl-1*-N-*benzoyl-5*-O-*(2,3,4,6-tetra*-O-*acetyl*-α-D-*galactopyranosyl)*-α-D-*arabinofuranosylamine* (**6**). — Compound **4** (178 mg) was acetylated with pyridine–acetic anhydride (13 mL) by the same procedure described for **3**. The resulting syrup was purified by preparative t.l.c. and gave **6** (197 mg, 68%), m.p. 125–128°, $[\alpha]_D^{20}$ +95.3° (*c* 0.5, chloroform); R_F 0.50.

Anal. Calc. for $C_{30}H_{37}NO_{16}$: C, 53.97; H, 5.54; N, 2.09. Found: C, 53.52; H, 5.83; N, 1.85.

2,3-Di-O-acetyl-1-N-benzoyl-5-O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-β-D-arabinofuranosylamine (**7**). — Compound **5** (47 mg) was acetylated with pyridine–acetic anhydride (10 mL) by the same procedure described for **3**. Crystallization from 1:3 methanol–water gave **7** (68 mg, 91%), needles, m.p. 76–78°, $[\alpha]_D^{20}$ +90.6° (*c* 1, chloroform); t.l.c. R_F 0.68.

Anal. Calc. for $C_{30}H_{37}NO_{16}$: C, 53.97; H, 5.54; N, 2.09. Found: C, 53.65; H, 5.42; N, 1.76.

Zemplén degradation of octa-O-benzoylmelibiononitrile (**1**). — Compound **1** (3.0 g) was dissolved in dichloromethane (6 mL), the solution cooled to 0°, and 0.5-mL aliquots of a 2% sodium methoxide in methanol solution were added portionwise, keeping the pH of the mixture over 8. After 2 min of mixing, a gelatinous mixture was obtained. It was kept for 10 min at 5°, and acetic acid was added until neutral. The organic layer was evaporated to dryness and gave 0.69 g (86.2%) of a syrup containing **8** and **9**.

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