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Note

A convenient method for shortening the sugar chain: degradation of D-glucose to D-arabinose

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As regards mildness and good yield, the most convenient methods for shortening the carbon chain of sugars are those which afford splitting of the chain by periodic acid or by lead tetraacetate. These methods require a pair of free hydroxyl groups on adjacent carbon atoms as the point of attack, and suitable protection of the other hydroxyl groups.

In connection with our studies[1] on the biosynthesis of the mitomycin antibiotics, we needed a convenient method for the preparation of labeled D-arabinose from labeled D-glucose. The present work describes a mild, simple method for the preparation of D-arabinose from D-glucose in 59% overall yield by the use of periodate oxidation.

The pair of free, 1,2-*cis* hydroxyl groups was elaborated from 1,2-*O*-isopropylidene-α-D-glucofuranose (**1**), which is readily prepared[2] from D-glucose in high yield. The hydroxyl groups in **1** were protected by benzoylation, giving 3,5,6-tri-*O*-benzoyl-1,2-*O*-isopropylidene-α-D-glucose (**2**). The benzoyl group was the protecting group of choice, as it is readily introduced, and is sufficiently stable to allow the removal of the isopropylidene group by acid hydrolysis without acyl migration. Compound **2** was hydrolyzed[3,4] with a mixture of acetic acid and hydrochloric acid, to afford 3,5,6-tri-*O*-benzoyl-D-glucose (**3**), which was oxidized with sodium metaperiodate, giving 2,4,5-tri-*O*-benzoyl-D-arabinose (**4**) as a foamy syrup. Chemical ionization mass-spectroscopic analysis of **4** showed *m/e* + at 463 (*m/e* 462 corresponds to the molecular formula $C_{26}H_{22}O_8$). Compound **4** was identified as the semicarbazone. Debenzoylation of **4** with 0.2M sodium methoxide afforded chromatographically pure D-arabinose (59% overall yield) which crystallized readily. Attempts to use the acetyl[5] group for protection were unsuccessful, as acid hydrolysis of the *O*-acetyl analog of **2** under a variety of conditions resulted not only in removal of the isopropylidene group but in removal of the acetyl groups as well.

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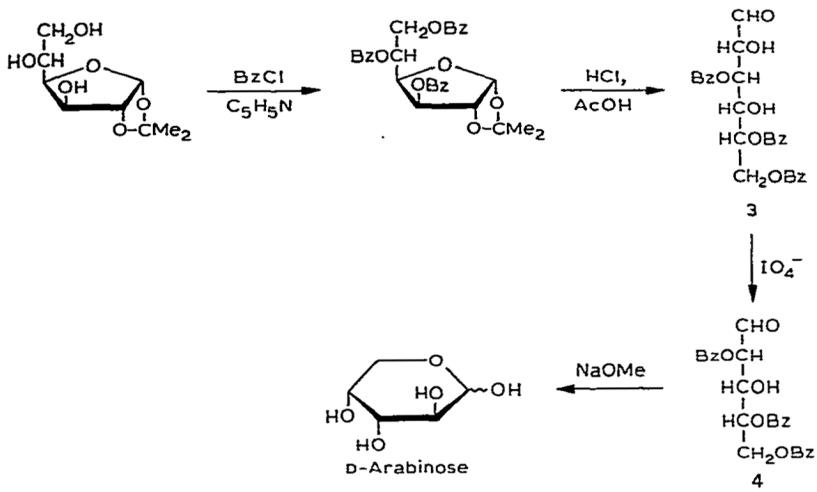

The method presented here may probably be generalized for the chain-shortening of all aldoses from which a 1,2-*O*-isopropylidene derivative can be prepared.

EXPERIMENTAL

General. — Evaporations were performed under diminished pressure below 50°. Thin-layer chromatography (t.l.c.) was conducted on silica gel (Kieselgel G, Merck) with the following solvent systems: *A*, benzene–methanol, (4:1) and *B*, pyridine–ethyl acetate–water (1:2:2, upper layer). Mass spectra were recorded with a Dupont 21–492B mass spectrometer. Combustion analyses were performed in the Department of Chemistry, Purdue University.

2,4,5-Tri-O-benzoyl-D-glucose (**4**). — A solution of 3,5,6-tri-*O*-benzoyl-D-glucose[3,4] (**3**; 4.5 g) in ethanol (200 mL) was cooled to 10°, and treated with a cold solution of 0.2M sodium metaperiodate (50 mL) with stirring. After addition of all of the periodate, the suspension was filtered from the precipitated sodium iodate, and the filtrate was kept for 1 h at room temperature; t.l.c. (solvent *A*) indicated complete consumption of **3**. The excess of periodate and iodate was removed by stirring with barium carbonate (1.89 g) and filtering. The filtrate was evaporated to dryness, and extracted with chloroform, and the extract was dried (anhydrous sodium sulfate), filtered, and concentrated, giving a chromatographically homogeneous (t.l.c.) syrup, R_F 0.78 (solvent *A*). The chemical-ionization mass-spectrum showed $m/e + 1$ at 463 (calc. m/e 462).

2,4,5-Tri-O-benzoyl-D-arabinose semicarbazone. — A solution of **4** (0.5 g) in ethanol (3 mL) was treated with equimolar amounts of semicarbazide hydrochloride and potassium acetate in the minimal volume of water, and kept for 5 h at room temperature. The mixture was evaporated to dryness, and extracted with ether, and the extract was dried (anhydrous sodium sulfate), and evaporated, affording a syrup which

crystallized from benzene or ethyl acetate as colorless needles, m.p. 178–180°, $[\alpha]_D^{24}$ +10.4° (*c* 0.8, methanol); t.l.c. (solvent A): single spot, R_F 0.84.

Anal. Calc. for $C_{27}H_{25}N_3O_8$: C, 62.42; H, 4.85; N, 8.08. Found: C, 62.26; H, 5.02; N, 8.10.

D-*Arabinose.* — A solution of **4** (3.5 g) in methanol (120 mL) was cooled to 0°, treated with a cold solution of 0.2M sodium methoxide (100 mL), and kept for four days at 5°. The solution was made neutral with solid carbon dioxide, concentrated to a small volume, and extracted with ether (3 × 100 mL) to remove methyl benzoate. The aqueous layer was demineralized by passage through a column of Amberlite IR-120 (H^+) cation-exchange resin, and evaporated to dryness; yield, 0.9 g (59% overall yield from D-glucose); t.l.c. (solvent *B*), one spot at the R_F of D-arabinose (R_F 0.68). The product was crystallized by dissolving in a small volume of hot methanol, adding ethanol, and refrigerating, m.p. and mixed m.p. 158–159°, $[\alpha]_D^{24}$ −102.3° (*c* 3.3, water) (lit.[6] $[\alpha]_D^{22}$ −102°).

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