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### A new synthesis of D-psicose (D-ribo-hexulose)

D-Psicose has previously been prepared by the epimerization of D-altrose<sup>1,2</sup>, and by the action of diazomethane on tetra-O-acetyl-D-ribonyl chloride with subsequent deacetylation of the resulting *keto*-D-psicose pentaacetate<sup>3</sup>. Recent work<sup>4,5</sup> in which methyl sulfoxide-acetic anhydride was used to oxidize secondary alcoholic groups to ketonic groups suggested that 1,2:4,5-di-O-isopropylidene- $\beta$ -D-erythro-2,3-hexodiulose (2) might be preparable by similar oxidation of 1,2:4,5-di-O-isopropylidene- $\beta$ -D-fructopyranose (1).

Reduction of this diulose acetal (2) should then afford a mixture of 1,2:4,5-di-Oisopropylidene- $\beta$ -D-*ribo*-hexulopyranose (3) and the corresponding D-fructose acetal (1). Study of a molecular model of 2 suggested that the favored conformer is that skew form (S<sup>0</sup><sub>3</sub>) in which both dioxolane rings are *exo* (2*a*), and indicated that borohydride reduction would favor formation of 3. From seven of the eleven conformations of 2 considered, the D-*ribo* isomer (3) alone would be expected, whereas, for the four others,



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# NOTES

there seemed to be little difference in the freedom of approach of the borohydride to the carbonyl group, and hence both the *ribo* and *arabino* isomers would be expected to be formed. Experimentally, it was found that 3 is formed almost exclusively; acid hydrolysis then gives 4. With this relatively simple procedure, D-psicose (4) becomes readily available.

# EXPERIMENTAL

General. — The oxidation, reduction, and hydrolysis reactions were followed by means of t.l.c. on Silica Gel G, with 3:1 (v/v) ethyl acetate-petroleum ether as the developer, and a spray of concentrated sulfuric acid, followed by charring, as the indicator:  $R_F$  of 1, unity; of 3-O-acetyl-1,2:4,5-di-O-isopropylidene- $\beta$ -D-fructose (5), 1.26; of 2, 1.18; of 3, 0.86; and of 4, 0.00.

1,2:4,5-Di-O-isopropylidene- $\beta$ -D-erythro-2,3-hexodiulo-2,6-pyranose (2). — Acetic anhydride (2 ml) was added to a solution of compound 1 (5.2 g; 0.02 mole) in 100 ml of methyl sulfoxide. After 48 h, t.l.c. indicated that compound 1 had been converted into 2 and 5. The reaction mixture was evaporated under diminished pressure to a syrup, from which 2 crystallized; yield 3.6 g (70%). Compound 2 was recrystallized from methanol, m.p. 101–102°;  $[\alpha]_{D}^{25} - 100.4^{\circ}$  (c 2.41, acetone).

Anal. Calc. for C<sub>12</sub>H<sub>18</sub>O<sub>6</sub>: C, 55.81; H, 7.03. Found: C, 56.15; H, 7.08.

The mother liquor contained both 2 and 5.

1,2:4,5-Di-O-isopropylidene- $\beta$ -D-psicopyranose (3). — To a solution of 2 (2.8 g; 0.011 mole) in 1:3 (v/v) water-methanol (80 ml), cooled in an ice bath, was added alkaline sodium borohydride (100% excess). After 30 min, the conversion of 2 into 3 was complete, and only a trace of 1 was detected in the product. After addition of 50 ml of water, the solution was evaporated to dryness under diminished pressure, and the residue was dissolved in water. The solution was repeatedly extracted with chloroform, and the extracts were combined, dried (sodium sulfate), and evaporated to dryness; the residue was dissolved in petroleum ether (b.p. 30-60°), and the solution cooled to give 3, yield 1.89 g (65%), m.p. 60-61°, lit. m.p.<sup>2</sup> 57-58.5°.

D-Psicose (4). — A solution of 3 (1 g) in water (5 ml) was mixed with 0.5 g of Dowex-50 W x8 (H<sup>+</sup>) cation-exchange resin, and the suspension was stirred for 75 min at 95°; t.l.c. then showed that hydrolysis was complete. The mixture was filtered through activated carbon, and the filtrated was evaporated to dryness under diminished pressure to a syrup that was identified as D-psicose by conversion into its phenyloso-triazole, m.p. 135–136°, lit. m.p.<sup>6</sup> 135–136°.

The product was also identified as D-psicose by high-voltage electrophoresis in sodium borate buffer. An authentic sample of 4 was prepared by an earlier procedure<sup>2</sup>. Both samples had  $R_{Fru}$  0.82. The electrophoresis was performed in an apparatus built according to the specifications of Gross<sup>7</sup>, and the separations were made under the following conditions: Whatman No. 3 MM filter paper; voltage gradient, 86 volts/cm; temp.,  $13 \pm 1^{\circ}$ ; time, 40 min; and buffer, 0.05M Na<sub>2</sub>B<sub>4</sub>O<sub>7</sub> (pH 9.2). Chromatograms were sprayed with an aqueous solution of urea (0.5M) and tartaric acid (M), and then

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heated<sup>8</sup> at 105° for 10 min. In the presence of borate ions, D-psicose (4) and D-fructose give a blue color with this reagent.

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Cane Sugar Refining Research Project, Southern Regional Research Laboratory, New Orleans, Louisiana 70119 (U. S. A.)

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EMMA J. MCDONALD