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Note

An improved synthesis of methyl 2,3-anhydro-α-D-lyxofuranoside

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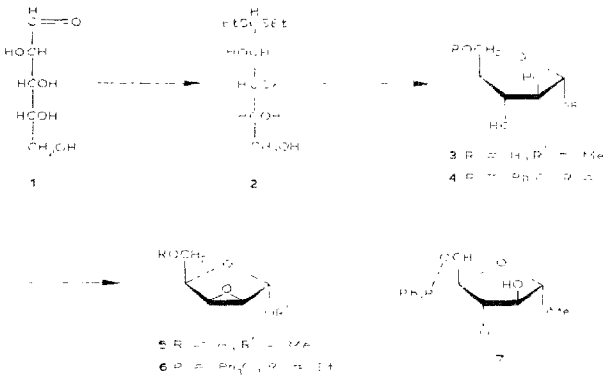
Methyl 2,3-anhydro-β-D-lyxofuranoside (**5**) is an important intermediate in the synthesis of 3-substituted derivatives of D-arabinose[1–3]. Compound **5** is most commonly prepared by a four-step conversion of D-xylose into methyl 2-*O*-mesyl-D-xylofuranoside, followed by methoxide-promoted epoxide formation[3,4]. Recently, one of us reported the synthesis of 4-deoxy-4-fluoro-D-mannose by a one-carbon chain-extension of 3-deoxy-3-fluoro-D-arabinose[5], which in turn was derived from **5**. The finding that 4-deoxy-4-fluoro-D-mannose is an effective inhibitor of protein glycosylation[6] prompted us to design a more convenient and high-yielding synthesis of methyl 2,3-anhydro-α-D-lyxofuranoside. Here we report a simple, three-step synthesis of **5** in 66% overall yield from D-arabinose.

Treatment of D-arabinose (**1**) with ethanethiol according to the procedure of Wolfrom *et al.*[7] afforded the diethyl dithioacetal **2** in 88% yield. By modifying the method first reported by Green and Paesu[8], dithioacetal **2** was oxidized in the pre-



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sence of methanolic $HgCl_2$–HgO, to give mainly the kinetic product, namely, methyl α-D-arabinofuranoside (**3**). Less then 5% of the β-furanoside was observed in the crude product. Triphenylphosphine (Ph_3P)–diethylazodicarboxylate (DEAD)[9,10] selectively converted the vicinal diol grouping in **3** into the *lyxo*-epoxide **5** in an overall yield of 76% from **2**.

The remarkable efficiency of this epoxidation paralleled the results obtained by Mengel and Bartke[9a] with 9-β-D-arabinofuranosyladenine[9] and by Guthrie and co-workers[10] with methyl α-D-fructofuranoside, but the mechanistic basis for these results is unclear. Favored formation of the primary phosphonium salt of **3** would lead, *via* the cyclic C-5–C-3 phosphorane **7**, to an activated C-3 phosphonium salt. However, trityl ether **4** was converted into its epoxide **6** in almost quantitative yield on treatment with Ph_3P–DEAD. Favored activation of C-3 has also been observed for aldopyranosides containing free 2- and 3-hydroxyl groups[11].

EXPERIMENTAL

General. — Melting points were determined with a Thomas–Hoover capillary melting-point apparatus and are uncorrected. Specific rotations were measured with a Perkin–Elmer Model 141 polarimeter. ^{1}H-N.m.r. spectra were recorded with a Bruker WM-300 spectrometer.

D-*Arabinose diethyl dithioacetal* (**2**). — D-Arabinose (**1**, 30 g) was subjected to the procedure of Wolfrom *et al.*[7], and the crude product was recrystallized from methanol (300 mL) to afford **2** (45.3 g, 88%), m.p. 125–126°; lit.[8] m.p. 125–126°.

Methyl 2,3-anhydro-α-D-*lyxofuranoside* (**5**). — To a rapidly stirred suspension of HgO (42 g, 194 mmol) and $HgCl_2$ (52 g, 192 mmol) in anhydrous methanol (600 mL) at −20° was added solid **2** (24.4 g, 95 mmol) portionwise during 5 min. The mixture was allowed to warm to room temperature during 5 h, and the suspension filtered. The filtrate was treated with pyridine (10 mL), and kept overnight at −20°. The precipitated mercury salts were filtered off, and the filtrate evaporated *in vacuo* to a semisolid paste which was dissolved in anhydrous oxolane (THF; 200 mL, distilled under N_2 from sodium benzophenone), and the solution evaporated in a rotary evaporator. This process was repeated with a fresh portion of THF (200 mL) to remove traces of methanol. The oily residue comprised virtually pure **3**, which was used in the next step without purification.

Crude **3** was dissolved in anhydrous THF (170 mL), Ph_3P (30 g, 114 mmol) was added, and the resulting solution was heated to reflux under N_2. A solution of DEAD (18 mL, 114 mmol) in THF (30 mL) was added dropwise, and, when addition was complete, water (3 mL) was introduced, and the mixture was cooled, and evaporated under diminished pressure to an oil. Hot diethyl ether (300 mL) was added, to precipitate triphenylphosphine oxide, and the two-phase mixture was kept overnight at −20°. The supernatant liquor was then decanted, and evaporated to an oil. After repeating this precipitation, the ether-soluble residue was dissolved in the minimal volume of CH_2Cl_2, and chromatographed on silica gel (200 g), elut-

ing first with CH_2Cl_2 (1.5 L), and then with 1:9 MeOH–CH_2Cl_2 (1 L). The second eluant afforded several fractions of epoxide **5**, contaminated with residual Ph_3PO. This material was distilled in a Kugelrohr apparatus (oven temperature, 130°) at 1.33 Pa, and crystallized from 1:1 $CHCl_3$–hexane, to furnish pure **5** (10.45 g, 75%) having m.p., specific rotation, and ^1H-n.m.r.-spectral data identical with the reported values[2,3].

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