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CARBON-CHAIN EXTENSION THROUGH C-1 OF 2-DEOXYALDOSE DITHIOACETAL DERIVATIVES: A ROUTE TO 1,3-DIDEOXY-2-KETOSES*†

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ABSTRACT

The 3,4 : 5,6-diisopropylidene acetal (**3**) of 2-deoxy-D-*arabino*-hexose underwent abstraction of H-1 by butyllithium in oxolane at −30°; iodomethane reacted readily with the resultant anion to give the 1,3-dideoxy-2-heptulose derivative **4**, and C-1 benzylation could likewise be effected. Attempted deacetonation of **4** gave mixtures, although 6,7-monodeacetonation could be achieved in high yield, affording access *via* glycol cleavage–reduction to the 1,3-dideoxy-2-hexulose derivative. Demercaptalation of **4** gave the acetal-protected 1,3-dideoxy-2-heptulose, which underwent methanolysis to give crystalline methyl 1,3-dideoxy-α-D-*arabino*-heptulopyranoside. Anions of the type derived from **3** have broad, synthetic potential for access to chain-extended, 2-keto sugar derivatives of interest as metabolic intermediates, and for synthesis of deoxy analogs of such nucleoside antibiotics as psicofuranine and decoyinine.

INTRODUCTION

There has been considerable interest in this laboratory in the development of routes to chain-extended sugars[2] for access to novel sugars, metabolites, and components of antibiotics. The synthetic potential of anions derived from the readily accessible dithioacetals of aldoses[3] prompted an earlier study[4] wherein it was shown that an oxygenated substituent vicinal to the dithioacetal undergoes ready elimination upon attempted generation of the carbanion, leading to a ketene dithioacetal, a type of intermediate that has proved very useful[5] for preparation of 2-deoxyaldoses and stereospecifically 2-deuterated analogs thereof. The use of such simple dithianyl anions as 2-lithio-1,3-dithiane as addends to epoxy and keto sugars is a well established[3] route[6] for carbon-chain extension and branching. By way of addition to suitable lactone derivatives, the reaction provides access to chain-extended dicarbonyl sugars[7].

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†For a preliminary account, see ref. 1.

As simple 2-alkyl-1,3-dithianes can be alkylated[8] at C-2 *via* an intermediate lithium salt, the possibility of applying this general method with sugar dithioacetals was considered feasible by employing a dithioacetal derivative lacking an oxygenated substituent at C-2. The present report describes the successful application of this procedure for the C-1 chain-extension of a diethyl dithioacetal of a 2-deoxyhexose derivative. The products are of interest in relation to synthesis of analogs of such nucleoside antibiotics as psicofuranine[9] (**1**) and decoyinine[10] (**2**), which are produced by *Streptomyces hygroscopicus*; these compounds may be regarded as C-1′-substituted glycofuranosyl nucleosides, and both interfere with the growth of microbial and mammalian cells[11,12]. This chain-extension sequence is also of interest in relation to practical syntheses of labeled 3-deoxy-D-*arabino*-heptulosonic acids; alternative routes to this key metabolic intermediate in the shikimic acid biosynthetic pathway are the subject of a separate, current investigation[13].

RESULTS AND DISCUSSION

Treatment of 2-deoxy-3,4:5,6-di-*O*-isopropylidene-D-*arabino*-hexose diethyl dithioacetal[14] (**3**, prepared as a distilled syrup in quantitative yield by acetonation of 2-deoxy-D-*arabino*-hexose diethyl dithioacetal) with butyllithium in oxolane at −30° generated the anion at C-1, and the solution turned from colorless to pale yellow. After 1–2 h at about −25°, the alkylating reagent (iodomethane or α-bromotoluene) was added, and the solution was warmed to 0° and kept at this temperature for 18 h. The corresponding C-1-substituted products **4** (or **5**) were obtained as oils in 83 and 76% yields, respectively. Although the starting material and the product had essentially identical R_F values in t.l.c., the starting material gave a distinct, black spot when sprayed with 5% sulfuric acid, whereas the C-1-alkylated product charred brownish-yellow. The products gave acceptable elemental analyses, and mass spectra verified that H-1 had, indeed, been replaced by a methyl (or benzyl) group. The most prominent high-molecular-weight peaks for both **4** and **5** included the molecule-ion (M^+) and $M^+ - 15$ ($-CH_3$). The mass spectrum of the alkylated product (**4**, *m/e* 364, M^+) showed no peak at *m/e* 335, indicating that no starting dithioacetal (**3**, mol. wt. 350) remained unreacted. Further characterizing details for **4** and **5**, including ^{1}H-n.m.r. data, are recorded in the Experimental section.

It is noteworthy that deprotonation of **3** was not effected when sodium methylsulfinyl carbanion in dimethyl sulfoxide (the reagent of choice[4] for converting acetal-protected aldose dithioacetals into ketene dithioacetals) was utilized, and recovery of **3** was essentially complete.

Having successfully established the high-yielding, C-1 alkylation of **3**, methods for selective deprotection of the products, in particular the 1-*C*-methyl derivative **4**, were examined. Deacetonation of **4** proved unexpectedly troublesome, but it was eventually found that methanol containing a trace of sulfuric acid, acting for 48 h at ~25°, removed a single *O*-isopropylidene group, and the 4,5-monoacetal (**6**) was obtained in 80% yield as a syrup that had a specific rotation close to zero. Conclusive

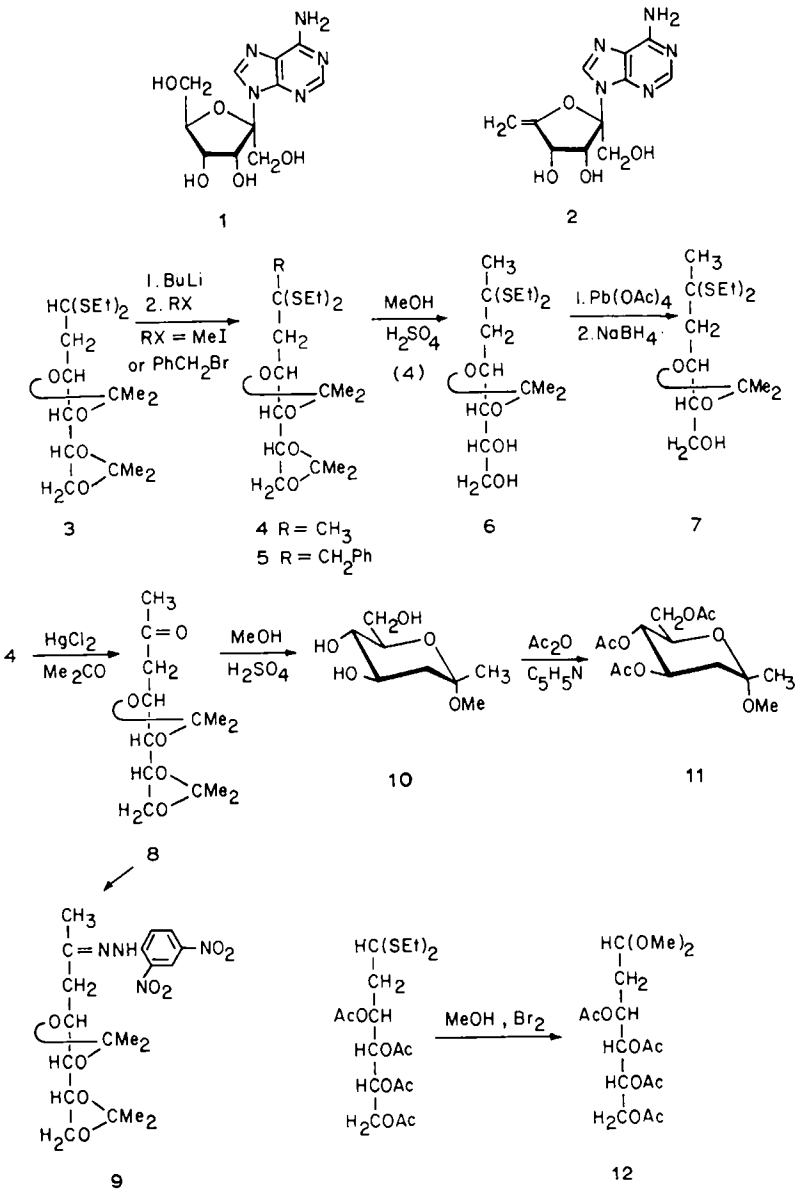
evidence that **6** was the 4,5- and not the 6,7-monoacetal ("evidence" from m.s. could be distinctly misleading) was provided by the sequence of lead tetraacetate oxidation–borohydride reduction, which gave the corresponding 1,3-dideoxyhexulose derivative **7**; *m/e* 294 (M^+).

In other attempts to achieve complete deacetonation of **4**, the results ranged from recovery of starting material (aqueous acetic acid for 72 h at ~25°) to immediate blackening of the solution (9:1 trifluoroacetic acid–water at ~25°) with extensive decomposition of the deacetonated product after 30 min. Use of sulfuric acid in methanol at higher acid concentration than that used preparatively for **6** gave a 1:5:1 mixture of three products having R_F values (3:17 methanol–chloroform) of 0.95, 0.45 (**6**), and 0.1. The fast-moving product ($C_{11}H_{16}O_3S$ by high-resolution m.s.) appeared to be a monoacetoxy-1-(ethylthio)-1-methyl-furan or -pyran, and the slowest-moving product was a fully deacetonated, methyl glycoside (**10**, to be described later); the procedure could not be modified to give a preparatively useful route of access to the fully deacetonated analog of **4**, nor did use of a cation-exchange resin as the acid catalyst significantly affect the product ratios.

Demercaptalation of the acetal-protected derivative **4** with mercuric chloride in acetone afforded an 85% yield of 1,3-dideoxy-4,5:6,7-di-*O*-isopropylidene-D-*arabino*-heptulose (**8**) as an analytically pure syrup, $[\alpha]_D$ +12° in chloroform, which showed typical, strong, carbonyl absorption in the infrared, and which gave a crystalline (2,4-dinitrophenyl)hydrazone (**9**) whose specific rotation was close to zero.

Methanolysis of the syrupy ketone **8** in the presence of a small proportion of sulfuric acid cleaved the protecting groups, and converted the keto sugar into its methyl α-pyranoside (**10**), obtained crystalline in 68% yield; its strong dextrorotation (+108° in methanol) illustrates the familiar increase, by one or two orders of magnitude, in the specific rotation attendant upon conversion from an acyclic-sugar precursor into a cyclic product. Its crystalline triacetate **11** gave a first-order, n.m.r. spectrum showing spin-couplings in excellent accord with the expected $^5C_2$ pyranoid conformation for **11**. The n.m.r. data are inconsistent with a furanoid tautomer. The α-D configuration was assigned to **10** and **11** on the basis of their high dextrorotations, and from expectations based on the anomeric effect[15], which would favor the product having the 1-methoxyl group axially disposed.

All compounds synthesized in this series, except for **10**, gave distinctive mass-spectral fragmentations largely dependent on the specific substituents. The isopropylidene acetals all showed observable molecule-ion peaks, followed by a strong peak for $M^+ - 15$. Cleavage between C-5 and C-6 gave rise to a prominent peak, as did C-2–C-3 cleavage. If diethyl dithioacetal groupings remained on the chain, loss of one ethylthio group was very prominent, as was the 1,1-bis(ethylthio)ethane fragment formed by C-2–C-3 cleavage. The acetylated product **11** gives rise to a mass spectrum characteristic of sugar acetates; the molecule-ion is prominent, but it readily loses the 1-methoxyl substituent, and conventional fragmentations, involving splitting out of acetic acid (60 m.u.), ketene (42 m.u.), and the elements of acetic anhydride (102 m.u.), are observed.



An attempt was made to prepare a 1-bromo derivative by replacement of one of the ethylthio groups in 3,4,5,6-tetra-*O*-acetyl-2-deoxy-D-*arabino*-hexose diethyl dithioacetal by the action of bromine in an inert solvent. The reaction, which proceeds readily[16] with the non-deoxygenated analogs, failed to give such a monobromo derivative; treatment of the mixture with methanol–silver carbonate gave the (sulfur-free) dimethyl acetal **12**. The latter could be prepared crystalline in 85% yield by conducting the reaction in methanol as the solvent and using 1 molar proportion of

bromine. The difference in reactivity of the deoxy derivative may arise from the absence of an electron-withdrawing substituent at C-2, but detailed studies designed to supply a plausible, mechanistic interpretation were not conducted.

EXPERIMENTAL

General methods. — I.r. spectra were recorded with a Perkin–Elmer Infracord spectrophotometer. X-Ray powder diffraction data give interplanar spacings in Å for CuKα radiation (camera diameter = 114.59 mm). Relative intensities were estimated visually; m, moderate; s, strong; vs, very strong; w, weak. Optical rotations were measured with a Perkin–Elmer Model 141 recording polarimeter. Electron-impact mass spectra were recorded by C. R. Weisenberger with an AEI MS-9 double-focusing instrument at an ionization potential of 70 eV and an accelerating potential at 8 kV. N.m.r. spectra were recorded, unless otherwise stated, with a Varian HA-100 n.m.r. spectrometer at ~25°. Samples were dissolved in the solvent indicated, and tetramethylsilane was used as the lock signal; n.m.r. data use the following conventions: d, doublet; m, multiplet; o, octet; q, quartet; s, singlet; and t, triplet. T.l.c. was performed on Silica Gel G activated at 120°. Preparative t.l.c. was performed on chromatoplates (200 × 200 × 1.5 mm) of Silica Gel G containing 1% of Lumilux Green 25. Silica Gel (No. 7734, E. Merck) was used for all column chromatography. Microanalyses were performed by W. N. Rond.

*2-Deoxy-α-*D-arabino-*hexopyranose and its diethyl dithioacetal.* — D-Glucal (10 g, 69 mmol) was kept for 16 h in 5% sulfuric acid (100 mL) at 0°. Neutralization with barium hydroxide, freeze-drying, and extraction with hot acetone yielded the deoxyaldose; m.p. 145–146° (lit.[17] m.p. 146°); yield 4.8 g (48%). Part of this product (2.0 g, 13 mmol) was shaken with conc. hydrochloric acid (2 mL) and ethanethiol (2 mL), to yield the crystalline dithioacetal; yield 2.5 g (69%); m.p. 133–134° (lit.[18] m.p. 133.5°).

*3,4,5,6-Tetra-*O*-acetyl-2-deoxy-*D-arabino-*hexose diethyl dithioacetal.* — Treatment of 2-deoxy-D-*arabino*-hexose diethyl dithioacetal with pyridine–acetic anhydride gave the crystalline acetate; yield 69%; m.p. 75–76° (lit.[19] m.p. 75.5°).

*2-Deoxy-3,4:5,6-di-*O*-isopropylidene-*D-arabino-*hexose diethyl dithioacetal* (**3**). — The following modification of the general literature procedure[14] gave superior yields. To a stirred solution of 2-deoxy-D-*arabino*-hexose diethyl dithioacetal (2.0 g, 7.4 mmol) in acetone (35 mL) was added conc. sulfuric acid (3 drops), and the solution was stirred for 24 h at ~25°. Concentrated, aqueous ammonia (1 mL, sufficient to basify the solution) was then added, and the resultant suspension was filtered, and the solvent removed from the filtrate. The desired product was obtained as a distillable, thin syrup; yield 2.51 g (97%), b.p. 110–115°/10 mtorr, $[\alpha]_D^{25}$ −1.2° (*c* 1.3, chloroform); R_F 0.55 (9:1 benzene–ethyl acetate) (spot charred black); λ_{max}^{film} 3.40 (C–H), 6.90, 7.30, 8.05–8.25, and 9.40 μm (C-O-C).

Anal. Calc. for $C_{16}H_{30}O_4S_2$: C, 54.85; H, 8.57; S, 18.28. Found: C, 54.72; H, 8.36; S, 18.02.

1,3-Dideoxy-4,5:6,7-di-O-*isopropylidene*-D-arabino-*heptulose diethyl dithioacetal* (**4**). — A reaction vessel that contained a solution of compound **3** (0.5 g, 1.43 mmol) in dry oxolane (10 mL), and had been purged with nitrogen, was sealed with a septum, and cooled to −30°. Butyllithium (2.4M, in hexane, Alfa Products, Beverly, Mass.; 1.3 mL, 3.12 mmol) was slowly added to the flask with slow stirring, and the solution was kept for 2 h at −20 to −30°. Iodomethane (1.0 mL, 15.5 mmol) was then slowly added, and the solution was allowed to warm to 0°, and kept for 18 h at that temperature. The yellowish solution was now poured into water (20 mL), made neutral with acetic acid, and extracted with pentane. The extracts were consecutively washed with 5% potassium hydroxide, sodium hydrogencarbonate, and water, dried (potassium carbonate), and evaporated to a thin syrup; yield 0.43 g (83%); b.p. 110–115°/6 torr, $[\alpha]_D^{25}$ 0°, $[\alpha]^{25}_{Hg578,546,436,365}$ 0° (*c* 0.5, chloroform); R_F 0.54 (9:1 benzene–ethyl acetate) (charred brown); λ_{max}^{film} 3.40 (C–H), 6.93, 7.28, 8.05, and 9.40 μm (C–O–C); n.m.r. (C_6D_6): δ 4.68 (m, H-4), 4.04 (m, H-5,6), 3.56 (m, H-7a,7b), 2.1 (m, H-3a,3b), and 1.88 (s, Me); *m/e* 364 (M^+), 349 ($M^+ - CH_3$), 303 ($M^+ - SEt$), 263 (C-5–C-6), and 149 (C-2–C-3).

Anal. Calc. for $C_{17}H_{32}O_4S_2$: C, 56.04; H, 8.79; S, 17.59. Found: C, 56.03; H, 9.00; S, 17.82.

1,3-Dideoxy-4,5:6,7-di-O-*isopropylidene-1-phenyl*-D-arabino-*heptulose diethyl dithioacetal* (**5**). — Compound **3** (0.75 g, 2.14 mmol) was dissolved in dry oxolane (25 mL) and the procedure for the preparation of **4** was used, except that α-bromotoluene (1.4 g, 3.18 mmol) was used instead of iodomethane. The excess of α-bromotoluene was removed from the product **5** by evacuation of the flask to ~15 torr for 48 h at 35°. The remaining syrup was chromatographed on a column (205 × 2.0 cm) of silica gel to yield syrupy **5**; yield 0.72 g (76%), $[\alpha]_D^{25}$ −1.2° (*c* 0.77, chloroform); R_F 0.52 (9:1 benzene–ethyl acetate); λ_{max}^{film} 3.45 (-CH_2-), 6.25, 6.95 (benzene ring), 7.35, 8.05–8.30, and 9.40 μm (C–O–C); n.m.r. ($CDCl_3$): δ 7.1–7.6 (m, 6 H, Ph), 3.32 and 3.06 (2 d *J* 7 Hz, CH_2 of benzyl), 1.29, 1.32, 1.37, and 1.41 (4 s, 12 H, CMe_2); *m/e* 440 (M^+), 425 ($M^+ - 15$), 379 ($M^+ - 61$), 213 (C-2–C-3), and 101 (C-5–C-6).

Anal. Calc. for $C_{23}H_{36}O_4S_2$: C, 62.73; H, 8.18; S, 14.54. Found: C, 62.71; H, 8.19; S, 14.37.

1,3-Dideoxy-4,5-O-*isopropylidene*-D-arabino-*heptulose diethyl dithioacetal* (**6**). — Compound **4** (1.0 g, 2.8 mmol) was dissolved in dry methanol (400 mL), one drop of conc. sulfuric acid was added, and the solution was stirred for 48 h at ~25°. At this point, virtually all of the starting material had disappeared, and the product **6** (R_F 0.45, 3:17 methanol–chloroform) had been formed. The methanolic solution was made neutral with aqueous ammonium hydroxide, the solvent removed, and the thin syrup taken up in acetone. The suspended material was filtered off, acetone was evaporated from the filtrate, and the solution of crude product **6** was placed on a column (205 × 2.0 cm) of silica gel that was eluted with 3:17 methanol–chloroform, to yield compound **6** as a syrup; yield 0.72 g (80%), $[\alpha]_D^{25}$ 0°, $[\alpha]^{25}_{Hg578,546,436,365}$ 0° (*c* 1.0, methanol); R_F 0.45 (3:17 methanol–chloroform); λ_{max}^{film} 2.95 (OH), 3.42 (C–H),

6.92, 7.30, 8.24, and 9.50 μm (C–O–C); n.m.r. ($CDCl_3$): δ 1.40 (s, 3 H, CH_3), and 1.05 and 0.95 (2 s, 6 H, CMe_2); *m/e* 324 (M^+), 319 ($M^+ - 15$), 263 ($M^+ - SEt$), 249 ($M^+ - CH_3 - SEt$), and 149 (C-2–C-3).

Anal. Calc. for $C_{14}H_{28}O_4S_2$: C, 51.85; H, 8.64; S, 19.75. Found: C, 51.98; H, 8.88; S, 19.33.

*1,3-Dideoxy-4,5:6,7-di-*O*-isopropylidene-*D-arabino*-heptulose* (**8**). — To a stirred mixture of mercuric chloride (5.2 g, 19.2 mmol) and cadmium carbonate (8.1 g, 46.5 mmol) in acetone (50 mL) was added a solution of **4** (1.7 g, 4.67 mmol) in acetone (20 mL), and the mixture was stirred for 24 h at ~25°, filtered through Celite, and the filtrate evaporated (water aspirator). The residue was extracted with several portions of warm chloroform, and the extract was successively washed with 30% aqueous potassium iodide and water, dried (sodium sulfate), and evaporated to a syrup which was applied to a column (20 × 1.5 cm) of silica gel that was then eluted with 4:1 benzene–ethyl acetate, to yield 1.02 g (85%) of **8** as a syrup, $[\alpha]_D^{25}$ +12° (*c* 0.67, chloroform); R_F 0.18 (3:17 methanol–chloroform); λ_{max}^{film} 3.40 (C–H), 5.8 (C=O), 7.30, 7.95–8.20, and 9.30 μm (C–O–C); n.m.r. [$(CD_3)_2CO$]: δ 4.36 (o, $J_{5,6}$ 4.7 Hz, H-6), 4.12 (q, $J_{4,5}$ 2.8 Hz, H-5), 3.84 (o, $J_{3a,4}$ 5.8, $J_{3b,4}$ 2.4 Hz, H-4), 2.85 and 2.66 (2 q, $J_{6,7a}$ 4.5, $J_{6,7b}$ 7.5, $J_{7a,7b}$ 14.8 Hz, H-7a,7b), 2.14 (s, 3 H, CH_3), 2.06 (m, H-3a,3b), and 1.09 (CMe_2); *m/e* 258 (M^+), 243 ($M^+ - CH_3$), 147 (C-5–C-6), and 101 (C-5–C-6).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.46; H, 8.53. Found: C, 60.13; H, 8.70.

*1,3-Dideoxy-4,5:6,7-di-*O*-isopropylidene-*D-arabino*-heptulose (2,4-dinitrophenyl)hydrazone* (**9**). — To a solution of compound **8** (0.15 g, 0.58 mmol) in methanol (5 mL) was added acetic acid (5 drops), and the solution was boiled for 30 min under reflux, cooled, and evaporated (water aspirator); the residue was taken up in ethanol, and water was added to faint opalescence. Refrigeration for 48 h afforded a mass of yellow needles; yield 0.13 g (51%), m.p. 80–81°, $[\alpha]_D^{25}$ 0°, $[\alpha]_{Hg578,546,436,365}^{25}$ 0° (*c* 1.25, chloroform); R_F 0.44 (9:1 benzene–ethyl acetate); λ_{max}^{KBr} 3.05 (N–H), 3.40 (C–H), 6.20 (C–H), 7.51, 7.70, 8.24, and 9.40 μm (C–O–C); n.m.r. [$(CD_3)_2CO$]: δ 8.98 m, 8.34 m, 7.98 (m, aromatic protons), 4.44–3.64 (m, H-4,5,6), 3.04–2.54 (m, H-7a,7b), 2.18 s, 2.14 (s, Me), and 1.34 (CMe_2); *m/e* 438 (M^+), 423 ($M^+ - CH_3$), 337 (C-5–C-6), 201 (C-3–C-4); X-ray powder diffraction data: 6.75 m (2), 6.00 m (3), 5.48 w, 4.98 w, 4.74 m, 4.41 s (1), 4.08 w, 3.89 w, 3.53 m, 3.16 w, 3.07 w, and 1.94 w.

Anal. Calc. for $C_{19}H_{26}N_4O_8$: C, 52.05; H, 5.93; N, 12.78. Found: C, 52.13; H, 6.21; N, 12.49.

*Methyl 1,3-dideoxy-*α*-*D*-arabino-heptulopyranoside* (**10**). — The syrupy ketose **8** (0.8 g, 3.1 mmol) was dissolved in methanol (40 mL), conc. sulfuric acid (2 drops) was added, and the solution was stirred for 2 h at ~25°. Aqueous ammonium hydroxide was added, the solvent removed (water aspirator), and the residue leached with acetone. The mixture was filtered, and the filtrate was evaporated to a syrup that crystallized spontaneously after 24 h at ~25°. Recrystallization was effected from acetone; yield 0.41 g (68%), m.p. 111–112°, $[\alpha]_D^{25}$ +108° (*c* 0.22, methanol); R_F 0.40 (3:17 methanol–chloroform); λ_{max}^{KBr} 2.95 (OH), 7.21, 8.05, and 9.45 μm

(C–O–); X-ray powder diffraction data: 5.96 vs (1), 5.03 s (2), 4.61 s (3), 4.27 s, 3.89 s, 3.65 s, 3.45 m, 2.71 m, 2.21 w, and 2.15 w.

Anal. Calc. for $C_8H_{16}O_5$: C, 50.99; H, 8.33. Found: C, 49.86; H, 8.92.

*Methyl 4,5,7-tri-*O*-acetyl-1,3-dideoxy-*α*-*D*-arabino-heptulopyranoside* (**11**). – A solution of **10** (0.37 g, 1.92 mmol) in pyridine (3 mL) was cooled to 0°, acetic anhydride (2 mL) was added, and the solution was kept overnight at ~25°, poured into ice–water (25 mL), and kept until crystallization occurred (4 h). Recrystallization from abs. ethanol gave **11**; yield 0.45 g (73%); m.p. 114–115°, $[\alpha]_D^{25}$ +91° (*c* 1.34, methanol); λ_{max}^{KBr} 5.70 (C=O of acetate), 7.30, 8.15, and 9.55 μm (C–O–C); n.m.r. ($CDCl_3$): δ 5.30 (o, $J_{4,5}$ 9.7, $J_{3e,4}$ 5.3, $J_{3a,4}$ 11.3 Hz, H-4), 4.95 (t, $J_{5,6}$ 9.7 Hz, H-5), 4.27 and 4.05 (2 q, $J_{7a,7b}$ 12.3, $J_{6,7a}$ 2.5, $J_{6,7b}$ 5.0 Hz, H-7a,7b), 3.82 (o, H-6), 3.21 (s, OMe), 2.28 and 1.68 (2 q, $J_{3e,4}$ 2.5, $J_{3a,4}$ 6.5, $J_{3a,3e}$ 12.9 Hz, H-3e,3a), 2.00, 2.04, and 2.07 (3 s) (OAc), and 1.37 s (CMe); *m/e* 318 (M^+), 303 ($M^+ - CH_3$), 287 ($M^+ - OMe$), 258 ($M^+ - HOAc$), and 167 ($M^+ - MeOH - 2\ HOAc$); X-ray powder diffraction data: 8.54 m, 6.53 s (2), 6.08 w, 5.33 w, 5.09 w, 4.77 vs (1), 3.90 w, 3.74 s (3), 3.60 w, 3.40 w, 2.83 w, and 2.32 w.

Anal. Calc. for $C_{14}H_{22}O_8$: C, 52.59; H, 6.92. Found: C, 52.72; H, 6.90.

*4,6-Dideoxy-2,3-*O*-isopropylidene-*aldehydo*-*D*-threo-hexos-5-ulose 5-(diethyl dithioacetal).* — The syrupy monoisopropylidene acetal **6** (0.42 g, 1.3 mmol) was dissolved in benzene (25 mL), lead tetraacetate[20] (0.6 g, 1.35 mmol) was added, and the solution was stirred for 30 min at ~25°. The mixture was then filtered, and the filtrate was washed successively with sodium hydrogencarbonate and water, dried (sodium sulfate), and evaporated to a syrup that was placed on a column (20 × 1.5 cm) of silica gel that was eluted with 2:1 benzene–ethyl acetate, to yield the crude aldehyde as a colorless syrup; yield 0.31 g (81%). This aldosulose was not purified further, but was used directly in the following reduction.

*1,3-Dideoxy-4,5-*O*-isopropylidene-*D*-threo-hexulose diethyl dithioacetal* (**7**). — The syrup from the preceding experiment (0.2 g, 0.68 mmol) was taken up in ether (30 mL), sodium borohydride (0.3 g, 0.789 mmol) was added, and the solution was boiled for 5 h under reflux. Water was slowly added, with cooling, and the solution was stirred for 30 min. The ethereal layer was separated, dried (sodium sulfate), and evaporated, and the residue was applied to a column (20 × 1.5 cm) of silica gel. Elution with 2:1 benzene–ethyl acetate gave pure **7** as a syrup; yield 0.8 g (90%); $[\alpha]_D^{25}$ 0°, $[\alpha]_{Hg578,546,436,365}^{25}$ 0° (*c* 0.43, chloroform); R_F 0.41 (2:1 benzene–ethyl acetate; *m/e* 294 (M^+), 280 ($M^+ - CH_3 + H$), 234 ($M^+ - SEt$), and 131 (C-3–C-4).

*3,4,5,6-Tetra-*O*-acetyl-2-deoxy-*D*-arabino-hexose dimethyl acetal* (**12**). — A solution of 3,4,5,6-tetra-*O*-acetyl-2-deoxy-*D*-*arabino*-hexose diethyl dithioacetal (0.1 g, 228 μmol) in methanol (10 mL) was cooled to 0°, and bromine (0.05 g, 0.25 mmol) in methanol (5 mL) was added. The solution was stirred for 30 min at 0°, silver carbonate (0.2 g, 9.72 mmol) was added, the suspension was allowed to warm to ~25°, and stirring was continued for 30 min. The mixture was filtered through Celite and decolorizing charcoal, to give a colorless filtrate that was concentrated, and kept at ~0°, resulting in crystallization; yield 73 mg (85%); m.p. 56–57°, $[\alpha]_D^{25}$ 0°,

$[\alpha]^{25}_{Hg578,546,436,365}$ 0° (*c* 1.0, methanol), R_F 0.55 (1:1 benzene–ethyl acetate); λ^{KBr}_{max} 5.70 (C=O of acetate), 7.35, 8.25, and 9.05–9.25 μm (C–O–C); n.m.r. ($CDCl_3$): δ 5.25 (m, H-1,3,4), 4.5–4.1 (m, H-5,6a,6b), 3.25, 3.30 (2 s, OMe), 2.09, 2.02 (OAc), and 1.8 (m, H-2a,2b); *m/e* 378 (M^+), 347 ($M^+ - OMe$), and 233 ($M^+ - C_6H_9O_4$); X-ray powder diffraction data: 9.20 w, 6.89 m (3), 6.06 w, 4.89 m (2), 3.56 w, 1.94 s (1), and 1.69 w.

Anal. Calc. for $C_{16}H_{26}O_{10}$: C, 50.79; H, 6.88. Found: C, 50.39; H, 6.79.

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