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Note

Synthesis of methyl 5-*O*-acetyl-7-deoxy-2,3-*O*-isopropylidene-hepto-furanosid-6-uloses*

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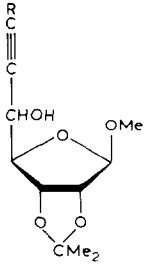
During recent studies of possible synthetic routes to sinefungin, a natural analog of *S*-adenosyl-L-methionine, we[1] prepared a series of propargylic alcohols (**1**) from methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside in high yield by a modification of the method of Berg and Kjolberg[2]. We now report conversion of the simplest of these propargylic carbohydrates (**1**, R = H) into methyl 5-*O*-acetyl-7-deoxy-2,3-*O*-isopropylidene-heptofuranosid-6-uloses (**2**) by mercuric acetate-catalyzed hydration.

Mercuric ion-catalyzed hydration–rearrangements are normally conducted under acidic conditions[3]. Because of the acid lability of **1** (R = H), milder conditions had to be employed. Kagan and coworkers[4] used mercuric acetate in boiling ethyl acetate to transform α-hydroxy-alkynyl steroids into α-acetoxy-keto steroids. By refluxing **1** (R = H) in abs. ethanol with mercuric acetate, we obtained **2** in 47% yield.

The i.r. spectrum of **2** showed carbonyl absorptions at 1745 and 1725 cm^{-1}, corresponding to the acetoxyl group and methyl ketone, respectively. Absorptions



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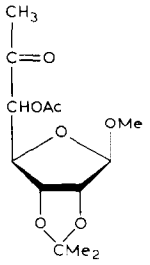

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*Taken in part from the disseratation of A.R.M., University of Kansas, Lawrence, KS, 1981.
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at 1385 and 1375 cm^{-1} supported the presence of the *O*-isopropylidene group. The absence of absorption at 3270 and 2170 cm^{-1} indicated modification of the acetylene group. The ^1H-n.m.r. spectrum showed five distinct singlets, each integrating for three protons, commensurate with the assigned structure. No exchangeable protons were detected in the ^1H-n.m.r. spectrum of **2**, supporting the absence of a free hydroxyl group.

The electon-impact mass spectrum of **2** demonstrated a parent ion at *m/z* 288, as well as key fragment-ions at *m/z* 273 $[M - 15]^+$, 257 $[M - 31]^+$, and 241 $[M - 47]^+$, suggesting that the isopropylidene and methoxyl groups were intact. A fragment at *m/z* 213 was thought to arise through loss of acetic acid from the *m/z* 273 ion. An ion at *m/z* 173 suggests a side chain located at C-5, having a mass of 115, in agreement with the assigned structure.

The conversion of **1** into **2** may involve the mercuric ion-catalyzed addition of acetate to the acetylene group of **1**, followed by acyl migration from C-6 to C-5 and subsequent rearrangement to the α-acetoxy-keto product **2**.

The relatively mild conditions employed for this hydration–rearrangement suggest the use of this reaction for preparation of chain-extended carbohydrates. Applied to an appropriately modified nucleoside, the reaction may allow preparation of a number of analogs of the natural product sinefungin[6].

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover capillary melting point apparatus and are uncorrected. ^1H-N.m.r. spectra were recorded with a Varian T-60 (60 MHz, ambient-temperature probe) spectrometer operated in the continuous-wave mode. Chemical shifts are reported in δ from tetramethylsilane as 0.00. Mass spectra were recorded with a Varian MAT-CH5 or Ribermag R-10-10 mass spectrometer interfaced to a digital computer.

Preparative-layer chromatography was performed on Woelm silica gel GF (Analtech, 1.00 mm). Methyl 2,3-*O*-isopropylidene-β-D-ribofuranoside[5] and methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanoside[3] were prepared by literature methods.

*Methyl 6,7-didehydro-6,7-dideoxy-2,3-O-isopropylidene-β-*D-allo- *and -α-*L-talo-*heptofuranoside* (**1**). — Freshly distilled, anhydrous oxolane(tetrahydrofuran, THF, 15 mL) was saturated with dry acetylene gas. Ethylmagnesium bromide (20 mmol) in 2:3 diethyl ether–THF (15 mL) was added dropwise to the solution, which was stirred for 3 h with continuous bubbling of acetylene through the mixture, and then chilled to 0–5°. A solution of methyl 2,3-*O*-isopropylidene-β-D-*ribo*-pentodialdo-1,4-furanoside[3] (1.00 g, 4.95 mmol) in anhydrous THF (15 mL) was added dropwise while more acetylene was bubbled through the mixture. The system was purged with nitrogen, stirred for 3 h at 0°, and then stirred overnight at room temperature. The mixture was then evaporated *in vacuo*, and the residue partitioned between diethyl ether (50 mL) and saturated ammonium chloride (50

mL). The ethereal solution was successively washed with saturated ammonium chloride (2 × 50 mL) and water (50 mL). The combined aqueous washings were again extracted with diethyl ether (50 mL). The combined extracts were dried (magnesium sulfate), filtered, and evaporated. Recrystallization (Skellysolve B) gave 1.00 g (89%) of **1** as a mixture of the two 5-epimers; m.p. 58–61° (lit.[2] α-L-*talo* epimer, 63–64°; β-D-*allo* epimer, 93–94°); ^{1}H-n.m.r. ($CDCl_3$): δ 5.00 (m, 1.5 H, H-1 and H-3), 4.83 (d, 0.5 H, H-3), 4.70–4.10 (m, 3 H, H-2,4,5), 3.82 (br. s, 1 H, OH, exchanges with D_2O), 3.49 (s, 1.5 H, OCH_3), 3.44 (s, 1.5 H, OCH_3), 2.46 (d, 1 H, H-7, *J* 2 Hz), 1.50 (s, 3 H, CCH_3), and 1.36 (s, 3 H, CCH_3); the ^{1}H-n.m.r. spectrum indicated a 1:1 mixture of the two diastereomers, ν_{max}^{KBr} 3400 (OH), 2370 (C≡C-H), 3000, 2940, and 2855 (CH), 2130 (C≡C), 1380 and 1370 cm^{-1} (CMe_2); *m/z* 213 (13.9, $[M - CH_3]^+$, 181 (10.1, $[213 - CH_3OH]^+$), 173 (100.0, $[M-C_3H_3O]^+$), 141 (8.7 $[173 - CH_3OH]^+$), 115 (25.3, $[173 - C_3H_6O]^+$), 113 (35.7, $[213 - CH_3 - CH_2O - C_3H_3O]^+$), 85 (18.6, $[115 - CH_2O]^+$), 59 (66.5, $[C_3H_6OH]^+$), and 55 (23.3, $[C_3H_3O]^+$).

*Methyl 5-O-acetyl-7-deoxy-2,3-O-isopropylidene-β-*D-allo- *and -α-*L-talo-*heptofuranosid-6-ulose* (**2**). — Compound **1** (R = H, 228 mg, 1.00 mmol) and mercuric acetate (637 mg, 2.00 mmol) were boiled under reflux in freshly distilled, anhydrous ethanol (30 mL) for 4 h. Treatment of the solution with hydrogen sulfide for 10 min at room temperaure afforded a black solution that was evaporated *in vacuo*. Microfine mercuric sulfide was removed by passing a solution of the residue in chloroform (1 mL) through a column of alumina (grade 1, 1 × 15 cm) with chloroform. The eluate was concentrated and applied to two preparative-layer chromatography plates. Elution with 8% ethanol in benzene gave 134 mg (47%) of **2** as an oil; ^{1}H-n.m.r. ($CDCl_3$): δ 5.05 (apparent d, 1 H, *J* 6 Hz, H-5), 4.93 (s, 1 H, H-1), 4.80–4.00 (m, 3 H, H-2,3,4), 3.33 (s, 3 H, OCH_3), 2.23 (s, 3 H, OAc), 2.14 (s, 3 H, OAc), 1.47 (s, 3 H, CCH_3), 1.30 (s, 3 H, CCH_3); ν_{max}^{NaCl} 2996, 2940, and 2845 (CH), 1745 (C=O), 1725 (C=O), 1385 and 1375 cm^{-1} (CMe_2); *m/z* 288 (0.2, M^+), 273 (15.1, $[M - CH_3]^+$), 257 (4.6, $[M - CH_3O]^+$), 241 (4.1, $[273 - CH_3OH]^+$), 213 (3.1, $[273 - AcOH]^+$), 199 (6.0, $[257 - C_3H_6O]^+$), 181 (13.7, $[241 - AcOH]^+$ or $[213 - CH_3OH]^+$), 173 (28.6, $[M - C_5H_7O_3]^+$), 171 (15.1, $[213 - C_2H_2O]^+$), 170 (15.7, $[213 - Ac]^+$), 143 (5.5, $[173 - CH_2O]^+$), 141 (5.5, $[173 - CH_3OH]^+$), 139 (24.2, $[199 - AcOH]^+$ or $[181 - C_2H_2O]^+$), 128 (70.4, $[171 - Ac]^+$ or $[170 - C_2H_2]^+$ or $[143 - CH_3]^+$), 115 (21.8, $[173 - C_3H_6O]^+$ or $[C_5H_7O_3]^+$), 97 (14.3, $[139 - C_2H_2O]^+$), 86 (100.0, $[128 - C_2H_2O]^+$), 85 (52.1, $[143 - C_3H_5O]^+$), and 59 (51.6, $[C_3H_6OH]^+$).

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