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Note

A convenient method for the preparation of methyl 2-deoxy-β-D-*erythro*-pentopyranoside

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Preparation of 2-deoxy-D-*erythro*-pentopyranosides appears to have remained rather difficult: the only related compounds reported thus far are methyl 2-deoxy-β-L-*erythro*-pentopyranoside (the enantiomer of **6**) and its α anomer, obtained (in 25 and 3.8% yields, respectively) by the treatment of 2-deoxy-L-*erythro*-pentose with 1% methanolic hydrogen chloride[1]. We report here a convenient preparative route to methyl 2-deoxy-β-D-*erythro*-pentopyranoside, which is of importance as a potential starting material for efficient synthesis of various 2-deoxy-D-*erythro*-pentose derivatives such as 2-deoxy-D-*erythro*-pentofuranose analogs having a ring-phosphorus atom[2].

Hughes and Maycock[3] suggested that treatment of pure methyl β-D-ribopyranoside (**1**) with acetone–sulfuric acid afforded a 1:2 mixture of methyl 2,3-*O*-isopropylidene-β-D-ribopyranoside (**2**) and its 3,4-*O*-isopropylidene isomer **3**; **2** and **3** were isolated in 23 and 46% yields, respectively. We have found that treatment of **1** with 2,2-dimethoxypropane–hydrochloric acid gave compound **3** in 59% yield after chromatographic separation. Compound **3** was then treated successively with sodium hydroxide, carbon disulfide, and methyl iodide[4] in dimethyl sulfoxide, affording methyl 3,4-*O*-isopropylidene-2-*O*-[(methylthio)thiocarbonyl]-β-D-ribopyranoside (**4**) in 89% yield.

Compound **4** was reduced with tri-butyltin hydride[5] in the presence of 2,2′-azobisisobutyronitrile[6] (AIBN) to give methyl 2-deoxy-3,4-*O*-isopropylidene-β-D-*erythro*-pentopyranoside[7] (**5**) in 74% yield. Compound **5** was partially hydrolyzed with 80% acetic acid to give methyl 2-deoxy-β-D-*erythro*-pentopyranoside (**6**) quantitatively. Physical data for the structural proof for these compounds are given in the Experimental section.

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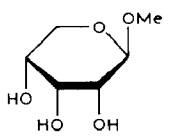

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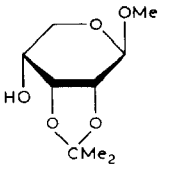

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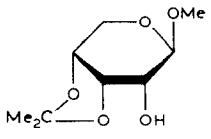

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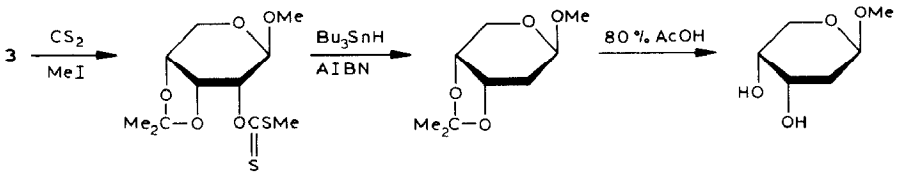

4 5 6

EXPERIMENTAL

General methods. — All reactions were monitored by t.l.c., and the products were detected with sulfuric acid–ethanol as the indicator. Column chromatography was performed by using Wako C-200 silica gel. T.l.c. was conducted on plates precoated with silica gel (0.25 mm, Merck). Melting points were measured with a Yanagimoto MP-S3 instrument and are uncorrected. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ at 27° with a Hitachi R-600 (60 MHz, FT) spectrometer. Chemical shifts are reported as δ values relative to Me_4Si. All signal assignments were verified by decoupling and by simulation analysis[8] using an NEC 9801F personal computer. Optical rotations were determined with a Nihonbunko DIP-4 polarimeter.

Acetonation of methyl β-D-ribopyranoside (**1**). — The glycoside **1** (5.0 g) was stirred for 2 h at 20° in 2,2-dimethoxypropane (90 mL) containing 4M hydrochloric acid in 1,4-dioxane (1.25 mL). The solution was made neutral with anhydrous sodium hydrogencarbonate, filtered, and evaporated *in vacuo*. The residue was chromatographed on silica gel (180 g) with 2:1 EtOAc–benzene, which was gradually changed to EtOAc. The elution gave first 2,3-acetal **2** (0.60 g, 9.6%), then a mixture (1.3 g, 21%) of **2** and the 3,4-acetal **3**, and finally pure **3** [colorless crystals, 3.7 g, 59%, m.p. 64–65° (from EtOAc–hexane), lit.[3] oil]. The ^{1}H-n.m.r. spectra of **2** and **3** were identical with those reported in ref. 3.

Methyl 3,4-O-isopropylidene-[(methylthio)thiocarbonyl]-β-D-ribopyranoside (**4**). — A solution of **3** (5.0 g) in dimethyl sulfoxide (5.6 mL) was treated for 10 min at 10–20° with 4M NaOH (5.6 mL) and CS_2 (3.8 mL). To this solution was added methyl iodide (3.8 g) and the whole was stirred for 25 min. The solution was then added to water (190 mL) at 0°. The syrupy precipitate was dissolved in MeOH (20 mL), and water (190 mL) was added at 0°. The syrupy precipitate was dissolved in

ether, and the solution was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to give **4** as yellow needles; yield 4.6 g (89%); m.p. 45–45.5° (hexane–EtOAc), $[\alpha]_D^{16}$ −134° (*c* 1.22, $CHCl_3$); R_F 0.83 (1:1 hexane–EtOAc); ^{1}H-n.m.r. 1.34, 1.57 (2 s, 6 H, CMe_2), 2.62 (s, 3 H, SMe), 3.43 (s, 3 H, OMe), 3.73 (1 H, $J_{5,5'}$ 11 Hz, H-5), 3.85 (1 H, H-5′), 4.33 (1 H, $J_{4,5}$ 2.0, $J_{4,5'}$ 2.5 Hz, H-4), 4.74 (1 H, $J_{3,4}$ 7.0 Hz, H-3), 4.90 (1 H, $J_{1,2}$ 5.8 Hz, H-1), and 5.76 (1 H, $J_{2,3}$ 3.3 Hz, H-2).

Anal. Calc. for $C_{11}H_{18}O_5S_2$: C, 44.88; H, 6.16%. Found: C, 44.93; H, 6.10%.

*Methyl 2-deoxy-3,4-*O*-isopropylidene-β-*D-erythro-*pentopyranoside*[7] (**5**). — Compound **4** (5 g) in dry benzene (150 mL) was added to a boiling solution of Bu_3SnH (9 mL) in dry benzene (100 mL) containing AIBN (280 mg) under reflux during a period of 1 h under argon. Refluxing was continued overnight. The mixture was evaporated *in vacuo* and the residue chromatographed on silica gel (150 g) with benzene, which was gradually changed to 2:1 hexane–EtOAc. The elution gave **5** as a syrup; yield 2.4 g (74%); $[\alpha]_D^{16}$ −105° (*c* 1.07, water) {lit.[7] oil, $[\alpha]_D^{20}$ −47.8° (*c* 1.04, water)}; R_F 0.48 (2:1 hexane–EtOAc); ^{1}H-n.m.r. 1.35, 1.51 (2 s, 6 H, CMe_2), 1.81 (1 H, $J_{2,2'}$ 15.0, $J_{2,3}$ 4.5 Hz, H-2), 2.15 (1 H, $J_{2',3}$ 5.0 Hz, H-2′), 3.39 (s, 3 H, OMe), 3.73 (1 H, $J_{5,5'}$ 15 Hz, H-5), 3.85 (1 H, H-5′), 4.15 (1 H, $J_{4,5}$ 2.6, $J_{4,5'}$ 2.8 Hz, H-4), 4.45 (1 H, $J_{3,4}$ 6.5 Hz, H-3), and 4.77 (1 H, $J_{1,2}$ 6.0, $J_{1,2'}$ 4.5 Hz, H-1).

*Methyl 2-deoxy-β-*D-erythro-*pentopyranoside* (**6**). — Compound **5** (350 mg) was dissolved in 80% AcOH (5 mL) and the solution was kept for 20 h at 20°. The solution was evaporated *in vacuo* to give **6** as colorless needles; yield 277 mg (100%); m.p. 83–84° (from benzene), $[\alpha]_D^{16}$ −200° (*c* 1.01, $CHCl_3$); R_F 0.5 (9:1 EtOAc–MeOH); ^{1}H-n.m.r. 1.73 (1 H, $J_{2,2'}$ 15, $J_{2,3}$ 0.5 Hz, H-2), 2.03 (1 H, $J_{2',3}$ 0.3 Hz, H-2′), 2.1–2.6 (m, 2 H, HO-3,4, D_2O exchangeable), 3.77 (m, 3 H, H-4,5,5′), 3.95 (m, 1 H, H-3), and 4.77 (1 H, $J_{1,2}$ 2.6, $J_{1,2'}$ 3.2 Hz, H-1). Although this compound was briefly mentioned in ref. 7, no detailed experimental data were given; compare physical data for methyl 2-deoxy-β-L-*erythro*-pentopyranoside[1], m.p. 83-84°, $[\alpha]_D^{20}$ +193° (*c* 0.64, $CHCl_3$).

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