## Note

## A synthesis of 2-deoxy-2-fluoro-D-xylose\*

JOHN A. WRIGHT AND JACK J. FOX

Division of Biological Chemistry, Sloan-Kettering Institute For Cancer Research, Sloan-Kettering Division of Cornell University Medical College, New York, N.Y. 10021 (U.S.A.) (Received July 15th, 1969; in revised form, September 25, 1969)

Recent interest<sup>1</sup> in the field of fluorocarbohydrates prompts us to report the synthesis of the previously unknown 2-deoxy-2-fluoro-D-xylose (8). As part of a program of synthesis of fluorocarbohydrates and nucleosides thereof<sup>2</sup>, we studied the action of potassium hydrogen fluoride-sodium fluoride on methyl 2,3-anhydro-5-O-benzyl- $\beta$ -D-lyxofuranoside (1) in ethylene glycol at reflux. Previous results<sup>2,3</sup> led us to expect a mixture of 2- and 3-fluorinated products, and this was indeed found to be the case.

Fractionation of the syrupy reaction mixture on a short column of Silica Gel G (Merck) resulted in the isolation of two major products (2) (31%) and 3 (23%) as chromatographically-pure syrups.

Compound 2 was identified as methyl 5-O-benzyl-3-deoxy-3-fluoro- $\beta$ -D-arabinofuranoside by hydrogenolysis to the glycoside 6, followed by acid hydrolysis to give 3-deoxy-3-fluoro-D-arabinose (5), identical in all respects with authentic material<sup>4</sup>.



The structure of compound 3 was established by benzoylation of the free hydroxyl group, which caused a downfield shift in the p.m.r. signal assigned to the geminal proton, resulting in a compound, 7, possessing a clearly-resolved first order

<sup>\*</sup>This investigation was supported in part by funds from the National Cancer Institute, National Institutes of Health, U.S. Public Health Service (Grant No. CA 08748).

p.m.r. spectrum. Signals at  $\delta$  5.64 (octet,  $J_{3,F}$  16.5,  $J_{3,4}$  5.5,  $J_{3,2}$  1.6 Hz), 5.07 (doublet,  $J_{1,F}$  13.4 Hz), and 5.00 p.p.m. (quartet,  $J_{2,F}$  49.5 Hz) were assigned to H-3, H-1, and H-2 respectively, and are consistent with a 2-deoxy-2-fluoro structure for 7, and therefore for 3. The very small (<1.0 Hz) H-1-H-2 coupling establishes the 1-2-transconfiguration, and on the basis of trans-scission of the epoxide 1, compound 3 is therefore methyl 5-O-benzyl-2-deoxy-2-fluoro- $\beta$ -D-xylofuranoside.

Hydrogenolysis of 3 afforded a quantitative yield of the glycoside 4 as a colorless, mobile syrup, which upon acid hydrolysis led to the free deoxyfluoropentose 8 as colorless needles, m.p.  $121-122^{\circ}$ .

On the basis of a mutarotation study  $([\alpha]_D^{25}+69 \rightarrow +32^\circ, \text{ after 1 h, of the free sugar 8, it was assigned the <math>\alpha$ -configuration. Compound 8 exhibited a medium-intensity, type-3 absorption<sup>5</sup> band at 757 cm<sup>-1</sup> which suggests that it possesses the pyranoid structure.

## EXPERIMENTAL

Melting points were determined with a Hoover-Thomas capillary apparatus, and are corrected. Thin-layer chromatography (t.l.c) was performed on microscope slides coated with Silica Gel GF 254 (Merck) using 1:2 ethyl acetate-light petroleum  $(30-60^\circ)$  (solvent A) and ethyl acetate (solvent B). Compounds were detected by spraying with 20% (v/v) sulfuric acid in ethanol, followed by heating to 130°. Reducing sugars were detected with the aniline hydrogen phthalate reagent. Evaporations were carried out *in vacuo*.

P.m.r. and i.r. spectra were recorded on Varian A-60 and Perkin-Elmer 221 instruments, respectively, and were found to be consistent with the proposed structures. Analytical samples of non-crystalline compounds (except 1) were purified by preparative t.l.c., and elementary analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan.

Methyl 2,3-anhydro-5-O-benzyl- $\beta$ -D-lyxofuranoside (1). — Methyl 2,3-anhydro- $\beta$ -D-lyxofuranoside<sup>6</sup> (26.5 g), silver oxide (37 g), benzyl bromide (32 ml), and anhydrous N,N-dimethylformamide (135 ml) were shaken together for 20 h at room temperature. The mixture was partitioned between chloroform (1 liter) and water (1 liter). The chloroform layer was separated, filtered, treated with pyridine (100 ml), and washed successively with water (6 × 500 ml), 2M hydrochloric acid (2 × 500 ml), saturated sodium hydrogen carbonate (500 ml), and water (500 ml), and then dried with magnesium sulfate and evaporated. The residual oil was vacuum-distilled to give 1 (32.9 g) as a mobile, colorless oil, b.p. (0.03 mmHg) 135–140°,  $[\alpha]_D^{23} - 67^\circ$  (c 2.0, ethanol).

Anal. Calc. for C<sub>13</sub>H<sub>16</sub>O<sub>4</sub>: C, 66.08; H, 6.83. Found: C, 66.17; H, 6.79.

Methyl 5-O-benzyl-2-deoxy-2-fluoro- $\beta$ -D-xyloside (3) and methyl 5-O-benzyl-3-deoxy-3-fluoro- $\beta$ -D-arabinoside (2). — The epoxide 1 (3.0 g), potassium hydrogen fluoride (3.0 g), and sodium fluoride (3.0 g) were heated for 2 h at reflux in ethylene glycol (60 ml). The cooled mixture was poured into saturated sodium hydrogen carbonate (500 ml) and extracted with chloroform ( $3 \times 100$  ml). Evaporation of the chloroform layer, dried with magnesium carbonate afforded a yellow oil which was chromatographed on a column of Silica Gel G (150 g). It was eluted with solvent A and 12-ml fractions were collected. Evaporation of fractions 34-48 gave compound **3** (0.75 g) as a pale-yellow syrup,  $[\alpha]_{\rm D}^{23} - 42^{\circ}$  (c 0.9, ethanol).

Anal. Calc. for C<sub>13</sub>H<sub>17</sub>FO<sub>4</sub>: C, 60.92; H, 6.69; F, 7.41. Found: C, 60.68; H, 6.68; F, 7.19.

Evaporation of fractions 59–90 gave compound 2 (1.00 g) as a colorless syrup. It was identified by hydrogenolysis, followed by acidic hydrolysis, as described below, to give 3-deoxy-3-fluoro-D-arabinose (5), m.p.  $118-120^{\circ}$  (lit.<sup>4</sup>: m.p.  $120^{\circ}$ ). P.m.r. and i.r. spectra of 5 were identical with those of authentic material.

Benzoylation of 3 with 2 moles of benzoyl chloride in pyridine for 2 h at 0° gave an 87% yield of the monobenzoyl ester 7 as a stiff syrup,  $[\alpha]_{D}^{23} - 63^{\circ}$  (c 1.2, ethanol); p.m.r. signals (chloroform-d, TMS internal standard) at  $\delta$  7.1-8 2 (11-12 protons, benzoyl and benzyl), 5.64 (1-proton octet, H-3,  $J_{3,F}$  16.5,  $J_{3,4}$  5.5,  $J_{3,2}$  1.6 Hz), 5.07 (1-proton doublet, H-1,  $J_{1,F}$  13.4 Hz), 5.00 (1-proton quartet, H-2,  $J_{2,F}$  49.5 Hz), 4.71 (1-proton pseudo-quartet, H-4,  $J_{4,5}$  5.5 Hz), 4.45 (2-proton singlet, benzyl CH<sub>2</sub>), 3.71 (2-proton doublet, H-5) and 3.39 p.p.m. (3-proton singlet, OMe). Coupling constants quoted are first order. P.m.r. and i.r. spectra indicated the presence of a small amount of benzoyl chloride in the sample.

Anal. Calc. for C<sub>20</sub>H<sub>21</sub>FO<sub>5</sub>: C, 63.82; H, 5.62; F, 5.04. Found: C, 66.55; H, 6.03; F, 4.73.

Methyl 2-deoxy-2-fluoro- $\beta$ -D-xylofuranoside (4). — A solution of 3 (500 mg) in ethanol (100 ml) containing 10% palladium-on-charcoal (100 mg) was hydrogenated on a Parr apparatus at ~ 24 p.s.i. until the uptake of hydrogen ceased (30 min). The filtered solution was evaporated to give a colorless oil (328 mg),  $[\alpha]_D^{23} - 102^\circ$  (c 1.4, ethanol).

Anal. Calc. for C<sub>6</sub>H<sub>11</sub>FO<sub>4</sub>: C, 43.37; H, 6.67; F, 11.44. Found: C, 43.39; H, 6.60; F, 11.72.

2-Deoxy-2-fluoro-D-xylose (8). — To a solution of 4 (496 mg) in water (50 ml), Dowex 50-W (X-8, H<sup>+</sup>, 5 ml, previously treated with boiling water) was added, and the mixture was heated for 1 h at reflux. After filtration, the solution was evaporated to dryness, and the syrupy residue was crystallized from ethanol-ether (294.5 mg, m.p. 109-111°). Two recrystallizations from propyl alcohol gave a product having m.p. 121-122°. Evaporation of the mother liquors, after treatment with charcoal, gave chromatographically pure 8 (102 mg) as a colorless syrup which slowly crystallized. A mixed m.p. of 8 and 5 gave a depression (101-116°), and on paper chromatography (4:1:5 butyl alcohol-ethanol-water, downward elution) 8 and 5 showed  $R_F 0.38$ and 0.32, respectively. Compound 8 showed  $[\alpha]_D^{23} + 69^\circ$  (1.5 min)  $\rightarrow +32^\circ$  (1 h) (c 0.9, ethanol).

Anal. Calc. for C<sub>5</sub>H<sub>9</sub>FO<sub>4</sub>: C, 39.48; H, 5.96; F, 12.49. Found: C, 39.60; H, 6.03; F, 12.48.

## ACKNOWLEDGMENT

The authors wish to thank Marvin J. Olsen for the determination of the p.m.r. spectra.

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