

3-DEOXY-2,5-DI-*O*-*p*-NITROBENZOYL- α -D-*threo*-PENTOFURANOSYL BROMIDE, A STARTING MATERIAL FOR THE SYNTHESIS OF NUCLEOSIDES*

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ABSTRACT

Hydrogenation (Raney nickel) of methyl 2,3-anhydro- α - and β -D-lyxofuranoside (3 and 12) for 12 h at 60°/60 lb in N_2 afforded methyl 3-deoxy- α - and β -D-*threo*-pentofuranoside (4 and 13). These were *p*-nitrobenzoylated to give the 2,5-di-*p*-nitrobenzoates (5b and 14b) which, on treatment with hydrogen bromide in acetyl bromide-acetic acid-dichloromethane, afforded the title compound (6b). The structure of compound 4 was established by conversion into the previously prepared 2,5-dibenzoate 5a of known structure, and the anomeric configuration of 6b was established by comparison of its optical rotation and the signals of its anomeric proton with those of methyl 3-deoxy-D-*threo*-pentofuranosides.

INTRODUCTION

The aim of this work was to devise a practical method for the synthesis of a 3-deoxy-D-*threo*-pentofuranosyl halide suitable for the preparation of nucleosides. Methyl 3-deoxy-D-*threo*-pentofuranosides that could be used for such a synthesis have previously been prepared by opening the oxirane ring of a suitably protected methyl 2,3-anhydro-D-lyxofuranoside with the α -toluenethiolate ion, followed by desulfurization with Raney nickel^{1,2}, or with iodide ion, followed by catalytic hydrogenation³. We have opened the oxirane ring of both methyl 2,3-anhydro- α - and β -D-lyxofuranoside (3 and 12) by hydrogenation under pressure with Raney nickel as the catalyst, a procedure first applied to methyl 2,3-anhydro- β -D-ribofuranoside^{4,5}. Hydrogenation of compounds 3 and 12 afforded the 3-deoxy derivatives 4 and 13 in high yield. The products were protected with *p*-nitrobenzoyl groups, and converted into the same 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl- α -D-*threo*-pentofuranosyl bromide (6b).

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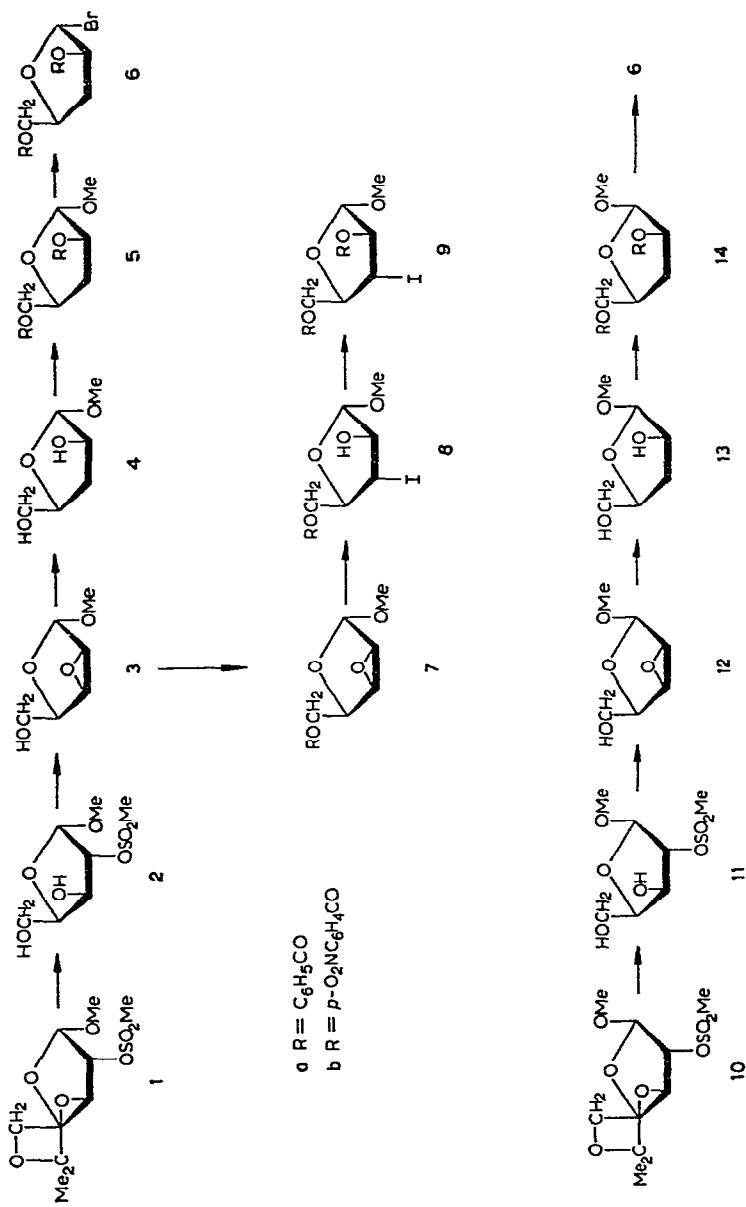
DISCUSSION

The starting material for this synthesis was methyl 3,5-*O*-isopropylidene-2-*O*-(methylsulfonyl)- α -D-xylofuranoside (**1**), obtained in three steps from D-xylose by using a slight modification of the procedure of B R Baker *et al.*⁶ (to permit the preparation of larger batches) Compound **1** and its partial-hydrolysis product, namely, methyl 2-*O*-(methylsulfonyl)- α -D-xylofuranoside (**2**), had been isolated¹ as syrups, but have now been obtained crystalline Treatment of the crystalline methanesulfonate **2** with sodium methoxide afforded the known^{3,4} epoxide **3**, which was catalytically hydrogenated under pressure in the presence of Raney nickel. The major product obtained was methyl 3-deoxy- α -D-*threo*-pentofuranoside (**4**), which we obtained crystalline Catalytic hydrogenation of **3** in the presence of 5% palladium-on-carbon proved unsatisfactory [Hydrogenation catalyzed with Raney nickel has been used to convert a similar epoxide, methyl 2,3-anhydro- β -D-ribofuranoside, into the 3-deoxy derivative, namely, methyl 3-deoxy- β -D-*erythro*-pentofuranoside^{4,5}]

To determine whether opening of the oxirane ring of compound **3** yielded the desired 3-deoxy derivative (**4**) (not the 2-deoxy compound), the product was converted into the di-*O*-benzoyl derivative, which proved to be identical with an authentic sample of methyl 2,5-di-*O*-benzoyl-3-deoxy- α -D-*threo*-pentofuranoside (**5a**) prepared by the procedure of Lemieux *et al.*³, which involves benzoylation of epoxide **3**, treatment of the monobenzoate **7a** with iodide to give the 3-iodo derivative (**8a**), benzoylation of **8a** to give **9a**, and catalytic reduction of **9a** to afford authentic **5a** It is noteworthy that *p*-nitrobenzoylation of epoxide **3** and treatment of the *p*-nitrobenzoate **7b** with iodide to give methyl 3-deoxy-3-iodo-5-*O*-*p*-nitrobenzoyl- α -D-*threo*-pentofuranoside (**8b**) proceeded satisfactorily and yielded crystalline derivatives in each step, but catalytic hydrogenation of the crystalline di-*p*-nitrobenzoate **9b** could not be achieved, presumably because the nitro groups were partially reduced, affording a mixture of products from which the 3-deoxy derivative **5b** could not be isolated

p-Nitrobenzoylation of the 3-deoxyglycoside **4** yielded crystalline methyl 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl- α -D-*threo*-pentofuranoside (**5b**), a new compound that was converted into crystalline 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl- α -D-*threo*-pentofuranosyl bromide (**6b**) by the action of hydrogen bromide in acetyl bromide-acetic acid-dichloromethane

The same 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl- α -D-*threo*-pentofuranosyl bromide (**6b**) was also obtained by starting from epoxide⁶ **12**, which, on hydrogenation in the presence of Raney nickel, gave crystalline methyl 3-deoxy- β -D-*threo*-pentofuranoside (**13**) as the major product Treatment of **13** with *p*-nitrobenzoyl chloride afforded methyl 3-deoxy-2,5-di-*O*-*p*-nitrobenzoyl- β -D-*threo*-pentofuranoside (**14b**), also in crystalline form Bromination of **14b** gave the same α -bromide (**6b**) as that obtained from the α -glycoside **5b** The anomeric configuration of bromide **6b** was apparent from its high, positive rotation ($[\alpha]_D +107.8^\circ$) and from the n m r. signal of its anomeric proton, which appeared as a singlet, like those of its precursors, the methyl

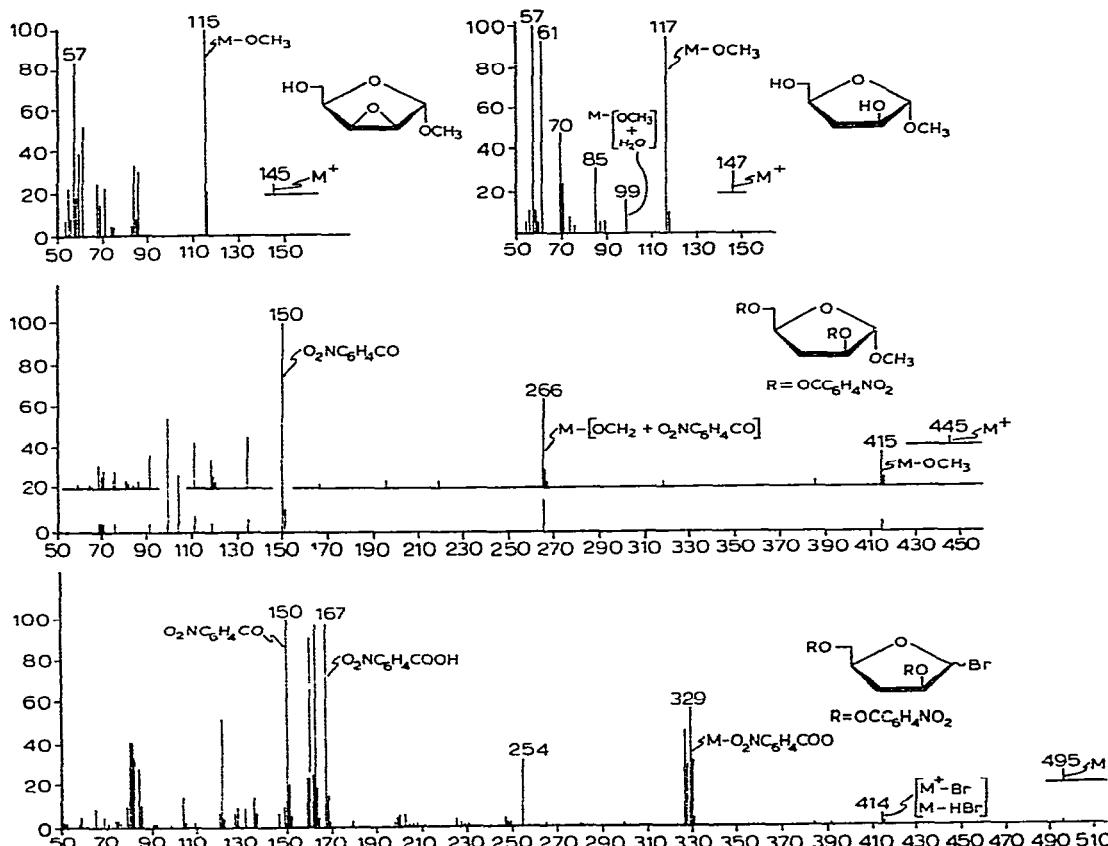


3-deoxypentofuranosides of the α -series. The optical rotation of the methyl 3-deoxy-D-threo-pentofuranosides of the β -series is negative, and their anomeric protons appear as doublets (see Table I). 3-Deoxy-2,5-di-O-p-nitrobenzoyl- α -D-threo-pentofuranosyl bromide (**6b**) is a stable compound that can be kept for weeks under refrigeration, and that is suitable for nucleoside synthesis.

TABLE I

SOME PROPERTIES OF THE ANOMERIC METHYL 3-DEOXY-D-threo-PENTOFURANOSIDES

α anomer	β anomer								
Compound	$[\alpha]_D$ (degrees)	m.p.	δ H-1	$J_{1,2}$	Compound	$[\alpha]_D$ (degrees)	m.p.	δ H-1	$J_{1,2}$
4b	+134.73	47	4.93	s 0	13b	-117.7	35	4.60	d 4.0
5b	+49.80	136	5.16	s 0	14b	-83.0	115	4.98	d 2.5

Fig. 1 Mass spectra of compounds **3**, **4**, **5b**, and **6b**

Whereas, in the *ribo* series, only the β -anomer (methyl 2,3-anhydro- β -D-ribofuranoside) may be used for the preparation of the 3-deoxyglycoside, and the α -anomer affords a mixture of 2- and 3-deoxy derivatives that is difficult to separate, the fact that hydrogenation of the anomers of methyl 2,3-anhydro-D-lyxofuranoside (3 and 12) affords the 3-deoxyglycosides (4 and 13) is remarkable. This behavior, of course, enables the preparation of high yields of bromide 6b from a given amount of D-xylose.

The n m.r. spectra of the methyl 3-deoxy-3-iodo- α -D-arabinofuranosides (8, 9a, and 9b), unlike those of the non-iodinated compounds studied, showed the proton attached to C-3 at lower field than the anomeric proton, this is attributed to deshielding by the iodine atom.

The mass spectra of methyl glycosides 3, 4, and 5 (see Fig 1) showed small molecular peaks, followed by stronger $M^+ - OMe$ ions. The bromide 6b also showed a weak molecular peak; it was followed by a peak corresponding to the loss of bromine and hydrogen bromide. A loss of a *p*-nitrobenzoyl group and a *p*-nitrobenzoate group was apparent for the *p*-nitrobenzoates 5b and 6b.

EXPERIMENTAL

General. — Melting points were determined on a Kofler block and are uncorrected. Evaporations were conducted under diminished pressure in a rotary evaporator at 40–45°. Specific rotations were measured, in a 0.2-dm tube, with a Bendix-NPL polarimeter. Infrared spectra were recorded, for potassium bromide pellets, with a Perkin-Elmer, grating, infrared spectrometer, model 621. N m.r. spectra were recorded at 60 and 100 MHz with Varian A-60 and HA-100 spectrometers, respectively. Mass spectra were recorded with a Varian M-66 mass spectrometer by Mr. M. P. Gilles. Thin-layer chromatography (tlc) was performed either on plates of Merck Silica Gel G or plates of silica gel pre-coated with a fluorescent indicator (Eastman Kodak catalog No. 6060), with sulfuric acid spray and u v light, respectively, for detection. For column chromatography, silica gel (60–200 mesh, J. T. Baker) was used with a Gibson automatic fraction-collector. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Michigan, U. S. A.

*Methyl 3,5-O-isopropylidene-2-O-(methylsulfonyl)- α -D-xylofuranoside*⁶ (1) — To a solution of methyl 3,5-O-isopropylidene- α -D-xylofuranoside⁶ (37.4 g) in pyridine (105 ml), cooled to –5°, methanesulfonyl chloride (25 ml) was added dropwise. The mixture was kept for 24 h at 20°, poured into crushed ice, stirred for 15 min, and then extracted with dichloromethane (4 × 250 ml). The extracts were combined and evaporated, and residual pyridine was removed by repeated co-evaporation with toluene–ethanol. The orange-colored residue crystallized from a mixture of carbon tetrachloride (50 ml) and hexane (10 ml), yield 43.7 g (84.5%), m.p. 85–86°. After recrystallization from carbon tetrachloride, the crystals had m.p. 86–87°, $[\alpha]_D^{22} + 103.8^\circ$ (*c* 1, methanol) (lit.⁶, for syrupy material, $[\alpha]_D + 65.7^\circ$), R_F 0.15 and 0.43 in hexane–acetone (3:1 and 1:1); n m.r. data ($CDCl_3$), δ 5.23 (d, $J_{1,2}$ 3 Hz, H-1), 4.90 (m, H-2), 4.42 (m, H-3), 4.16 (m, H-4), 3.96 (m, H-5,5'), 3.48 (s, OMe), 3.08 (s, SO_2Me), and 1.56 (s, Me_2C).

Anal Calc for $C_{10}H_{18}O_7S$ C, 42.70, H, 6.04, S, 11.37 Found C, 42.69, H, 6.15, S, 11.43

*Methyl 2-O-(methylsulfonyl)- α -D-xylofuranoside*⁶ (2) — A solution of compound 1 (40 g) in a mixture of acetic acid (120 ml) and water (60 ml) was heated for 2.5 h at $50 \pm 1^\circ$. After removal of the solvent, and coevaporation with toluene (3×10 ml), a yellow residue was obtained which crystallized from ether in colorless plates; yield 32.8 g (95%), m.p. 89° , $[\alpha]_D^{22} + 166.7^\circ$ (c 1, methanol), R_F 0.11 and 0.22 in hexane-acetone (3:1 and 1:1), $\nu_{\text{max}}^{\text{KBr}}$ 3375 cm^{-1} (OH), n.m.r. data (D_2O) δ 5.11 (d, $J_{1,2}$ 4 Hz, H-1), 5.05 (m, H-2), 4.96 (m, H-3), 4.32 (m, H-4), 3.83 (m, H-5,5'), 3.43 (s, OMe), and 3.33 (s, SO_2Me)

Anal Calc for $C_7H_{14}O_7S$ C, 34.71; H, 5.78, S, 13.22 Found C, 34.82, H, 5.72, S, 13.28

*Methyl 2,3-anhydro- α -D-lyxofuranoside*⁶ (3). — To a solution of compound 2 (30.5 g, 125 mmoles) in methanol (150 ml) cooled to -10° was added a freshly prepared solution of 2M sodium methoxide (70 ml) in methanol, with stirring, during 1 h. After 2 h at -10° , the mixture was kept for 3 days at $0 \pm 1^\circ$ under anhydrous nitrogen. Filtration through Celite, followed by washing with methanol (5×70 ml) removed most of the sodium methanesulfonate. The filtrate and washings were combined, made neutral with acetic acid (3.5 ml), and evaporated to dryness. The residue was dissolved in water (30 ml), and the solution extracted with dichloromethane (5×50 ml). The extracts were combined, dried, and evaporated to a light-yellow solid, which was recrystallized from hot benzene (20 ml) plus hexane (2 ml), yield 17.4 g (94.5%), m.p. $81-82^\circ$ [lit. m.p. $80-82^\circ$ (ref. 3) and $82-83^\circ$ (ref. 6)], R_F 0.22 in 13:7 hexane-acetone, n.m.r. data ($CDCl_3$) δ 4.95 (s, H-1), 4.16 (m, H-2), 4.06 (m, H-3), 3.75 (m, H-4, H-5,5'), and 3.43 (s, OMe)

Methyl 3-deoxy- α -D-threo-pentofuranoside (4) — Compound 3 (5 g, 35 mmoles) in ethanol (100 ml) containing Raney nickel (two teaspoonsful) was hydrogenated for 12 h at $60-65^\circ/60$ lb in N_2 . The suspension was filtered through Celite, and the catalyst washed with ethanol (5×50 ml). The filtrate and washings were combined and evaporated to a syrup (5 g) which was chromatographed on a column (3 \times 48 cm) of silica gel with 4:1 hexane-acetone for elution. Fractions (15 ml each) were collected, and examined by tlc, fractions 38-50 (2.59 g) were pure, whereas fractions 34-37 and 51-56 contained traces of impurities that could be removed by one recrystallization from ethanol. Total yield of 4 (after purification) 4.6 g (88.9%), m.p. 47° , $[\alpha]_D^{22} + 134.8^\circ$ (c 1, methanol); R_F 0.169 in 13:7 hexane-acetone; n.m.r. data δ 4.93 (s, H-1), 4.21 (m, H-2, H-4), 3.66 (m, H-5,5'), 2.45 (m, H-3), and 1.61 (m, H-3')

Methyl 3-deoxy-2,5-di-O-p-nitrobenzoyl- α -D-threo-pentofuranoside (5b) — To a solution of compound 4 (22.2 g, 150 mmoles) in pyridine (600 ml), cooled to -5° , was added *p*-nitrobenzoyl chloride (84.6 g, 450 mmoles). After 2 h at -5° , the mixture was stirred for 24 h at 20° , poured onto crushed ice (3.5 liters), and kept for 15 h at 5° . The solid that separated was filtered off, washed with cold water, dissolved in hot benzene (500 ml), and the solution passed through a column (2 \times 30 cm) of silica gel which was then eluted with benzene (1.5 liters). The eluate was concentrated

to 150 ml, hexane (20 ml) was added, and the product crystallized slowly as light-yellow needles, yield 44.6 g (66.6%), m.p. 135–136°, $[\alpha]_D^{22} +49.8^\circ$ (c 1, chloroform), R_F 0.67 in 13:7 hexane–acetone, $\nu_{\text{max}}^{\text{KBr}}$ 1745, 1625, and 1550 cm^{-1} (*p*-O₂NC₆H₄CO), n.m.r. data (CDCl₃) δ 5.35 (m, H-2), 5.16 (s, H-1), 4.53 (m, H-4, H-5,5'), 3.40 (s, OMe), 2.75 (m, H-3), and 2.0 (m, H-3')

Anal. Calc for C₂₀H₁₈N₂O₁₀: C, 53.81, H, 4.03, N, 6.27. Found: C, 53.65, H, 3.96; N, 6.22.

3-Deoxy-2,5-di-O-p-nitrobenzoyl- α -D-threo-pentofuranosyl bromide (6b). — *Method A* A suspension of compound 5 (10 g, 25 mmoles) in acetic acid (45 ml), acetyl bromide (3 ml), and dichloromethane (45 ml) was gently warmed until dissolution occurred, and then cooled to 5°. Cold, anhydrous hydrogen bromide in acetic acid (33% w/v, 45 ml) was added, and the mixture was stirred for 1.25 h at 0 ± 2°. Co-evaporation with toluene (3 × 30 ml) gave a yellow solid, which was recrystallized from dichloromethane (20 ml) plus ether (15 ml), to afford light-yellow plates, yield 8.6 g (77.0%), m.p. 152–154°, $[\alpha]_D^{22} +107.8^\circ$ (c 1, chloroform), R_F 0.210 in 3:1 hexane–acetone, n.m.r. data (CDCl₃) δ 6.63 (s, H-1), 5.80 (d, $J_{2,3}$ 6 Hz, H-2), 4.88 (m, H-4), 4.60 (m, H-5,5'), 2.91 (m, H-3), 1.95 (m, H-3'), and 8.16 (m, 2C₆H₄).

Anal. Calc for C₁₉H₁₅BrN₂O₉: C, 46.08, H, 3.05, Br, 16.13, N, 5.65. Found: C, 46.05, H, 3.04, Br, 16.17, N, 5.57.

Method B A suspension of compound 14b (10 g) in acetic acid and dichloromethane was treated as just described. The product (7.72 g, 73%) had m.p. and mixed m.p. 153–154°.

Anal. Found: C, 46.01, H, 3.08, Br, 16.26, N, 5.58.

Methyl 2,3-anhydro-5-O-p-nitrobenzoyl- α -D-lyxofuranoside (7b) — To a solution of compound 3 (2.9 g, 20 mmoles) in pyridine (120 ml), cooled to 5°, was added *p*-nitrobenzoyl chloride (5.5 g, 30 mmoles). After 30 min at 5°, the mixture was stirred for 5 h at 20°, and processed as for 5b, the product crystallized from 1:6 acetone–ethanol in pale-yellow needles, yield 5.65 g (96.1%), m.p. 131–132°, $[\alpha]_D^{22} +34.7^\circ$ (c 1, chloroform), R_F 0.26 in 7:3 hexane–acetone, $\nu_{\text{max}}^{\text{KBr}}$ 1745, 1625, and 1550 cm^{-1} (*p*-O₂NC₆H₄CO), n.m.r. data (CDCl₃) δ 5.00 (s, H-1), 4.60 (m, H-2, H-3), 4.23 (m, H-4), 3.76 (m, H-5,5'), 3.45 (s, OMe), and 8.26 (m, C₆H₄).

Anal. Calc for C₁₃H₁₃NO₇: C, 52.88, H, 4.40, N, 4.74. Found: C, 52.85, H, 4.57, N, 4.73.

Methyl 3-deoxy-3-iodo-5-O-p-nitrobenzoyl- α -D-arabinofuranoside (8b) — A mixture of compound 7b (2.9 g, 0.01 mole), sodium acetate (0.5 g), sodium iodide (7 g), acetic acid (12 ml), and acetone (100 ml) was boiled under reflux for 40 h, evaporated to dryness, the residue dissolved in chloroform (200 ml), and the solution successively washed with water (3 × 10 ml), 0.5M sodium thiosulfate (3 × 20 ml), dried (magnesium sulfate), evaporated, and the residue crystallized from ether (50 ml) plus petroleum ether (b.p. 60–80°) (5 ml) as light-yellow needles, yield 3.5 g (81.9%), m.p. 101–102°, $[\alpha]_D^{22} +79.5^\circ$ (c 1, chloroform), R_F 0.18 in 3:1 hexane–acetone, $\nu_{\text{max}}^{\text{KBr}}$ 3400–3300 (OH), 1745, 1625, and 1550 cm^{-1} (*p*-O₂NC₆H₄CO), n.m.r.

data (CDCl_3) δ 5.00 (d, $J_{1,2}$ 2 Hz, H-3), 4.63 (s, H-1), 4.58 (m, H-2), 4.53 (m, H-5,5'), 3.52 (m, H-4), 3.40 (s, OMe), and 8.26 (s, C_6H_4).

Anal Calc for $\text{C}_{13}\text{H}_{14}\text{INO}_7$ C, 36.90, H, 3.34; N, 3.31. Found C, 37.38, H, 3.57, N, 2.93

Methyl 3-deoxy-3-iodo-2,5-di-O-p-nitrobenzoyl- α -D-arabinofuranoside (9b) — To a solution of compound 8b (3.1 g, 7.5 mmoles) in pyridine (25 ml), cooled to 5°, was added *p*-nitrobenzoyl chloride (1.85 g, 10 mmoles), the mixture was processed as before. After two recrystallizations from dichloromethane (15 ml) plus hexane (2 ml), light-yellow needles were obtained, yield 3.15 g (74%), m.p. 185°, $[\alpha]_D^{22} -1.09^\circ$ (c 1.0, dichloromethane), R_F 0.21 in 3:1 hexane-acetone, n.m.r. data (CDCl_3) δ 5.63 (m, H-3), 5.20 (s, H-1), 4.83 (m, H-2, H-5,5'), 3.35 (m, H-4), 3.46 (s, OMe), and 8.23 (s, 2 C_6H_4).

Anal Calc for $\text{C}_{20}\text{H}_{17}\text{INO}_{10}$ C, 41.98, H, 2.99, N, 4.89. Found C, 42.08, H, 3.01, N, 4.83

Methyl 5-O-benzoyl-3-deoxy-3-iodo-2-O-p-nitrobenzoyl- α -D-arabinofuranoside. — Compound 8a was prepared from 3a by the method of Lemieux *et al.*³ To a solution of 8a (3.8 g, 0.01 mole) in pyridine (25 ml), cooled to 5°, was added *p*-nitrobenzoyl chloride (2.6 g, 15 mmoles). The mixture was stirred for 15 h at 20°, and processed as for 9b. Two recrystallizations from acetone (5 ml) plus hexane (10 ml) yielded colorless needles (3.78 g, 93.5%), m.p. 122°, $[\alpha]_D^{22} -18.51^\circ$ (c 1, chloroform), R_F 0.29 in 9:1 hexane-acetone; $\nu_{\text{max}}^{\text{KBr}}$ 1745, 1625, and 1550 cm^{-1} , n.m.r. data (CDCl_3) δ 5.63 (d, 4 Hz, H-3), 5.10 (s, H-1), 4.78 (m, H-2, H-5,5'), 4.13 (m, H-4), 3.46 (s, OMe), 8.10, 8.00, and 7.40 (m, C_6H_5 and C_6H_4).

Anal Calc for $\text{C}_{20}\text{H}_{19}\text{INO}_8$ C, 45.89, H, 3.48, I, 24.04, N, 2.65. Found C, 45.84, H, 3.38, I, 24.12, N, 2.74

Methyl 3,5-O-isopropylidene-2-O-(methylsulfonyl)- β -D-xylofuranoside (10b) — Methanesulfonylation of methyl 3,5-O-isopropylidene- β -D-xylofuranoside by the method of Baker *et al.*⁶ afforded a syrup that crystallized from 5:1 carbon tetrachloride-hexane to yield colorless, prismatic needles, m.p. 58°, $[\alpha]_D^{22} -50.9^\circ$ (c 1, chloroform) (lit.⁶, for syrupy compound, $[\alpha]_D -34.5^\circ$), R_F 0.42 in 13:7 hexane-acetone; n.m.r. data (CDCl_3) δ 4.96 (s, H-1), 4.76 (s, H-2), 4.30 (d, $J_{3,4}$ 4 Hz, H-3), 4.10 (m, H-4), 3.86 (m, H-5,5'), 3.36 (s, OMe), 3.01 (s, SO_2Me), and 1.5 (s, Me_2C).

Anal Calc for $\text{C}_{10}\text{H}_{18}\text{O}_7\text{S}$ C, 42.70, H, 6.04, S, 11.37. Found C, 42.56, H, 6.14; S, 11.35

Methyl 3-deoxy-2,5-di-O-p-nitrobenzoyl- β -D-threo-pentofuranoside (14b) — Compound 12b (ref. 6) (20 g) was hydrogenated in the presence of Raney nickel (four teaspoonsful) for 12 h at 60°/60 lb in H_2 . Filtration followed by evaporation of the solvent afforded a thick, colorless syrup that was *p*-nitrobenzoylated with *p*-nitrobenzoyl chloride (55.6 g) in pyridine (600 ml) as described for 5b, the product crystallized from benzene (20 ml) in light-yellow needles (35 g, 58%). After recrystallization, it had m.p. 115°, $[\alpha]_D^{22} -83.0^\circ$ (c 1, chloroform); R_F 0.36 in 13:7 hexane-acetone, n.m.r. data (CDCl_3) δ 5.2 (m, H-2), 4.98 (d, $J_{1,2}$ 2.5 Hz, H-1), 4.58 (m, H-4, H-5,5') 3.40 (s, OMe), and 2.53 (m, H-3,3').

Anal Calc for $C_{20}H_{18}N_2O_{10}$: C, 53.81, H, 4.03, N, 6.27. Found C, 53.81, H, 4.05; N, 6.21

*Methyl 3-deoxy- β -D-*threo*-pentofuranoside (13)* — Saponification of compound **14b** was accomplished with 30% aqueous potassium hydroxide in 1,4-dioxane (12 ml) for 4 h at 40° under nitrogen. The mixture was then kept for 18 h at 0°, the precipitated potassium *p*-nitrobenzoate was filtered off, and the filtrate was diluted with water (75 ml), and passed through a column (2 × 50 cm) of Dowex 50W X-8 (H^+). *p*-Nitrobenzoic acid was removed by filtration, and the filtrate was passed through a column (2 × 30 cm) of Dowex 1 X-8 (OH^-). The eluate (1.8 liters) was evaporated to a thick syrup (1.1 g, 79%) which crystallized, m.p. 35°, $[\alpha]_D^{22} -117.7^\circ$ (c 1.1, methanol), $R_F 0.10$ in 13.7 hexane-acetone, n.m.r. data (D_2O): δ 4.60 (d, $J_{1,2} 3.5$, H-1), 4.03 (m, H-2, H-4), 3.43 (m, H-5,5'), 3.25 (s, OMe), 1.86 (m, H-3), and 1.46 (m, H-3')

Methyl 2,3-anhydro-5-O-p-nitrobenzoyl- β -D-lyxofuranoside (15b) — Compound **12** was *p*-nitrobenzoylated as described for **7b**. The product crystallized in quantitative yield from acetone-ethanol, m.p. 92°, $[\alpha]_D^{22} -54.6^\circ$ (c 1, chloroform), $R_F 0.24$ in 7.3 hexane-acetone, n.m.r. data ($CDCl_3$): δ 5.03, (s, H-1), 4.63 (d, $J_{2,3} 4$ Hz, H-2, H-3), 4.26 (m, H-4), 3.53 (s, H-5,5'), 3.36 (s, OMe), and 8.23 (s, C_6H_4)

Anal Calc for $C_{13}H_{13}NO_7$: C, 52.88, H, 4.40, N, 4.74. Found C, 52.76, H, 4.49, N, 4.62

REFERENCES

- 1 G CASONI AND L GOODMAN, *J Amer Chem Soc*, 86 (1964) 1427, 4167
- 2 T VAN ES, *Carbohydr Res*, 21 (1972) 156
- 3 R U LEMIEUX, K A WATANABE, AND A A PAVIA, *Can J Chem*, 47 (1969) 4413
- 4 E WALTON, F W HOLLY, G E BOXER, AND R F NUTT, *J Med Chem*, 8 659 (1965)
- 5 R F NUTT AND E WALTON, in W W ZORBACH AND R S TIPSON (Eds.), *Synthetic Procedures in Nucleic Acid Chemistry*, Vol 1, Wiley, New York, 1968, p 339
- 6 B R BAKER, R E SCHAUB, AND J H WILLIAMS, *J Amer Chem Soc*, 77 (1955) 7