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ABSTRACT

A synthesis of 5,6-dideoxy-L-arabino-hexose (II) from methyl β -D-galactofuranoside is described.

INTRODUCTION

The isolation of 6-deoxy-5-keto-D-arabino-hexose (6-deoxy-D-arabino-hexos-5-ulose) (I) from hygromycin has recently been described (1). This substance was converted by reduction to 5,6-dideoxy-D-arabino-hexose, which was then characterized as its dithio-acetal (1). The purpose of this communication is to describe the synthesis of its optical isomer, 5,6-dideoxy-L-arabino-hexose (II). The elimination of tosyloxy (tolyl-p-sulphonyl-oxy) groups situated on vicinal primary and secondary alcoholic groups by heating the esters with sodium iodide is a general reaction (2) which has been observed in the hexitol (3), hexose (4), and inositol series (5).

Crystalline derivatives of ethyl α - and β -D-galactofuranosides are known, but their preparation is tedious. It was observed that an impure syrupy preparation of methyl β -D-galactofuranoside (6) which had been converted to the 2,3,5,6-tetra-toluene-*p*-sulphonate gave, when heated with a solution of sodium iodide in acetone, a crystalline methyl 5,6-didehydroxy-2,3-di-*O*-tosyl- α -L-arabino-hexoside (III; R = tosyl = tolyl-*p*-sulphonyl).



Removal of the tosyl groups by reductive saponification yielded crystalline methyl 5,6-didehydroxy- α -L-arabino-hexoside (III; R = H) which, when it was reduced (Raney nickel catalyst), furnished 5,6-dideoxy- α -L-arabino-hexoside (IV). This substance (IV) was also produced when the unsaturated tosyl derivative of III was reduced by boiling its solution in ethanol in the presence of Raney nickel, followed by reductive saponification of the tosyl groups.

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Tosylation of IV yielded a product indistinguishable from the substance III (R = H) produced by reduction of III (R = tosyl). This experiment proved that inversion of hydroxyl groups had not occurred during removal of the tolyl-*p*-sulphonyl groups in the preparation of III (R = H) and IV.

Both III (R = H) and IV were oxidized by aqueous sodium metaperiodate and yielded significant quantities of iodoform when the oxidized products were allowed to stand in iodine solution. When IV was shaken with ethanethiol and concentrated hydrochloric acid it yielded the diethyl dithioacetal of II. The p-isomer of this derivative was isolated from hygromycin.

When III (R = tosyl) was shaken with silver nitrate and iodine in acetonitrile solution (7), a crystalline deoxy-iodonitrate of III (R = tosyl) was produced. The location of the iodine group in this new product is undecided, as is the decision as to whether the substance is a derivative of L-altrose or of D-galactose.

EXPERIMENTAL

Solutions were evaporated under reduced pressure; optical rotations were determined at $20^{\circ} \pm 2^{\circ}$ C (unless otherwise stated).

Synthesis of Methyl 5,6-Didehydroxy-2,3-di-O-tolyl-p-sulphonyl- α -L-arabino-hexoside (III; R = Tosyl)

Crude methyl β -D-galactofuranoside (from 50 g of D-galactose (6)) was dissolved in pyridine (500 ml), and toluene-*p*-sulphonyl chloride (250 g) was added to the solution. After 20 hours, the solution was poured (with stirring) onto crushed ice. The syrupy tosyl derivatives were isolated in the usual way. The syrup, without further purification, was heated in acetone solution (500 ml) with sodium iodide (70 g) under reflux. The solution rapidly became brown because of the separation of iodine, and sodium toluene*p*-sulphonate precipitated. The mixture was filtered at intervals to minimize uneven boiling. (Yield of the sodium salt of toluene-*p*-sulphonic acid, 36.5 g.)

The acetone was removed and the residue was extracted with chloroform. The extracts were washed successively with a solution of sodium thiosulphate and then with water. The chloroform extract was dried (MgSO₄) and evaporated to a syrup which rapidly crystallized. The crystals (32 g) were recrystallized from methanol, m.p. 109–110° C, $[\alpha]_{\rm D} - 62^{\circ} \pm 2^{\circ}$ (c, 0.5 in chloroform). Anal. Calc. for C₂₁H₂₄O₈S₂: C, 53.8; H, 5.1; S, 13.7; OMe, 6.5. Found: C, 53.7; H, 5.5; S, 14.7; OMe, 6.5.

Methyl 5,6-Didehydroxy- α -L-arabino-hexoside (III; R = H)

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The di-O-tosyl derivative (above) (1 g) was dissolved in ethanol (100 ml), and sodium amalgam (100 g of 3%) was added portionwise with stirring. During the addition, water (150 ml) was added at such a rate that precipitation of the tosyl derivative was avoided. After 12 hours, the solution was made neutral with sulphuric acid and evaporated to dryness. The solid residue was extracted exhaustively with acetone and the extracts were evaporated. The crude crystalline residue (0.21 g) was volatile at 100° C and accordingly it was purified by sublimation at 12 mm/100° C. The product, after sublimation, had m.p. 60° C, $[a]_{p}^{23} - 110^{\circ} \pm 2^{\circ}$ (c, 0.67), and was analytically pure. The substance moved at 2.4 times the speed of rhamnose in *n*-butyl alcohol – ethanol – water (9:2:2) solvent, and gave a yellow coloration when it was heated with *p*-anisidine hydrochloride. Anal. Calc. for C₇H₁₂O₄: C, 52.5; H, 7.6; OMe, 19.4. Found: C, 52.4; H, 7.8; OMe, 22.3.

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Methyl 5,6-Dideoxy- α -L-arabino-hexoside (IV) (Methyl 5-Deoxy-5-C-methyl- α -L-arabino-side)

The unsaturated arabinoside derivative (above, 89 mg) was dissolved in methanol and hydrogenated at 20° in the presence of a Raney nickel catalyst (0.5 g). After 20 minutes, the hydrogen uptake (53.4 ml at S.T.P.) was constant. The solution was filtered and the filtrate evaporated. The product was purified by sublimation at 16 mm/100° C. The product had m.p. 63° C and $[\alpha]_D$ 126°±6° (c, 0.18). Anal. Calc. for C₇H₁₄O₄: C, 51.8; H, 8.7; OMe, 19.1. Found: C, 51.9; H, 8.7; OMe, 19.8.

Both this compound and the unsaturated glycoside were oxidized by sodium metaperiodate solution, with the consumption of more than one mole of reagent, per mole, and with the formation of iodine and iodoform. No formic acid was detected.

Methyl 5,6-Dideoxy-2,3-di-O-tosyl-a-L-arabino-hexoside

The unsaturated tosyl derivative (III; R = tosyl) (116 mg) was dissolved in ethanol (20 ml) and boiled under reflux in the presence of Raney nickel catalyst (0.5 g) for 4 hours. The odor of acetaldehyde was detectable during the reaction. The solution was cooled and filtered, and the filtrate evaporated to a crystalline solid which was purified by recrystallization from ethanol. The product had m.p. $93-94^{\circ}$ C, $[\alpha]_{\rm D} - 61^{\circ}$ (c, 2.23 in chloroform). A product which had the same properties was produced when methyl 5,6-dideoxy- α -L-arabino-hexoside (IV; 0.1 g) was allowed to react with toluene-*p*-sulphonyl chloride (0.3 g) in pyridine (5 ml) solution overnight. The substance, which was isolated after the pyridine solution had been poured onto ice, weighed 0.21 g and had m.p. $93-94^{\circ}$ C, not depressed on admixture with an authentic specimen. Anal. Calc. for C₂₁H₂₆O₈S₂: C, 53.6; H, 5.6; S, 13.6; OMe, 6.6. Found: C, 53.8; H, 6.0; S, 12.9; OMe, 6.6.

5,6-Didehydroxy-L-arabino-hexose Diethyl Dithioacetal

Methyl 5,6-dideoxy- α -L-*arabino*-hexoside (0.1 g) was shaken with ethanethiol (0.5 ml) and 6 N hydrochloric acid (0.5 ml) for 5 hours. The mixture was twice extracted with chloroform (2-ml portions) and the extracts were washed with sodium bicarbonate solution and then dried (MgSO₄). Removal of the chloroform left a syrupy diethyl dithioacetal which crystallized. It was recrystallized from water and had m.p. 110°. Anal. Calc. for C₁₀H₂₂O₃S₂: C, 47.3; H, 8.7; S, 25.2. Found: C, 47.4; H, 8.8; S, 24.8.

Iodonitration of Methyl 5,6-Didehydroxy-2,3-di-O-tolyl-p-sulphonyl- α -L-arabino-hexoside

Methyl 5,6-didehydroxy-2,3-di-O-tolyl-p-sulphonyl- α -L-arabino-hexoside (2.34g; 5 millimole) was dissolved in acetonitrile (50 ml), and to the solution was added silver nitrate (1.70 g; 10 millimole) and iodine (1.27 g; 5 millimole). An immediate precipitate of silver iodide was observed. The mixture was shaken at room temperature for 7 days in a stoppered flask from which light was excluded. The mixture was then filtered and the silver iodide was washed with acetonitrile and air-dried; yield 1.22 g. (The reaction of silver nitrate with iodine to give silver iodide and iodonium nitrate would give 1.17 g of silver iodide from the above amounts of reactants.)

The filtrate was boiled under reflux for 24 hours and a light precipitate was removed by filtration. Concentration of the filtrate afforded a yellow syrup which yielded a further precipitate (probably silver nitrate) when diluted with chloroform. The mixture was again filtered and the filtrate was evaporated to a syrup which crystallized from chloroform – light petroleum (b.p. 60–80° C). Total yield 0.36 g after recrystallization from the same solvents; i.e. 11.0% calculated as the iodonitrate. The compound had

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m.p. 125–126° C and $[\alpha]_D - 49^\circ$ (c, 5.0 in chloroform). Anal. Calc. for $C_{21}H_{24}INO_{11}S_2$: C, 38.4; H, 3.7; I, 19.3; N, 2.1; S, 9.8. Found: C, 38.4; H, 3.8; I, 18.6; N, 2.6; S, 9.5.

The infrared absorption spectrum showed a strong band at 1642 cm⁻¹ which was absent from the spectrum of the parent olefinic compound and is presumably due to the nitrate group. The residual syrup (1.85 g) gave an infrared absorption spectrum with bands of the same relative intensity and therefore probably contains one or more of the other three possible iodonitrates.

A portion of the crystalline iodonitrate (0.10 g) was dissolved in hot ethanol and the solution was refluxed for 90 minutes with hydrazine hydrate (0.03 ml) (8). Excess hydrazine was destroyed by boiling the solution for a further 15 minutes with Raney nickel. The mixture was then filtered and the filtrate was concentrated to an oil which was soluble in water but not soluble in chloroform. The properties of this product indicate that nitrate and tolyl-p-sulphonyl groups had both been removed. It was not further examined.

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