1073. *The Synthesis and Reactions of Unsaturated Sugars. Part I.* The Synthesis of Methyl* 4-O-*Benzyl*-2,3-*didehydro*-2,3-*dideoxy*-β-L-*ribopyranoside.*

By N. F. Taylor and (Mrs.) G. M. Riggs.

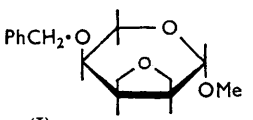
Methyl 2,3-anhydro-β-L-ribopyranoside, prepared by a modified existing procedure, was converted smoothly into methyl 2,3-anhydro-4-*O*-benzyl-β-L-ribopyranoside. Scission of this epoxide with methylmagnesium iodide yielded an iodohydrin, methyl 4-*O*-benzyl-3-iodo-3-deoxy-β-L-xylopyranoside. The 2-*O*-toluene-*p*-sulphonyl derivative of this compound, after treatment with sodium iodide in acetone, was converted by an elimination reaction into methyl 4-*O*-benzyl-2,3-didehydro-2,3-dideoxy-β-L-ribopyranoside.

Unsaturated sugars with a double bond at the 2,3-position have usually been made by the rearrangement of glycals (review by Helferich [1]) or 2-hydroxyglycals (review by Blair [2]). More recently 3,4,6-tri-*O*-acetyl-D-glucal has been rearranged to *p*-nitrophenyl 4,6-di-*O*-acetyl-2,3-didehydro-2,3-dideoxy-D-*erythro*-hexosides by treatment with *p*-nitrophenol.[3] Alternative methods, for the direct introduction of a double bond into carbohydrates, depend upon elimination reactions at suitably substituted terminal 1,2-glycols (*e.g.*, the 5,6-glycoseens [4] and hexatoleens [5]). Apart from the reported methyl 4,6-*O*-benzylidene-2,3-didehydro-2,3-dideoxy-α-D-glucopyranoside,[6-8] however, little attention has been given to the direct introduction of a 2,3-double bond into hexoses and pentoses. Our interest in the preparation of a suitably blocked 2,3-pentoseen was prompted initially by the possibility of addition reactions leading to 2- and 3-substituted pentoses.

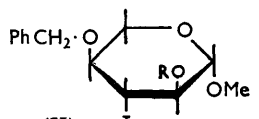
* Preliminary communication, Taylor and Riggs, *Chem. and Ind.*, 1963, 209.

[1] Helferich, *Adv. Carbohydrate Chem.*, 1952, **7**, 210.
[2] Blair, *Adv. Carbohydrate Chem.*, 1954, **9**, 97.
[3] Ferrier, Overend, and Ryan, *J.*, 1962, 3667.
[4] Helferich and Himmen, *Ber.*, 1928, **61**, 1825; Ohle and Varghe, *Ber.*, 1929, **62**, 2425.
[5] Bladen and Owen, *J.*, 1950, 598.
[6] Bollinger and Prins, *Helv. Chim. Acta*, 1946, **29**, 1061.
[7] Richards, *J.*, 1954, 4511.
[8] Newth, *J.*, 1956, 471.

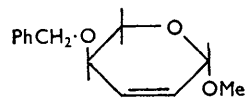
Methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside [9] was converted into the 2-*O*-*p*-nitrobenzenesulphonyl derivative, and the isopropylidene residue was removed by shaking with methanol containing concentrated hydrochloric acid, to give methyl 2-*O*-*p*-nitrobenzenesulphonyl-β-L-arabinopyranoside which, on treatment with 2N-sodium hydroxide, gave methyl 2,3-anhydro-β-L-ribopyranoside, identical with that prepared by Mukherjee and Todd.[10] Introduction of the 4-*O*-benzyl group into methyl 2,3-anhydro-β-L-ribopyranoside without extensive epoxide scission was achieved initially by an adaptation of the method developed by Sowden and Fischer [11] involving the use of the sodium–naphthalene reagent: [12] the monosodium salt of the compound was treated with benzyl bromide in 1,2-dimethoxyethane, and refluxing for 48 hours yielded methyl 2,3-anhydro-4-*O*-benzyl-β-L-ribopyranoside (I) in 50% yield. A 60% yield was obtained in later



(I)



(II) I



(III)

preparations by shaking methyl 2,3-anhydro-β-L-ribopyranoside with an excess of benzyl bromide and silver oxide in dimethylformamide at room temperature for 24 hours. This method appears to be generally applicable to the preparation of benzyl ethers of sugar epoxides since it had already been successfully used for the preparation of 4,6-di-*O*-benzyl ethers of methyl 2,3-anhydro-α-D-allo- and -manno-pyranosides.[13]

The scission of the epoxide ring in (I) by methylmagnesium iodide was most readily achieved when ether was the solvent.[7] Only one crystalline product containing iodine was isolated; the structure of this iodohydrin (II; R = H) was established by hydrogenation, using Raney nickel, which removed the 4-*O*-benzyl group and iodine to give a glycoside which did not consume periodate and was, therefore, assigned the structure of methyl 3-deoxy-β-L-xylopyranoside. This structure was confirmed when the latter was hydrolysed by acid to give a sugar which was chromatographically identical with 3-deoxy-D-xylose.[14] The 2,3-*trans*-arrangement of groups in methyl 4-*O*-benzyl-3-iodo-3-deoxy-β-L-xylopyranoside (II; R = H) is in agreement with the many examples of epoxide scission by Grignard reagents in the sugar series (review by Newth [15]). This was further supported when (II; R = H) was converted into the 2-*O*-toluene-*p*-sulphonyl derivative (II; R = $SO_2 \cdot C_6H_4Me$-*p*) and treated with sodium iodide in acetone. Reaction occurred at room temperature with the elimination of iodine and the toluene-*p*-sulphonyloxy-group (as sodium toluene-*p*-sulphonate) to give methyl 4-*O*-benzyl-2,3-didehydro-2,3-dideoxy-β-L-ribopyranoside (III) as a colourless liquid which solidified on standing. Compound (III) did not reduce Fehling's solution in the cold but immediately decolourised cold potassium permanganate solution.

The conversion of (II; R = $SO_2 \cdot C_6H_4Me$-*p*) into (III) provides a further example of this type of elimination, which has been discussed by Newth,[8] who showed that by heating methyl 4,6-*O*-benzylidene-3-iodo-3-deoxy-2-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside with sodium iodide in acetone at 100°, elimination occurred to give the corresponding 2,3-didehydro-2,3-dideoxy-α-D-glucopyranoside. It is perhaps significant that elimination occurs much more readily with (II; R = $SO_2 \cdot C_6H_4Me$-*p*) than with the glucose compound.

[9] Jones, Kent, and Stacey, *J.*, 1947, 1341.
[10] Mukherjee and Todd, *J.*, 1947, 969.
[11] Sowden and Fischer, *J. Amer. Chem. Soc.*, 1941, **63**, 3244.
[12] Scott, Walker, and Hansley, *J. Amer. Chem. Soc.*, 1936, **58**, 2442.
[13] Taylor, unpublished results.
[14] Allerton and Overend, *J.*, 1951, 1480.
[15] Newth, *Quart. Rev.*, 1959, **13**, 10.

Unlike the latter, compound (II; R = SO_2·C_6H_4Me-*p*) can readily undergo C1–1C interconversion, giving rise to a *trans*-axial–axial relationship of iodine and toluene-*p*-sulphonyloxy-groups, thereby facilitating the mechanism of elimination suggested by Foster and Overend.[16]

Experimental

M. p.s were determined by an Electrothermal apparatus and are uncorrected. Chromatography was carried out with Whatman No. 1 paper, using the water-poor phase of butan-1-ol–ethanol–water (4 : 1 : 5 v/v), and reducing sugars were detected by aniline hydrogen phthalate.[17]

Methyl 2-O-p-*Nitrobenzenesulphonyl*-3,4-O-*isopropylidene*-β-L-*arabinopyranoside*.—Methyl 3,4-*O*-isopropylidene-β-L-arabinopyranoside [9] (1·0 g.) was dissolved in dry pyridine (10 c.c.). *p*-Nitrobenzenesulphonyl chloride (1·6 g., 50% excess) was added and the solution set aside at room temperature for 24 hr., after which it was poured into ice-cold water (100 c.c.). The *product* separated immediately as a solid, m. p. 154° (from anhydrous ethanol) (1·6 g.), $[\alpha]_D^{20}$ +196·5° (*c* 1·45 in chloroform) (Found: C, 45·1; H, 4·7; S, 8·2. $C_{15}H_{19}NO_9S$ requires C, 45·1; H, 4·7; S, 8·0%).

Methyl 2-O-p-*Nitrobenzenesulphonyl*-β-L-*arabinopyranoside*.—Methyl 2-*O*-*p*-nitrobenzenesulphonyl-3,4-*O*-isopropylidene-β-L-arabinopyranoside (2·0 g.) was shaken overnight with methanol (100 c.c.) containing concentrated hydrochloric acid (0·4 c.c.). The solution was neutralised ($PbCO_3$), filtered, and evaporated to dryness *in vacuo*, to leave a syrup which was extracted with hot ethyl acetate (15 c.c.), and filtered. Light petroleum (b. p. 40—60°) was added to the filtrate to produce incipient turbidity; on standing, a crystalline solid (1·3 g.) separated, m. p. 131° (from ethyl acetate–light petroleum), $[\alpha]_D^{20}$ +185° (*c* 1·2 in ethyl acetate) (Found: C, 41·5; H, 4·4. $C_{12}H_{15}NO_9S$ requires C, 41·3; H, 4·3%). The 3,4-di-*O*-acetate had m. p. 122° (Found: C, 44·1; H, 4·4. $C_{16}H_{19}NO_{11}S$ requires C, 44·4; H, 4·4%).

Methyl 2,3-*Anhydro*-β-L-*ribopyranoside*.—Methyl 2-*O*-*p*-nitrobenzenesulphonyl-β-L-arabinopyranoside (7·0 g.) was dissolved in ethanol (150 c.c.) and heated with stirring to 60°. 2N-sodium hydroxide was added dropwise until the solution was distinctly alkaline, and the heating continued for a further 15 min. When cool, the mixture was filtered from sodium *p*-nitrobenzenesulphonate and the filtrate concentrated to ¾ of its value. Water (200 c.c.) was added to the concentrate and the solution extracted with chloroform (3 × 100 c.c.); the extract was dried (Na_2SO_4) and evaporated to dryness, to leave a colourless syrup (3 g.), b. p. 194°(bath)/0·8 mm., $[\alpha]_D^{20}$ +33° (*c* 0·5 in chloroform), identical with that prepared by Mukherjee and Todd.[10] Treatment of the compound (0·39 g.) with acetic anhydride (1·0 c.c.) in pyridine (7·0 c.c.) for 48 hr. afforded *methyl* 4-O-*acetyl*-2,3-*anhydro*-β-L-*ribopyranoside*, m. p. 70—71° [from light petroleum (b. p. 60—80°)], $[\alpha]_D^{20}$ +22·6° (*c* 2·2 in chloroform) (Found: C, 51·4; H, 6·1. $C_8H_{12}O_5$ requires C, 51·1; H, 6·4%). *Methyl* 2,3-*anhydro*-4-O-p-*nitrobenzenesulphonyl*-β-L-*ribopyranoside*, m. p. 151° (from absolute ethanol) (Found: C, 43·5; H, 3·7; S, 9·5. $C_{12}H_{13}NO_8S$ requires C, 43·5; H, 3·9; S, 9·6%), was also readily formed from the anhydro-sugar (0·2 g.), pyridine (7 c.c.), and *p*-nitrobenzenesulphonyl chloride (0·4 g.), by setting the solution aside overnight.

Methyl 2,3-*Anhydro*-4-O-*benzyl*-β-L-*ribopyranoside* (I).—*Method* 1. Methyl 2,3-anhydro-β-L-ribopyranoside (5·0 g.) in 1,2-dimethoxyethane (10 c.c.) was added with shaking to sodium–naphthalene reagent [12] [prepared from sodium (0·8 g.) and a molal solution of naphthalene in 1,2-dimethoxyethane (35 c.c.)] until the green colour of the solution disappeared. Benzyl bromide (12·5 c.c.) was added, the solution refluxed for 48 hr., cooled, and filtered, and the solvent (naphthalene and excess of benzyl bromide) removed by distillation *in vacuo*. The residue distilled as a mobile liquid, b. p. 128°/0·17 mm. (3·95 g.), which, on standing, gave a solid, m. p. 44—45° [from light petroleum (b. p. 40—60°)], $[\alpha]_D^{20}$ −12·0° (*c* in chloroform) (Found: C, 66·4; H, 7·1. $C_{13}H_{16}O_4$ requires C, 66·2; H, 6·8%).

Method 2. To methyl 2,3-anhydro-β-L-ribopyranoside (6·0 g.), dissolved in dry dimethylformamide (15 c.c.), were added benzyl bromide (6·0 g.) and silver oxide (6·0 g.). The mixture was shaken vigorously at room temperature for 24 hr., filtered, and the residues washed with chloroform. Water (300 c.c.) was added to the filtrate and washings, and the chloroform layer

[16] Foster and Overend, *J.*, 1951, 3452.
[17] Partridge, *Biochem. J.*, 1948, **42**, 238.

separated. The aqueous layer was extracted with chloroform (3 × 100 c.c.) and the combined extracts dried (Na_2SO_4). Evaporation of the chloroform left a mobile liquid which was distilled to give methyl 2,3-anhydro-4-*O*-benzyl-β-L-ribopyranoside (5·2 g.), which solidified on standing, m. p. 44—45°.

Methyl 4-O-*Benzyl*-3-*iodo*-3-*deoxy*-β-L-*xylopyranoside* (II; R = H).—Methyl 2,3-anhydro-4-*O*-benzyl-β-L-ribopyranoside (4·0 g.), in dry ether (200 c.c.), was added rapidly with stirring to methylmagnesium iodide [from methyl iodide (5·3 g.) and magnesium (0·9 g.) in ether (80 c.c.)] at room temperature. After being stirred for 1 hr., the solution was poured with stirring into crushed ice, acidified with dilute hydrochloric acid, and the ether layer separated. The aqueous layer was extracted with ether (3 × 50 c.c.) and the combined ether extracts washed with sodium carbonate solution, sodium thiosulphate solution, and water, dried (Na_2SO_4), and evaporated to dryness. Addition of a small volume of ether to the residue gave a crystalline solid (2·8 g.), m. p. 135° (from ethanol), $[\alpha]_D^{20}$ +19·4° (*c* 1·2 in chloroform) (Found: C, 42·8; H, 4·6; I, 35·1. $C_{13}H_{17}IO_4$ requires C, 42·9; H, 4·6; I, 34·9%). The structure of the *product* was shown as follows: the iodohydrin (150 mg.), in ethanol (10 c.c.) and water (3 c.c.), was refluxed with Raney nickel (50 g.) and barium carbonate (1·0 g.) for 2 hr. The mixture was filtered and the filtrate evaporated *in vacuo* to give a colourless syrup, which was dissolved in water (15 c.c.), extracted with chloroform (3 × 15 c.c.), and the aqueous layer evaporated to dryness *in vacuo*. The residue was dissolved in a small amount of ethanol, the solution filtered, and the filtrate evaporated to leave a colourless syrup which was non-reducing (Fehling's) and did not consume periodate. Hydrolysis of the syrup with N-sulphuric acid at 100° for 4 hr. gave only one reducing sugar, chromatographically identical with 3-deoxy-D-xylose,[15] R_F 0·45 (cf. 2-deoxy-D-ribose in the same solvent system, R_F 0·375).

Methyl 4-O-*Benzyl*-3-*iodo*-3-*deoxy*-2-O-*toluene*-p-*sulphonyl*-β-L-*xylopyranoside* (II; R = $SO_2{\cdot}C_6H_4Me$-*p*).—To methyl 4-*O*-benzyl-3-iodo-3-deoxy-β-L-xylopyranoside (4·0 g.) in dry pyridine (40 c.c.) was added toluene-*p*-sulphonyl chloride (4·0 g.). The solution was set aside at room temperature for 3 days, after which it was poured into ice-cold water; the solid which separated (4·0 g.) had m. p. 174° (from aqueous ethanol), $[\alpha]_D^{19}$ +2·1° (*c* 2·4 in chloroform) (Found: C, 46·5; H, 4·3; I, 24·5; S, 6·5. $C_{20}H_{23}IO_6S$ requires C, 46·3; H, 4·4; I, 24·5; S, 6·2%).

Methyl 4-O-*Benzyl*-2,3-*didehydro*-2,3-*dideoxy*-β-L-*ribopyranoside* (III).—Methyl 4-*O*-benzyl-3-iodo-3-deoxy-2-*O*-toluene-*p*-sulphonyl-β-L-xylopyranoside (2·0 g.) was dissolved in dry acetone (25 c.c.). Dry sodium iodide (2·0 g.) was added, and sodium toluene-*p*-sulphonate separated almost immediately. The mixture was refluxed on the water bath for 15 min., allowed to cool, and filtered. The filtrate and washings were evaporated to dryness *in vacuo*, water (100 c.c.) added to the residue, the aqueous solution extracted with chloroform (2 × 100 c.c.), and the extract washed with sodium thiosulphate solution and water. After drying (Na_2SO_4) the chloroform solution was evaporated to dryness to leave a pale yellow syrup which distilled as a colourless mobile liquid, b. p. 98°/0·05 mm. (0·7 g.), $[\alpha]_D^{20}$ −81·9° (*c* 1·2 in chloroform), n_D^{19} 1·5240 (Found: C, 70·6; H, 7·1. $C_{13}H_{16}O_3$ requires C, 70·7; H, 7·2%), which did not reduce Fehling's solution but immediately decolourised cold potassium permanganate solution.

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