84. *Synthesis of* 4-*Deoxy*-L-*ribose from* D-*Lyxose.*

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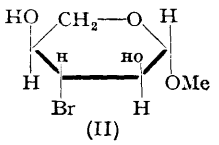
2 : 3-*iso*Propylidene α-methyl-D-lyxoside furnished a crystalline 4-toluene-*p*-sulphonate. After removal of the *iso*propylidene group, treatment of the product in alkaline conditions gave α-methyl-3 : 4-anhydro-D-lyxoside from which 4-bromo-4-deoxy-α-methyl-D-lyxoside was obtained. Hydrogenation of the bromo-compound gave β-methyl-4-deoxy-L-riboside. Neither this glycoside nor the corresponding free deoxy-sugar gave a positive Dische reaction.

THE principal known deoxyriboses are 2-deoxy- (Deriaz, Overend, Stacey, Teece, and Wiggins, *J.*, 1949, 1879), 3-deoxy- (Kent, Stacey, and Wiggins, *J.*, 1949, 1232), and 2 : 3-dideoxy-compounds (Allerton, Overend, and Stacey, *J.*, 1952, 255). We now report the synthesis of 4-deoxy-L-ribose.

Yields of deoxypentoses are, in general, poor by the arabinal method (cf. Meisenheimer and Jung, *Ber.*, 1927, **60**, 1462; Deriaz, Overend, Stacey, and Wiggins, *J.*, 1949, 2836). Methods depending on the cleavage of an ethylene oxide ring have been used by Kent, Stacey, and Wiggins (*loc. cit.*), Mukherjee and Todd (*J.*, 1947, 969), and Prins (*J. Amer. Chem. Soc.*, 1948, **70**, 3955).

α-Methyl-D-lyxoside, formed by the action of methanolic hydrogen chloride on D-lyxose (Phelps and Hudson, *J. Amer. Chem. Soc.*, 1926, **48**, 503), gave a 2 : 3-*iso*propylidene compound which readily yielded crystalline 2 : 3-*iso*propylidene 4-toluene-*p*-sulphonyl α-methyl-D-lyxoside. Hydrolysis by dilute acetic acid furnished 4-toluene-*p*-sulphonyl α-methyl-D-lyxoside, whence the anhydro-sugar (I) was obtained by sodium methoxide at

room temperature. Scission of the anhydro-ring with hydrobromic acid gave a single bromo-sugar, which differed from the known 3-bromo-3-deoxy-β-methyl-L-xyloside (II) and was shown by its ready oxidation with lead tetra-acetate under the conditions described by Hockett and McClenahan (*J. Amer. Chem. Soc.*, 1939, **61**, 1667) to be 4-bromo-4-deoxy-α-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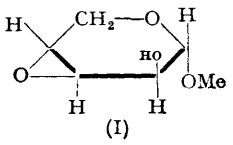
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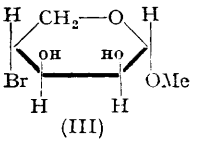
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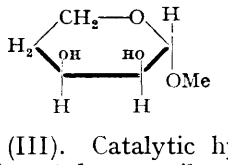
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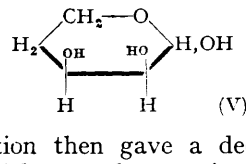
(V)

methyl-D-lyxoside (III). Catalytic hydrogenation then gave a deoxy-glycoside (IV), hydrolysed by acid to 4-deoxy-L-ribose (V), which was characterised as the crystalline *N'*-benzyl-*N'*-phenylhydrazone.

Although the Dische diphenylamine test (*Mikrochem.*, 1930, **8**, 4) is not completely specific to 2-deoxy-sugars (Allerton *et al.*, *loc. cit.*), neither 4-deoxyribose nor its methyl glycoside gives a positive result when heated with the reagent for 3·25 minutes at 100° (cf. Deriaz, Stacey, Teece, and Wiggins, *J.*, 1949, 1222).

On paper chromatography with a butanol–ethanol–water system (Hirst, Hough, and Jones, *J.*, 1949, 928), 3-deoxyribose moved somewhat faster than 2- or 4-deoxyribose, although all had similar R_G values in these solvents.

The configurational designation D or L of 4-deoxyribose depends on the configuration of $C_{(3)}$, since $C_{(4)}$ and $C_{(5)}$ are both symmetrical. Hydrogenation of 4-bromo-4-deoxy-α-methyl-D-lyxoside yields, consequently, 4-deoxy-β-methyl-L-riboside.

Experimental

α-Methyl-D-lyxoside.—D-Lyxose (5 g.) was refluxed for 5 hours with 0·5% methanolic hydrogen chloride (100 c.c.). The solution was neutralised by dry silver carbonate and evaporated *in vacuo*. α-Methyl-D-lyxoside crystallised and, recrystallised from ethyl acetate (yield, 4 g.), had m. p. 108—109°, $[\alpha]_D^{22}$ +51·8° (*c*, 0·6 in H_2O) (Found: OMe, 18·4. Calc. for $C_6H_{12}O_5$: OMe, 18·9%).

2 : 3-iso*Propylidene α-Methyl-D-lyxoside.*—The foregoing glycoside (3 g.) was shaken at room temperature with dry acetone (50 c.c.) and concentrated sulphuric acid (0·5 c.c.) for 24 hours. The acid was neutralised with anhydrous sodium carbonate and, after removal of the solvent, the syrupy product was distilled with a trace of barium carbonate in a high vacuum. It had m. p. 40—41°, b. p. 65°/0·02 mm., n_D^{23} 1·4575, $[\alpha]_D^{22}$ +42·7° (*c*, 0·8 in EtOH) (yield 2·8 g.) (Found: C, 53·5; H, 7·8; OMe, 15·0. Calc. for $C_9H_{16}O_5$: C, 53·5; H, 7·85; OMe, 15·2%).

2 : 3-iso*Propylidene* 4-*Toluene*-p-*sulphonyl α-Methyl-D-lyxoside.*—The above *iso*propylidene derivative (1·5 g.) in pyridine (10 c.c.) at 0° was treated with toluene-*p*-sulphonyl chloride (4 g.), After 24 hours at room temperature, pouring the solution into cold water and recrystallisation from ethanol gave the *ester*, m. p. 96—97°, $[\alpha]_D^{22}$ −10·2° (*c*, 1·85 in EtOH) (Found: C, 53·5; H, 6·1; S, 8·0. $C_{16}H_{22}O_7S$ requires C, 53·5; H, 6·15; S, 8·95%).

4-*Toluene*-p-*sulphonyl α-Methyl-D-lyxoside.*—The previous compound (1·15 g.) was warmed at 90—100° for 3 hours with 0·1% acetic acid (25 c.c.), then evaporated in a vacuum-desiccator (KOH). The *product*, which did not crystallise, had n_D^{21} 1·5240, $[\alpha]_D^{21}$ +30° (*c*, 1·4 in $CHCl_3$) (Found: OMe, 9·8. $C_{13}H_{18}O_7S$ requires OMe, 9·8%).

α-Methyl-3 : 4-anhydro-D-lyxoide (I).—4-Toluene-*p*-sulphonyl α-methyl-D-lyxoside (0·4 g.) in chloroform (10 c.c.) at 0° was treated with sodium methoxide in methanol (2 g. of sodium and 50 c.c. of methanol). After 12 hours at room temperature, the solution was diluted with chloroform (50 c.c.) and shaken with water (100 c.c.). The aqueous layer was neutralised with dilute sulphuric acid, and evaporated to dryness. The residue was extracted repeatedly with hot ethyl acetate, and the extract evaporated to dryness. The product distilled at 115° (bath-temp.)/0·02 mm. and became semicrystalline. The *anhydro*-compound had $[\alpha]_D^{22}$ +98·6° (*c*, 1·4 in $COMe_2$), n_D^{22} 1·4350 (Found: OMe, 21·25. $C_6H_{10}O_4$ requires OMe, 21·4%).

Scission of α-Methyl-3 : 4-anhydro-D-lyxoside with Hydrobromic Acid.—The anhydro-glycoside (I) (0·2 g.) was heated in acetone (50 c.c.) containing 2·04N-hydrobromic acid (5 c.c.) under reflux for 5 hours. The solution was neutralised by addition of lead carbonate and the filtrate concentrated to a small volume. The solid *4-bromo-4-deoxy-α-methyl-D-lyxoside* (III) (0·1 g.), which separated, was recrystallised twice from ethyl acetate and had m. p. 134—135°, $[\alpha]_D^{21}$ +14·6° (*c*, 0·7 in MeOH) (Found : Br, 33·3. $C_6H_{11}O_4Br$ requires Br, 35·2%). 3-Bromo-3-deoxy-β-methyl-D-xyloside has m. p. 101—102° $[\alpha]_D^{14}$ −16·4° (*c*, 0·4 in MeOH).

No evidence was obtained of another bromo-compound.

Oxidation of 4-Bromo-4-deoxy-α-methyl-D-lyxoside with Lead Tetra-acetate.—The rate of oxidation of the bromo-compound with lead tetra-acetate in acetic acid was compared with that of α-methyl-mannoside and -glucoside under the conditions recorded by Hockett and McClenahan (*loc. cit.*) in darkness. To about 10 mg. of the glycoside in acetic acid (12 c.c.) were added 12·5 c.c. of a standard solution of lead tetra-acetate (approx. 30 g./l. in acetic acid). The final volume was made up to 25·0 c.c. with acetic acid. At intervals, 5-c.c. portions were removed and transferred immediately into 10 c.c. of aqueous potassium iodide containing a little potassium sulphate. The iodine liberated was titrated with 0·02N-sodium thiosulphate. A control test was carried out on 12·5 c.c. of the lead tetra-acetate solution diluted to 25 c.c. with " AnalaR " acetic acid. The following results were obtained (corrected for control) :

Bromo-pentoside				
Time (hr.)	0·33	3	6	20
$Pb(OAc)_4$ consumed (mole/mole)	0·0031	0·031	0·048	0·106
α-Methylmannoside				
Time (hr.)	0·33	3	6	20
$Pb(OAc)_4$ consumed (mole/mole)	0·0052	0·030	0·054	0·099
α-Methylglucoside				
Time (hr.)	0·33	3	6	20
$Pb(OAc)_4$ consumed (mole/mole)	0·0006	0·006	0 012	0·026

Hydrogenolysis of 4-Bromo-4-deoxy-α-methyl-D-lyxoside (III).—A methanolic solution (30 c.c.) of the bromo-sugar (III) (0·2 g.) was shaken at room temperature in hydrogen, in the presence of freshly prepared Raney nickel (*ca.* 1 g.) and calcium hydroxide (0·1 g.). After 8 hours, the solution gave positive tests for bromide and was saturated with carbon dioxide and filtered. The filtrate was evaporated to dryness and the residue extracted exhaustively with hot ethyl acetate. Concentration of this extract yielded *β-methyl-4-deoxy-L-riboside* (IV) (0·12 g.), $[\alpha]_D^{21}$ +39·2° (*c*, 0·2 in H_2O), n_D^{21} 1·4815 (Found : OMe, 20·5. $C_6H_{12}O_4$ requires OMe, 21·0%).

4-Deoxy-L-ribose (V).—β-Methyl-4-deoxy-L-riboside (IV) (0·1 g.) was hydrolysed at 100° with N-sulphuric acid (20 c.c.). In 4 hours the optical rotation changed from +39° to +23° (const.). The solution was neutralised (phenolphthalein) with sodium carbonate, then evaporated to dryness, and the residue extracted with hot ethyl acetate. Evaporation of the extract gave 4-deoxy-L-ribose (V) (0·06 g.), which reduced Fehling's solution readily and had n_D^{22} 1·4920, $[\alpha]_D^{21}$ +23·1° (*c*, 0·2 in H_2O).

In 75% aqueous ethanol at 70° (1 hour) this gave a *benzylphenylhydrazone*, m. p. 102—103° (from aqueous ethanol) (Found : N, 8·3. $C_{18}H_{22}O_3N_2$ requires N, 8·9%).

Dische Tests.—The reagent was prepared from pure diphenylamine (2 g.) (twice recrystallised from ligroin) (Dische, *loc. cit.*). The test was carried out simultaneously on D-ribose (1·6 mg.) 2-deoxy-L-ribose (1·93 mg.), 3-deoxy-D-ribose (1·1 mg.), and 4-deoxy-L-ribose (1·2 mg.), each in water (2 c.c.) containing the reagent (4 c.c.). The solutions, and a control consisting of water (2 c.c.) and reagent (4 c.c.) alone, were heated in a boiling-water bath for 3·25 minutes, then cooled in ice for 15 minutes. The intensities of the colours were measured on a Spekker photo-electric colorimeter with Ilford filter 606. The following molecular extinction coefficients were obtained: D-ribose, 0; 2-deoxy-L-ribose, 2720; 3-deoxy-D-ribose, 146; 4-deoxy-L-ribose, 0.

Chromatography of 2-, 3-, and 4-Deoxyribose.—With butanol–ethanol–water (4 : 1 : 5) and Whatman No. 1 filter paper, as described by Hirst *et al.* (*loc. cit.*), the following R_G values were determined at 20° (bands were observed after spraying with aniline hydrogen phthalate) : D-ribose, 0·34, 2-, 0·50, 3-, 0·60, and 4-deoxyribose, 0·53.

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