113. *The Preparation of 2 : 3-Anhydromethyl-*D*-lyxoside from 2-Toluene-*p*-sulphonyl Methyl-*D*-xylofuranoside, and Synthesis of 2-Methyl* D*-Xylose, 3-Methyl* D*-Arabinose, and 3 : 5-Dimethyl* D*-Arabinose.*

By E. E. PERCIVAL and ROLF ZOBRIST.

Crystalline 2 : 3-anhydromethyl-D-lyxoside has been prepared; hydrolysis of the anhydro-ring with sodium methoxide led to the isolation and characterisation of crystalline 2-methyl D-xylose and syrupy 3-methyl D-arabinose.

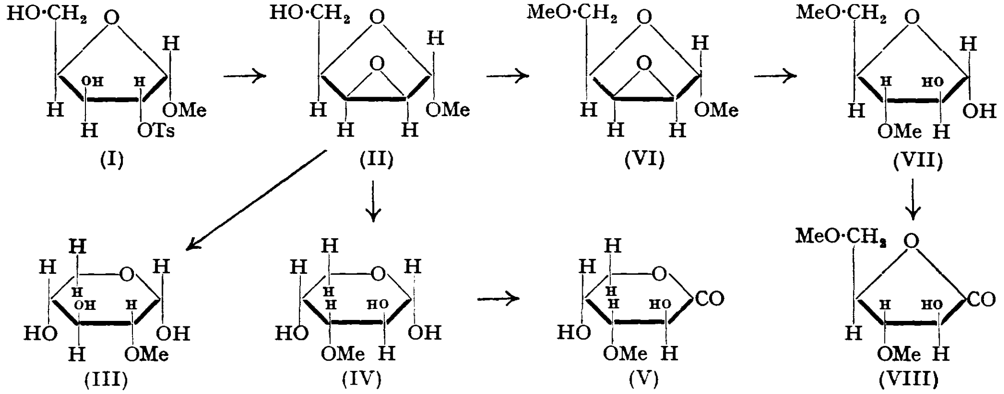
Methylation of the anhydro-compound gave crystalline 5-methyl 2 : 3-anhydromethyl-D-lyxoside. Fission of the anhydro-ring, followed by hydrolysis of the glycosidic methoxyl group, gave only one dimethyl pentose which has been identified as 3 : 5-dimethyl D-arabinose.

EARLIER work (Haworth, Hirst, and Panizzon, *J.*, 1934, 154; Peat and Wiggins, *J.*, 1938, 1088) furnished evidence that the alkaline hydrolysis of toluene-*p*-sulphonyl groups from methylglucosides results in the formation of ethylene oxide rings provided that there is a free hydroxyl group, in the *trans*-position, on the carbon atom adjacent to that carrying the toluenesulphonyl group. If these conditions prevail hydrolysis is accompanied by Walden inversion on the carbon atom which formerly carried the toluenesulphonyl residue. If was also shown by these workers that scission of the oxide ring with sodium methoxide gives two products. The ring can apparently break on either side of the oxygen atom, and at the point of entry of the methoxy-group inversion takes place. It is not always possible to isolate both products, since the proportions vary, that is, the chances of the two oxygen bridges being split are not equal in all such compounds owing to steric factors.

We decided to investigate some of these steric effects and at the same time attempt to synthesise different methylated derivatives of pentoses and methylpentosides. 2-Toluene-*p*-sulphonyl methyl-D-xylofuranoside (I) was used as the starting material. Hydrolysis with alkali gave 2 : 3-anhydromethyl-D-lyxoside (II) and fission of the anhydro-ring gave 2-methyl D-xylose (III) and syrupy 3-methyl D-arabinose (IV) in the ratio of 1 : 2. 2-Methyl xylose had m. p. 134°, not depressed on admixture with an authentic specimen, and on treatment with ethanolic aniline yielded the characteristic anilide (Percival and Willox, *J.*, 1949, 1608). 3-Methyl D-arabinose was a colourless syrup, $[\alpha]_D$ $-90°$ (*c*, 0·84 in H_2O) (initial). Oxidation with bromine water gave a crystalline lactone (V), m. p. 81°, which on treatment with methyl-alcoholic ammonia gave a crystalline amide, m. p. 132°. Hirst, Jones, and Williams (*J.*, 1947, 1062) record m. p. 78° and m. p. 132° for the same derivatives from 3-methyl L-arabinose.

2 : 3-Anhydromethyl-lyxoside was methylated with a view to ascertaining whether a 5-methoxyl group would influence the fission of the oxide ring. Treatment of crystalline 5-methyl 2 : 3-anhydromethyl-lyxoside (VI) with sodium methoxide gave a syrup containing only one dimethyl pentose, 3 : 5-dimethyl D-arabinose, contaminated with traces of trimethyl, monomethyl, and unmethylated pentoses. No evidence for the presence of 2 : 5-dimethyl xylose could be obtained.

Similar treatment of syrupy 2 : 3-anhydromethyl-lyxoside gave an identical syrup. These syrups were combined and freed from traces of impurity by separation on a column of powdered cellulose. Demethylation and chromatographic analysis of the resulting syrup revealed only the presence of arabinose and partially methylated arabinose. No xylose or methylated xyloses could be found. The pure dimethyl pentose separated from the column was identified as 3 : 5-dimethyl D-arabinose (VII) by oxidation with bromine water to the corresponding dimethyl D-arabonolactone (VIII). This lactone was crystalline (m. p. 74—75°) and its slow rate of mutarotation in aqueous solution ($[\alpha]_D$ $+85°$ changing to $+57°$ in 27 days) indicated that it belonged to the γ-series of arabonolactones (cf. Smith and Cunneen, *J.*, 1948, 1146, who record m. p. 75°, $[\alpha]_D$ $-84°$ changing to $-69°$ in 28 days for 3 : 5-dimethyl L-arabonolactone), and it gave a crystalline phenylhydrazide (Hirst, Jones and Williams, *loc. cit.*). The possibility of the simultaneous formation of 2 : 3- and 2 : 5-anhydromethyl-lyxosides had been envisaged, but no proof of the presence of fission products from the 2 : 5-ring compound could be obtained. It is conceivable, however, that part of the 2-methyl xylose isolated might have been derived from this source.



It is interesting that in the absence of substitution on $C_{(5)}$ hydrolysis of the ethylene oxide compound caused fission of both oxygen bridges and the two expected monomethyl derivatives, 2-methyl D-xylose and 3-methyl D-arabinose, were isolated. However, when a methyl group occupied $C_{(5)}$ a preferential splitting of the ring occurred between the oxygen atom and $C_{(3)}$, and only 3 : 5-dimethyl D-arabinose was obtained. No trace of the other isomer, 2 : 5-dimethyl D-xylose, could be found. Similar results have been obtained with methylated anhydro-derivatives of rhamnose and of fucose (unpublished work).

EXPERIMENTAL

2 : 3-*Anhydromethyl*-D-*lyxoside*.—2-Toluene-*p*-sulphonyl methylxylofuranoside (24 g.) (Percival and Zobrist, *J.*, 1952, 4306) was dissolved in ethanol (400 c.c.) and hydrolysed with 2N-sodium hydroxide at 75° until permanently pink to phenolphthalein (36·3 c.c., 96%). The solvents were removed under diminished pressure. Repeated extraction of the residue with ethyl acetate and removal of the solvent gave a syrup (11 g.) which partly crystallised. The crystals (A) (2·7 g., 23%) were separated and after recrystallisation from benzene had m. p. 81°, $[\alpha]_D^{15}$ +57° (*c*, 1·0 in H_2O) (Found: C, 49·3; H, 6·5; OMe, 20·7. $C_6H_{10}O_4$ requires C, 49·3; H, 6·85; OMe, 21·2%). The residual syrup (B) (8·3 g.) had $[\alpha]_D^{15}$ +4° (*c*, 0·95 in H_2O) (Found: OMe, 20·5%).

Alkaline Hydrolysis of 2 : 3-*Anhydromethyl*-D-*lyxoside*.—Crystalline 2 : 3-anhydromethyl-D-lyxoside (A) (0·1 g.) was heated at 95° for 12 hours with methanol (5 c.c.) containing 4% of sodium. Thereafter, the solution was diluted with water (5 c.c.), neutralised with solid carbon dioxide, and evaporated to dryness. Extraction with chloroform and removal of the solvent gave a colourless syrup. This was hydrolysed at 100° with 0·1N-sulphuric acid (10 c.c.) until no further change in rotation occurred ($[\alpha]_D^{15}$ $+63° \longrightarrow -4·7°$ in 3 hours). Neutralisation of the solution with barium carbonate and evaporation to dryness gave a colourless syrup (C). Examination on a paper chromatogram with butanol–ethanol–water (4 : 1 : 5) revealed the presence of 2-methyl xylose (R_G 0·38), a second nomomethyl pentose (R_G 0·26), and unmethylated pentose (R_G 0·19).

The residual syrup (B) (6·0 g.) was hydrolysed as described for the crystalline material (A) and, after removal of the glycosidic methoxyl group, gave a pale yellow syrup (D) (4·1 g.). Comparison on a paper chromatogram of the spots given by this syrup with those given by syrup (C) showed the two syrups to be identical. The above results together with the difference in rotation suggest that the crystals (A) are the α-form of 2 : 3-anhydromethyl-D-lyxoside and that the residual syrup (B) is a mixture of the α- and the β-form of this sugar.

The syrups (C) and (D) (4·0 g.) were combined and separated on a column of powdered cellulose (Chanda, Hirst, and Percival, *J.*, 1951, 1240). Elution was by purified light petroleum (b. p. 100—120°)–*n*-butanol (1 : 9) saturated with water. Fraction 1 (1·05 g.) was crystalline 2-methyl xylose, m. p. 134°, unchanged on admixture with an authentic specimen, $[\alpha]_D^{18}$ −22° (initial), +26° (3 days) (*c*, 0·61 in H_2O) (cf. Percival and Willox, *loc. cit.*) (Found: C, 44·1; H, 7·4; OMe, 18·5. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·3; OMe, 18·9%). Fraction 2 (2·16 g.) was syrupy 3-*methyl* D-*arabinose*, $[\alpha]_D^{15}$ −90° (initial), −43° (3 days) (*c*, 0·84 in H_2O) (Found: OMe, 18·6. $C_6H_{12}O_5$ requires OMe, 18·9%). Hirst, Jones, and Williams (*loc. cit.*) record

+110° (*c*, 3·6 in H_2O) for 3-methyl L-arabinose. Aqueous extraction of the column and removal of the water gave a syrup (0·4 g.). Quantitative determination of the sugars present by the method of Hirst, Hough, and Jones (*J.*, 1949, 928) with butanol–ethanol–water (4 : 1 : 5) as the eluting solvent gave arabinose (78%) and xylose (22%).

On being heated with alcoholic aniline (0·15 g. in 5 c.c.) 2-methyl D-xylose (0·1 g.) gave a crystalline aniline compound, m. p. 125—126°, $[\alpha]_D$ +212° (*c*, 0·5 in EtOAc) (cf. Percival and Willox, *loc. cit.*).

Characterisation of 3-*Methyl* D-*Arabinose*.—3-Methyl D-arabinose (0·23 g.) was oxidised to the lactone (0·13 g.), which crystallised immediately and was purified by sublimation in a vacuum; it had m. p. 81°, $[\alpha]_D^{18}$ +99° (5 min.), +104° (30 min.), +80° (3 days), +75° (22 days) (*c*, 2·994 in H_2O) (Found : 43·9; H, 6·7; OMe, 19·1. $C_6H_{10}O_5$ requires C, 44·4; H, 6·2; OMe, 19·1%). With alcoholic ammonia the *lactone* gave 3-methyl D-arabonamide, m. p. 132° (from alcohol and acetone), which gave a positive Weerman test.

5-*Methyl* 2 : 3-*Anhydromethyl-lyxoside*.—Crystalline 2 : 3-anhydromethyl-D-lyxofuranoside (0·60 g.) was methylated 3 times with methyl iodide and silver oxide, and a very volatile crystalline product (0·56 g.) was isolated. This was purified by sublimation in a vacuum and then had m. p. 43° (constant), $[\alpha]_D^{18}$ +60° (*c*, 4·45 in MeOH) (Found : C, 50·8; H, 7·7; OMe, 36·7. $C_7H_{12}O_4$ requires C, 52·5; H, 7·65; OMe, 38·7%).

Methylation of the syrupy 2 : 3-anhydromethyl-lyxofuranoside ($[\alpha]_D$ +4°) (6·0 g.) gave syrupy 5-methyl 2 : 3-anhydromethyl-D-lyxoside (5·5 g.), $[\alpha]_D^{18}$ +24° (*c*, 1·2 in H_2O) (Found : OMe, 39·5%).

Alkaline Hydrolysis of 5-*Methyl* 2 : 3-*Anhydromethyl*-D-*lyxoside*.—Following the procedure used for the unmethylated material, crystalline 5-methyl 2 : 3-anhydromethyl-lyxoside (0·40 g.) was treated with 4% sodium methoxide solution (25 c.c.). Neutralisation, however, was effected by passage through a column of cation exchange resin (Amberlite I.R.-100H). Evaporation of the solvents gave a colourless syrup (0·26 g.), $[\alpha]_D^{18}$ +64° (*c*, 0·92 in H_2O) (Found : OMe, 47·3. Calc. for $C_8H_{16}O_5$: OMe, 48·45%).

This syrup (0·25 g.) was hydrolysed with N-sulphuric acid at 100° for 1 hour, by which time the rotation had changed to $[\alpha]_D^{20}$ +37° (constant). After neutralisation and evaporation of the solvent a yellow syrup (E) (0·18 g.) was obtained. Chromatographic examination of this syrup with *n*-butanol–ethanol–water (4 : 1 : 5) indicated one main spot (R_G 0·77) and very faint spots corresponding to a trimethyl pentose (R_G 0·94), 2-methyl xylose (R_G 0·38), 3-methyl arabinose (R_G 0·27), and a pentose (R_G 0·19). 2 : 4-Dimethyl xylose, 2-methyl xylose, and xylose were run on the paper as controls.

Hydrolysis of syrupy 5-methyl 2 : 3-anhydromethyl-lyxoside ($[\alpha]_D$ +24°) (5·4 g.) with sodium methoxide gave a yellow syrup (3·8 g.), $[\alpha]_D^{18}$ −17° (*c*, 1·0 in H_2O) (Found : OMe, 47·4. Calc. for $C_8H_{16}O_5$: OMe, 48·45%). Hydrolysis with sulphuric acid gave a syrup (1·8 g.), $[\alpha]_D$ +38°, which revealed the same spots on a paper chromatogram as those given by the syrup (E) obtained from crystalline 5-methyl 2 : 3-anhydromethyl-lyxoside. Purification by passage through a column of powdered cellulose with light petroleum (b. p. 100—120°)–butanol (50 : 50) saturated with water as eluant gave a dimethyl pentose (F) (1·1 g.), $[\alpha]_D^{18}$ +47° (*c*, 0·76 in H_2O; const.) (Found : OMe, 33·9. $C_7H_{14}O_5$ requires OMe, 34·8%).

The purified syrup (F) (0·01 g.) was demethylated by hydriodic acid (1 c.c.) at 100° for 10 minutes. The solution was diluted with water (10 c.c.) neutralised with silver carbonate and filtered. Silver ions were removed by treatment with cation exchange resin (Amberlite I.R.-100H), and the solution was concentrated. Examination on a paper chromatogram with butanol–pyridine–water–benzene (5 : 3 : 3 : 1) as eluant revealed the presence of arabinose and unchanged dimethyl pentose. There was no evidence for the presence of xylose.

Characterisation of 3 : 5-*Dimethyl* D-*Arabinose*.—The sugar (F) (120 mg.) was oxidised with bromine (1 c.c.) in water (5. c.c.) at 20° for 48 hours. The 3 : 5-*dimethyl* D-*arabonolactone* (98 mg.) isolated in the usual way crystallised. The crystals, after recrystallisation from ether, had m. p. 74—75°, $[\alpha]_D^{15}$ +85° (after 15 min., *c*, 0·40 in H_2O), +80° (3 days), +77° (6 days), +57° (27 days) (Found: C, 47·4; H, 6·95; OMe, 34·9. $C_7H_{12}O_5$ requires C, 47·7; H, 6·9; OMe, 35·2%). A portion of the lactone (50 mg.) was heated with alcoholic phenylhydrazine for 2 hours. On cooling, the phenylhydrazide was deposited, as plates, m. p. 144—145°.

The authors are very grateful to Professor E. L. Hirst, F.R.S., for his interest and advice, and thank the Schweizerischen Schulrat, Eidgenössische Technische Hochschule, Zürich, and the University of Edinburgh for the award of an Exchange Studentship to one of them (R. Z.).

KING'S BUILDINGS, UNIVERSITY OF EDINBURGH. [*Received, November 6th,* 1952.]