## 335. 2 : 5-*Dimethyl Xylofuranose and* 2 : 3-*Dimethyl Xylose.*

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In the course of a research (unpublished) on the conversion of xylose into an isomeric pentose by means of optical inversions within the molecule, material became available for the preparation of 2 : 5-*dimethyl xylofuranose* and 2 : 3-dimethyl xylose. The former sugar has now been prepared for the first time; the latter, which has only been obtained from a natural source by the hydrolysis of methylated xylan (Hampton, Haworth, and Hirst, J., 1929, 1739), has now been prepared by synthetic methods. Of all the mono- and di-methyl derivatives of xylose which may be expected to exist, only 4-methyl xylose and 3 : 5-dimethyl xylofuranose (known in the form of a lactone) remain to be prepared.

Convenient starting points were found in 3-*p*-toluenesulphonyl 5-benzoyl 1 : 2-monoacetone xylose and 5-benzoyl 1 : 2-monoacetone xylose, which may be obtained by the methods of Svanberg and Sjöberg (*Ber.*, 1923, **56**, 863, 1448) and Levene and Raymond (*J. Biol. Chem.*, 1933, **102**, 317).

2:5-*Dimethyl Xylofuranose.*—The benzoyl group was removed from 3-*p*-toluenesulphonyl 5-benzoyl 1 : 2-monoacetone xylose by treatment with sodium methoxide, and 3-p-*toluenesulphonyl* 1 : 2-*monoacetone xylose* was obtained in crystalline form, which, on methylation with the Purdie reagents, gave a theoretical yield of crystalline 3-p-*toluenesulphonyl* 1 : 2-*monoacetone* 5-*methyl xylose*. This substance, on treatment with methyl-alcoholic hydrogen chloride, yielded a mixture of 3-p-*toluenesulphonyl* 5-*methyl* γ-*methylxylosides* which was separated into crystalline 3-p-*toluenesulphonyl* 5-*methyl* β-*methylxylofuranoside* and a syrup which was essentially the corresponding α-*methylxylofuranoside*. Moreover, it was possible, by means of treatment with methyl-alcoholic hydrogen chloride, to convert the syrupy

α-form into an equilibrium mixture from which the pure β-form could be isolated and *vice versa*.

The α- and the β-form of 3-*p*-toluenesulphonyl 5-methyl methylxylofuranoside were converted successively into the corresponding 3-p-*toluenesulphonyl* 2 : 5-*dimethyl methylxylofuranosides* and 2 : 5-*dimethyl methylxylofuranosides* and finally into 2 : 5-*dimethyl xylofuranose*. The same final product was obtained in each series of experiments. The structure assigned to the resultant sugar was proved by its conversion into the *p*-bromophenylosazone of 5-methyl xylose, identical with that obtained by Levene and Raymond (*loc. cit.*, p. 331).

2 : 3-*Dimethyl Xylose*.—5-Benzoyl monoacetone xylose was converted successively into 5-benzoyl γ-methylxyloside, 5-*benzoyl* 2 : 3-*dimethyl* γ-*methylxyloside*, 2 : 3-*dimethyl* γ-*methylxyloside*, and so into 2 : 3-dimethyl xylose. The identity of the sugar was proved by its conversion into 2 : 3-dimethyl β-methylxyloside and 4-*p*-toluenesulphonyl 2 : 3-dimethyl β-methylxyloside (Robertson and Speedie, J., 1934, 829). It is noteworthy that there was no indication of acyl migration during the methylation of 5-benzoyl γ-methylxyloside.

A similar synthesis was attempted from 5-*p*-toluenesulphonyl 1 : 2-monoacetone xylose *via* 5-p-*toluenesulphonyl* 3-*methyl* 1 : 2-*monoacetone xylose*. This substance was treated with methyl-alcoholic hydrogen chloride to effect removal of the acetone residue and its replacement with the methylxylosidic group. Unexpectedly, the *p*-toluenesulphonyl residue was eliminated at the same time, and the resulting product was a monomethyl methylxyloside. Similar experiments with 5-*p*-toluenesulphonyl 1 : 2-monoacetone xylose confirmed the unusual behaviour of the *p*-toluenesulphonyl group in position 5.

## Experimental.

Xylose was converted successively into diacetone xylose and 1 : 2-monoacetone xylose as described by Svanberg and Sjöberg (*loc. cit.*). The latter was converted into 3-*p*-toluenesulphonyl 5-benzoyl 1 : 2-monoacetone xylose, and 5-benzoyl 1 : 2-monoacetone xylose by the methods of Levene and Raymond (*loc. cit.*).

3-p-*Toluenesulphonyl* 1 : 2-*Monoacetone Xylose*.—3-*p*-Toluenesulphonyl 5-benzoyl 1 : 2-monoacetone xylose (10 g.) was dissolved in benzene (100 c.c.), and a solution of sodium (0·3 g.) in methyl alcohol (15 c.c.) added. The resulting homogeneous solution was kept at room temperature for 1 hour, then poured into water (100 c.c.). The benzene layer was separated, washed with dilute acid and water, dried, and evaporated to dryness. The product (6 g.) crystallised on cooling. On recrystallisation from ethyl alcohol–light petroleum, 3-p-*toluenesulphonyl* 1 : 2-*monoacetone xylose* was obtained as fine needles, m. p. 89—90°; $[\alpha]_D^{17°}$ — 28·6° in chloroform ($c$ = 2) (Found : S, 9·28. $C_{15}H_{20}O_7S$ requires S, 9·3%).

3-p-*Toluenesulphonyl* 1 : 2-*Monoacetone* 5-*Methyl Xylose*.—This substance was prepared in theoretical yield by methylating the above compound with methyl iodide and silver oxide. It crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 81—82°, $[\alpha]_D^{18°}$ — 31·8° in chloroform ($c$ = 2·412) (Found : MeO, 8·6. $C_{16}H_{22}O_7S$ requires MeO, 8·66%).

3-p-*Toluenesulphonyl* 5-*Methyl* γ-*Methylxylosides*.—The foregoing compound (2·5 g.), dissolved in methyl alcohol (150 c.c.) containing dry hydrogen chloride (4·5 g.), was kept at room temperature till no further change in rotation was observed. The initial value, $[\alpha]_D$ — 18·9°, changed to a constant value of + 11·3° (corrected for change in concentration) in 24 hours. The solution was neutralised with lead carbonate, filtered, and evaporated to dryness. The residue was extracted with ether, and the ethereal extract, after being decolorised with charcoal, was evaporated to give a clear syrup (2·0 g.) which partly crystallised on standing. On crystallising this material from ether–light petroleum (b. p. 40—60°), and then from carbon tetrachloride, 3-p-*toluenesulphonyl* 5-*methyl* β-*methylxylofuranoside* was obtained as colourless plates (0·8 g.), m. p. 89°, $[\alpha]_D^{18°}$ — 51·7° in chloroform ($c$ = 1·798) (Found : MeO, 18·9. $C_{14}H_{20}O_7S$ requires MeO, 18·97%).

The mother-liquors from the above crystallisations yielded a syrup (1·1 g.), which had the same empirical composition as the crystals described above, but differed markedly in showing $[\alpha]_D^{17°}$ + 44·5° in chloroform ($c$ = 2·207). This material is probably contaminated with traces of the β-form but is essentially 3-p-*toluenesulphonyl* 5-*methyl* α-*methylxylofuranoside* (Found : MeO, 18·78%).

A larger-scale experiment, in which 12 g. of starting material were used, gave the same end

point, $[\alpha]_D$ − 19·2° ⟶ + 11° (corrected), and yielded 4·2 g. of crystalline β-form along with 6·5 g. of the syrupy α-form.

*Interconversion of the α- and the β-Form of* 3-p-*Toluenesulphonyl 5-Methyl Methylxylofuranoside.*—The α-form (0·52 g.), purified as far as possible from the crystalline isomer and showing $[\alpha]_D^{17°}$ + 44·5° in chloroform, was dissolved in methyl alcohol (20 c.c.). The rotation of the solution was $[\alpha]_D^{17°}$ + 26·3°. After addition of a 10% solution of hydrogen chloride in methyl alcohol (1 c.c.), the solution was maintained at room temperature, and the course of the reaction observed polarimetrically. The rotation gradually fell, and after 48 hours was constant at + 11·7°. When the product was isolated as described above, 0·2 g. of the crystalline β-form was obtained on crystallisation.

In the same way the pure β-form was converted into an equilibrium mixture, $[\alpha]_D$ + 11·7°, from which a specimen of the α-form could be isolated. Unsuccessful attempts were made to change the equilibrium point by changing the conditions of reaction. The configuration of the methylxylosidic group in the two forms was determined by studying the hydrolysis of the 2 : 5-dimethyl methylxylofuranosides derived from them (see below).

3-p-*Toluenesulphonyl 2 : 5-Dimethyl Methylxylofuranosides.*—3-*p*-Toluenesulphonyl 5-methyl β-methylxylofuranoside was methylated by means of the Purdie reagents. After 12 such treatments, the 2 : 5-*dimethyl* compound was obtained in 70% yield as a colourless viscous syrup, $[\alpha]_D^{18°}$ − 49·9° in chloroform (*c* = 1·794), $n_D^{18°}$ 1·5037 (Found: MeO, 26·8. $C_{15}H_{22}O_7S$ requires MeO, 26·8%).

In similar fashion methylation of the syrupy α-isomer (20 treatments) yielded 3-p-*toluenesulphonyl* 2 : 5-*dimethyl* α-*methylxylofuranoside* as a viscous syrup which showed $[\alpha]_D^{17°}$ + 34·7° in chloroform (*c* = 1·976), $n_D^{18°}$ 1·5050 (Found: MeO, 26·1%).

2 : 5-*Dimethyl Methylxylofuranosides.*—3-*p*-Toluenesulphonyl 2 : 5-dimethyl β-methylxylofuranoside (7 g.) was dissolved in ethyl alcohol (50 c.c.), and a solution of potassium hydroxide (7·5 g.) in water (100 c.c.) added. The mixture was boiled for 10 hours. Polarimetric control was impossible owing to the rapid darkening of the solution. The alkali was neutralised with carbon dioxide, and the solvent removed under diminished pressure. The dry residue was extracted with ether, and the ethereal extract, on evaporation, yielded a dark syrup (3·1 g.), which on distillation gave 2 : 5-*dimethyl* β-*methylxylofuranoside* as a mobile colourless syrup (2·5 g.), b. p. 85° (bath temp.)/0·02 mm., $n_D^{17°}$ 1·4501, $[\alpha]_D^{17°}$ − 56° in chloroform (*c* = 2·26) (Found: MeO, 47·8. $C_8H_{16}O_5$ requires MeO, 48·4%).

In similar fashion, the α-methylxylofuranoside (5·3 g.) was converted into 2 : 5-*dimethyl* α-*methylxylofuranoside*, which was obtained as a colourless syrup (1·7 g.), b. p. 110° (bath temp.)/0·03 mm., $n_D^{18°}$ 1·4507, $[\alpha]_D^{17°}$ + 54·3° in chloroform (*c* = 2·696) (Found: MeO, 47·5%).

2 : 5-*Dimethyl Xylofuranose.*—2 : 5-Dimethyl β-methylxylofuranoside (2 g.) was dissolved in a mixture of water (75 c.c.), acetone (75 c.c.), and hydrogen chloride (4·5 g.). The hydrolysis was observed polarimetrically and was carried out at room temperature. The initial rotation $[\alpha]_D$ − 49·1° changed in 10 hours to a constant value of + 32·4° (corrected for change in concentration). The solution was neutralised with lead carbonate, filtered, and evaporated to dryness. Extraction of the dry residue with acetone, followed by evaporation to dryness, yielded 2 : 5-*dimethyl xylofuranose* as a viscous syrup, which reduced Fehling's solution on warming and showed $n_D^{14°}$ 1·4706, $[\alpha]_D^{17°}$ + 46° in water (*c* = 1·21) and + 16·4° in ethyl alcohol (*c* = 1·85) (Found: MeO, 34·0. $C_7H_{14}O_5$ requires MeO, 34·8%).

When 2 : 5-dimethyl α-methylxylofuranoside (1·3 g.) was submitted to similar treatment, the initial rotation $[\alpha]_D$ + 32·3° changed to a constant value of + 27° (corrected for change in concentration) in 5 hours. In this experiment, however, a different proportion of acetone and water was used, and this accounts for the discrepancy in the value of the end point. The product was isolated as above, and the 2 : 5-dimethyl xylofuranose so obtained showed $n_D^{17°}$ 1·4699, $[\alpha]_D^{16°}$ + 16·6° in ethyl alcohol (*c* = 1·327) (Found: MeO, 33·8%).

The results of the above hydrolyses corroborate the configurations assigned to the two series of xylofuranosides which have been described.

*Conversion of* 2 : 5-*Dimethyl Xylofuranose into the* p-*Bromophenylosazone of* 5-*Methyl Xylose.*—2 : 5-Dimethyl xylofuranose (0·3 g.) was dissolved in water (20 c.c.), and *p*-bromophenylhydrazine (0·8 g.) in 10% acetic acid (8 c.c.) added. The mixture was heated at 60° for an hour, after which the temperature was gradually raised to 90° and maintained at that point for 1½ hours. The osazone, together with a large amount of tarry material, separated, and after cooling, the aqueous liquor was decanted. Several crystallisations from ethyl alcohol and finally from ether were necessary to free the osazone from tarry material. The *p*-bromophenylosazone was finally obtained as flat, blunt, yellow-brown needles (0·04 g.), m. p. 167—169° (decomp.). Levene

and Raymond quote m. p. 170—171° (Found : MeO, 6·2. Calc. for $C_{18}H_{20}O_3N_4Br_2$ : MeO, 6·2%).

5-*Benzoyl* γ-*Methylxyloside.*—5-Benzoyl 1 : 2-monoacetone xylose (5 g.) was dissolved in methyl alcohol (60 c.c.) containing hydrogen chloride (0·6 g.), and the solution was boiled until the rotation became constant. The hot solution was neutralised with lead carbonate, cooled, filtered, and evaporated to dryness. The residue was extracted with boiling chloroform, and after filtration and evaporation, a mixture of the α- and the β-form of 5-benzoyl γ-methylxyloside was obtained as a yellow syrup (4·2 g.). The product was contaminated with methyl benzoate, but it was decided to remove this impurity at a later stage.

5-*Benzoyl* 2 : 3-*Dimethyl* γ-*Methylxyloside.*—The mixture of 5-benzoyl γ-methylxylosides (17·5 g.) was methylated three times with methyl iodide and silver oxide. The resulting syrup, $n_D^{15°}$ 1·4920, was dissolved in benzene, and the solution repeatedly extracted with water to remove trimethyl γ-methylxyloside which might have resulted through the loss of benzoyl content and consequent exposure of the hydroxyl group to methylation. The benzene solution, after drying over anhydrous sodium sulphate and evaporation, yielded a mixture of the α- and the β-form of 5-*benzoyl* 2 : 3-*dimethyl* γ-*methylxyloside* as a mobile syrup (16·3 g.), $n_D^{15°}$ 1·4918 (Found : MeO, 32·3. $C_{15}H_{20}O_6$ requires MeO, 31·4%). The high methoxyl value is undoubtedly due to the persistence of traces of methyl benzoate in the product.

2 : 3-*Dimethyl* γ-*Methylxyloside.*—The benzoyl group was removed from 5-benzoyl 2 : 3-dimethyl γ-methylxyloside (18 g.) by boiling it for 1 hour with *N*/5-aqueous-alcoholic sodium hydroxide solution. The reaction mixture was diluted with water, and the alcohol evaporated; the aqueous residue was almost saturated with potassium carbonate and extracted repeatedly with chloroform; the combined extracts were dried and evaporated to dryness. As the resulting syrup might contain unchanged material in addition to the desired product, it was dissolved in benzene, and the solution extracted repeatedly with water until an aqueous extract showed no optical activity. The combined aqueous extracts were almost saturated with potassium carbonate and exhaustively extracted with chloroform. The combined chloroform extracts, on drying and evaporation, yielded a syrup (7·7 g.), which was distilled to give 2 : 3-*dimethyl* γ-*methylxyloside* (6·5 g.) as a colourless mobile syrup, b. p. 95° (bath temp.)/0·15 mm., $n_D^{15°}$ 1·4518, and $[\alpha]_D^{16°}$ + 12·5° in chloroform ($c$ = 2·104) (Found : MeO, 48·9. $C_8H_{16}O_5$ requires MeO, 48·4%).

2 : 3-*Dimethyl Xylose.*—2 : 3-Dimethyl γ-methylxyloside (5·8 g.) was hydrolysed by boiling with *N*/10-hydrochloric acid (200 c.c.). The initial rotation, $[\alpha]_D$ + 16·7°, changed to a constant value of + 22·3° (corrected for change in concentration) in 90 mins. The hot solution was neutralised with lead carbonate, filtered, and evaporated, and the residue was extracted with hot acetone. On evaporation of the acetone, 2 : 3-dimethyl xylose (4·8 g.) was obtained as a pale yellow syrup, which showed $n_D^{16°}$ 1·4727, and $[\alpha]_D$ + 18·9° changing to + 19·6° in chloroform ($c$ = 1·7) (Found : MeO, 34·6. Calc. for $C_7H_{14}O_5$ : MeO, 34·8%). The above constants are almost identical with those quoted by Robertson and Speedie (*loc. cit.*) for 2 : 3-dimethyl xylose obtained from xylan by the method of Hampton, Haworth, and Hirst (*loc. cit.*).

2 : 3-Dimethyl xylose was characterised by conversion into 2 : 3-dimethyl β-methylxyloside and 4-*p*-toluenesulphonyl 2 : 3-dimethyl β-methylxyloside by the methods described by Robertson and Speedie (*loc. cit.*).

2 : 3-Dimethyl β-methylxyloside was a clear syrup, b. p. 95° (bath temp.)/0·03 mm., $n_D^{17°}$ 1·4538, $[\alpha]_D^{18°}$ — 5·7° in chloroform ($c$ = 1·8) (Found : MeO, 48·1. Calc. for $C_8H_{16}O_5$ : MeO, 48·4%). The material prepared from xylan showed b. p. 90—95° (bath temp.)/0·03 mm., $n_D^{15}$ 1·4540, $[\alpha]_D$ — 5·8° in chloroform ($c$ = 2·20).

4-*p*-Toluenesulphonyl 2 : 3-dimethyl β-methylxyloside was a crystalline solid, m. p. 59—60°, $[\alpha]_D^{17°}$ —8·5° in chloroform ($c$ = 1·2). Robertson and Speedie quote m. p. 56—59°, $[\alpha]_D$ — 8·8° in chloroform ($c$ = 2·50) for the same substance derived from xylan.

5-p-*Toluenesulphonyl Monoacetone* 3-*Methyl Xylose.*—5-*p*-Toluene sulphonyl 1 : 2-monoacetone xylose, prepared by the method of Levene and Raymond (*loc. cit.*), was converted into 5-p-*toluenesulphonyl monoacetone* 3-*methyl xylose* by methylation with the Purdie reagents. It crystallised from methyl alcohol in needles, m. p. 114°, $[\alpha]_D$ — 27·2° in chloroform ($c$ = 2·173) (Found : MeO, 8·6. $C_{16}H_{22}O_7S$ requires MeO, 8·66%).

*Treatment of* 5-p-*Toluenesulphonyl Monoacetone* 3-*Methyl Xylose with Methyl Alcohol containing Hydrogen Chloride.*—The material (4·0 g.), dissolved in methyl alcohol (100 c.c.) containing dry hydrogen chloride (1 g.), was kept at room temperature for 10 hours. No polarimetric observation was possible owing to the rapid development of colour. The solution was neutralised with lead carbonate, filtered, and evaporated to dryness. The resultant syrup

(1·2 g.) was taken up in ether, boiled with norit, filtered, and the solution evaporated. The purified product contained no sulphur and corresponded with a monomethyl methylxyloside (Found : MeO, 34·9. Calc. for $C_7H_{14}O_5$ : MeO, 34·8%). The *p*-toluenesulphonyl group had been eliminated. Similar results were obtained when 5-*p*-toluenesulphonyl monoacetone xylose was submitted to the above treatment.

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