

CCXXVI.—*The Transformation of Monomethyl  
Fructose into Derivatives of  $\gamma$ -Fructose.*

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WITH the object of explaining the anomalous position of fructose as compared with glucose in respect to the oxide ring system (Charlton, Haworth, and Peat, this vol., p. 98), attention is directed to the monomethyl fructose prepared by Irvine and Hynd (J., 1909, 95, 1220) from  $\alpha$ -fructose diacetone. This monomethyl fructose belongs to the normal fructose series, since it is lævo-rotatory and methylation leads to normal crystalline tetramethyl fructose. In allocating the methyl group to the terminal position (6) in the chain, Irvine and Hynd relied on the results of oxidation.

These, however, are open to criticism on the grounds that the oxidation product was not distilled, analytical data were recorded for material manifestly non-homogeneous, and contact with methyl alcohol may have led to partial esterification, thus complicating the methoxyl value.

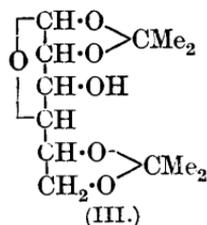
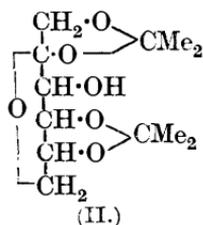
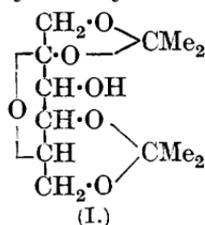
The monomethyl fructose, if it is indeed 6-methyl fructose, should on current views be incapable of conversion into a  $\gamma$ -methylfructoside having a 2 : 6-oxide ring. A methyl  $\gamma$ -methylfructoside has, however, been prepared from it, further methylation of which gave a product apparently identical in its properties with tetramethyl  $\gamma$ -methylfructoside which, on hydrolysis, was converted into tetramethyl  $\gamma$ -fructose.

Thus the amylenoxide structure applied to  $\gamma$ -fructose derivatives is inconsistent with the presence of a methyl group in the sixth position in monomethyl fructose, and cumulative evidence furnishes grounds for the recognition of the latter as 3-methyl fructose.

$\alpha$ -Fructose diacetone is definitely a derivative of normal fructose (Irvine and Patterson, J., 1922, **121**, 2146) and the difficulties in its formulation arising through the unusual isopropylidene linking between two non-adjacent hydroxyl groups (I) are obviated in (II), which represents  $\alpha$ -fructose diacetone as based on a 2 : 6-oxide ring structure for normal fructose. The second acetone residue may be attached either to carbon atoms 3 and 4 or to 4 and 5, but the relationship existing between monomethyl fructose and monomethyl glucose (prepared from the diacetone compounds) in the identity of their osazones enables a choice to be made in favour of the 4 : 5-attachment,  $\gamma$ -glucose being assumed to be butylene oxidic; glucose diacetone will then be represented by (III).

The above considerations combined with other experimental results obtained in these laboratories are inconsistent with the formula ascribed to normal fructose by Irvine and Patterson (J., 1922, **121**, 2702), who regard it as a butylene oxide sugar. On the basis of the new formula for glucose, it may require alteration to the amylenoxide structure. Conversely, the amylenoxide constitution applied by Haworth and Linnell (J., 1923, **123**, 294) to derivatives of  $\gamma$ -fructose is also involved in this adjustment. Work now proceeding under Prof. Haworth indicates the necessity for this revision in view of the non-homogeneous nature of the oxidation products of  $\gamma$ -fructose derivatives causing fortuitous analytical results. The proposed structures bring into harmony the relationship of glucose and fructose diacetones and elucidate the properties of the monomethyl sugars. The inability of  $\gamma$ -methylfructoside to condense with acetone is also explained.

Incidentally during the course of the work a crystalline monomethyl methylfructoside was isolated.



#### EXPERIMENTAL.

*Preparation of Monomethyl Fructose.*—Methyl  $\alpha$ -fructose diacetone, m. p. 118°, obtained by methylating  $\alpha$ -fructose diacetone by Irvine and Hynd's method (*loc. cit.*), was hydrolysed with dilute hydrochloric acid, and the monomethyl fructose obtained was recrystallised from ethyl acetate–methyl alcohol.

*Monomethyl Methylfructoside and Monomethyl  $\gamma$ -Methylfructoside.*—In a preliminary experiment on the condensation of monomethyl fructose with cold methyl alcohol containing hydrogen chloride, a syrup was obtained having a slight reducing action towards Fehling's solution. After several extractions with ether and ethyl acetate the syrup gradually crystallised in large, colourless tetrahedra, m. p. 143°,  $[\alpha]_D - 34.6^\circ$  in ethyl alcohol ( $c = 1.1$ ), and then had the composition of a monomethyl methylfructoside, probably of the normal form (Found: C, 45.7; H, 7.6; OMe, 29.5.  $\text{C}_8\text{H}_{16}\text{O}_6$  requires C, 46.1; H, 7.8; OMe, 29.8%).

In cold methyl alcohol containing 0.5% of hydrogen chloride the specific rotation of monomethyl fructose increased from  $-29.5^\circ$  to the constant value  $+35.4^\circ$  in 40 minutes. After neutralisation of the acid and removal of the solvent, the syrup obtained, which was devoid of reducing power, was shown to be monomethyl  $\gamma$ -methylfructoside by its conversion, by two treatments with silver oxide and methyl iodide, into tetramethyl  $\gamma$ -methylfructoside (b. p. 93–94°/0.03 mm.; OMe, 58.6%;  $n_D 1.4468$ ;  $[\alpha]_D + 13.7^\circ$  in ethyl alcohol,  $+15.0^\circ$  in methyl alcohol). The value for the specific rotation, which is lower than most of those recorded, is due to the predominance of one isomeric form. In methyl alcohol containing 0.5% of hydrogen chloride an equilibrium value of  $+36.0^\circ$  was obtained after the mixture had been heated at 100° for 2 hours in a sealed tube. Hydrolysis of the fructoside gave tetramethyl  $\gamma$ -fructose [OMe, 49.2%;  $n_D 1.4520$ ;  $[\alpha]_D$  (final)  $+24.3^\circ$  in water ( $c = 0.8$ )]. Menzies (*J.*, 1922, **121**, 2238) gives  $[\alpha]_D + 24.6^\circ$ .

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