CLXIX.—*Sugar Carbonates. Part III. Derivatives of γ-Methylfructoside, γ-Ethylfructoside, and Normal Methylfructoside.*

By CHARLES FREDERICK ALLPRESS, WALTER NORMAN HAWORTH, and JOHN JAMES INKSTER.

SINCE the fructose residue in sucrose is not the normal, but the γ- or labile form, it seems to be a necessary preliminary to the synthesis of sucrose that derivatives of γ-methylfructoside should be made available. The fructoside is readily prepared from ordinary fructose by standard methods, and is characterised by the ease with which its methyl residue can be eliminated. This property induced us to attempt to substitute carbalkyloxy-groups for the hydrogen atoms of the remaining hydroxyls in γ-methylfructoside, and in this we have succeeded. The methods employed are described below, but we have not yet been successful in exposing the reducing hydroxyl group of the substituted ketose. Similar experiments have also been undertaken with *γ-ethylfructoside*.

Condensation of γ-methylfructoside with methyl chloroformate in presence of pyridine gave rise to *tetracarbomethoxy γ-methylfructoside*. A series of experiments on the graded hydrolysis of this compound with aqueous-alcoholic solutions containing 0·5% up to 2·5% of hydrogen chloride gave distinct evidence of hydrolysis as indicated by the Fehling's test, and although the methoxyl content of the product (28% OMe) approximated to that (30·1% OMe) required for tetracarbomethoxy γ-fructose, yet the other analytical data showed that the product was not homogeneous. The corresponding *tetracarbethoxy γ-methylfructoside* was also prepared.

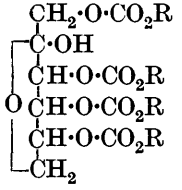
Condensation of γ-ethylfructoside with ethyl chloroformate gave *tetracarbethoxy γ-ethylfructoside*, which distilled without difficulty and showed $[\alpha]_D$ + 27·5° in ethyl alcohol. The dextrorotatory character of the product would appear to indicate that the γ-ethylfructoside residue has been retained, and indeed the compound gave the usual test with neutral permanganate, which was decolorised instantly. Hydrolysis of the glucosidic ethoxyl residue was not effected completely by heating with 1·25% aqueous hydrogen chloride for 3 hours at 80°, but seemed to proceed with greater ease at 90°, and the product reduced Fehling's solution normally; we have, however, not yet isolated pure tetracarbethoxy γ-fructose. The results of our experiments indicate that the introduction of carbonic ester residues into the γ-fructosides tends considerably to increase the stability of the alkylfructoside residue.

Compounds of the desired type but related to normal fructose

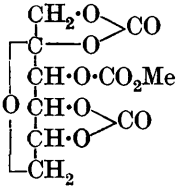
have already been described (Allpress and Haworth, J., 1924, **125**, 1228). These are tetracarbomethoxy fructose and tetracarbethoxy fructose, and both these compounds are represented on the basis of the revised structural formula for normal fructose (I). It was previously stated that, although these two crystalline products displayed little, if any, mutarotation in chloroform or acetone, they were probably to be formulated as containing a free reducing group. This conclusion has now been confirmed by the preparation of the corresponding methylfructosides by methylation. These are devoid of action on Fehling's solution, and are recognised as *tetracarbomethoxy methylfructoside* and *tetracarbethoxy methylfructoside*. The carboxylated methylfructosides of the two structural types, the stable and the unstable form, are therefore made available.

In the γ- or unstable series we have not encountered an example of the formation of a true carbonate of the type represented by (II) derived from the normal fructose. The formulation of this crystalline substance, monocarbomethoxy fructose dicarbonate, is, however, now revised on the basis of the new fructose formula (compare Allpress and Haworth, *loc. cit.*).

(I.)



(II.)



Experimental.

Tetracarbomethoxy γ-Methylfructoside.—To a well-cooled mixture of γ-methylfructoside (13 g.; prepared by Menzies' method, J., 1922, **121**, 2238) and dry chloroform containing pyridine (6 mols.), methyl chloroformate was gradually added. The γ-methylfructoside dissolved after agitation for several hours and the reaction was then at an end. Chloroform was removed under diminished pressure, pyridine hydrochloride extracted with water, and the remaining syrup was dissolved in acetone, dried, and distilled after removal of the solvent (b. p. 226—227°/0·1 mm.). Yield, 10—14 g. *Tetracarbomethoxy γ-methylfructoside* was thus obtained as a pale yellow, viscid syrup which showed no tendency to crystallise and did not reduce Fehling's solution. It had $[\alpha]_D$ + 19·8° in acetone (c = 1·5) (Found : C, 42·2; H, 5·1; OMe, 33·5; *M*, ebullioscopic in acetone, 415. $C_{15}H_{22}O_{14}$ requires C, 42·3; H, 5·2; OMe, 36·4%; *M*, 426). The compound displayed unexpected stability towards boiling 0·5% aqueous-alcoholic hydrogen chloride; although the product reduced Fehling's solution, it consisted largely of the unaltered fructoside.

Tetracarbethoxy γ-Methylfructoside.—The above procedure being imitated throughout, γ-methylfructoside (3·6 g.) was condensed with ethyl chloroformate, and the product (5·2 g.), consisting of a pale yellow syrup, was twice distilled (yield, 3·8 g.); b. p. 235—238°/0·07 mm., $[\alpha]_D$ + 22·5° in ethyl alcohol. It was devoid of action towards Fehling's solution, but readily reduced cold neutral permanganate (Found: C, 46·8; H, 6·2; OR, 41·9.* $C_{19}H_{30}O_{14}$ requires C, 47·3; H, 6·2; OR,* 43·8%).

This product was submitted to hydrolysis with aqueous-alcoholic hydrogen chloride, and it appeared that with concentrations of acid below 1% no significant change occurred on heating at 80° for 3 hours. Concentrations of acid varying from 1·75% to 2% gave rise to a product which reduced Fehling's solution actively and showed a diminution of rotation to a value which remained constant during several hours.

γ-Ethylfructoside.—Dried ethyl alcohol containing 0·5% of hydrogen chloride was mixed with dried and sieved fructose (1·25 g. for each 100 c.c. of solution), and the solution was observed polarimetrically:

Time (mins.)	0	3	5	7	10	13	18
$[\alpha]_D^{17°}$	−55°	−9·5°	+3°	+10·5°	15·5°	16·5°	17·5°
Time (mins.)	24	27	30	36	47	65	
$[\alpha]_D^{17°}$	17·5°	17·5°	16·5°	16·5°	15·5°	14·5°	

The rotation thus became positive after about 4 minutes, and attained a maximum rotation in 18 to 27 minutes from the time of adding the acid. After this the value slowly decreased, and became negative after several hours.

The following procedure was adopted for the preparation of larger quantities. Fructose (7·5 g.) was shaken with pure ethyl alcohol (500 c.c.) for an hour. Thereafter, alcohol containing hydrogen chloride was added in such quantity as to give a concentration of 0·5% of hydrogen chloride, and this mixture was shaken for 25 minutes, a clear solution being obtained. At this stage the condensation was arrested by neutralising the acid with sodium ethoxide dissolved in dry alcohol. Silver carbonate was then added, which removed the last traces of hydrogen chloride. Filtration and evaporation under diminished pressure yielded a syrup, from which the last traces of alcohol were removed by heating at 80° in a high vacuum. The product, which contained a small quantity of sodium chloride, was extracted four times with boiling ethyl acetate, and the extract yielded on evaporation of the solvent a clear syrup which hardened on cooling. The last traces of solvent were removed by heating for an hour at 100° under 0·05 mm. pressure.

* OR calculated as 4OEt + 1OMe.

The *γ-ethylfructoside* was readily soluble in water, alcohol, acetone, or pyridine, and showed in alcohol $[\alpha]_D$ + 28°. It was devoid of any action towards Fehling's solution except after prolonged boiling, but decolorised neutral permanganate readily (Found: C, 45·7; H, 7·8. $C_8H_{16}O_6$ requires C, 46·2; H, 7·7%).

Tetracarbethoxy γ-Ethylfructoside.—A solution of γ-ethylfructoside (1 mol.) in dry pyridine (7 mols.) was diluted with four times its volume of dry chloroform and cooled to 0°. A chloroform solution of ethyl chloroformate was then added gradually with stirring. After being kept at room temperature for an hour, the solvent was removed under diminished pressure, and the pyridine hydrochloride, which crystallised, was extracted with water. The viscid, yellow residue was dissolved in acetone, reprecipitated by water, and again dissolved in acetone; this solution was dried over magnesium sulphate, and the solvent distilled; the residue, in the absence of traces of pyridine hydrochloride, distilled without difficulty; b. p. 228°/0·05 mm.

The *tetracarbethoxy γ-ethylfructoside* showed in ethyl alcohol, $[\alpha]_D$ + 27·5°. It was also soluble in acetone and chloroform. It was not affected by Fehling's solution, but decolorised neutral permanganate (Found: C, 48·3; H, 6·45; OEt, 43·2. $C_{20}H_{32}O_{14}$ requires C, 48·4; H, 6·45; OEt, 45·3%). Towards aqueous-alcoholic hydrogen chloride, this completely substituted derivative of γ-ethylfructoside behaved like the corresponding derivative of γ-methylfructoside, and showed considerable stability even at 100°. Hydrolysis of the glucosidic ethyl group was therefore considerably retarded by the introduction of the carbethoxy-groups.

The Normal Forms of Tetracarbomethoxy Methylfructoside and Tetracarbethoxy Methylfructoside.—*Tetracarbomethoxy methylfructoside* was prepared by subjecting tetracarbomethoxy fructose (m. p. 126°) to two methylations by Purdie's reagents. The isolated product was crystallised from ethyl acetate; it melted at 107° and showed $[\alpha]_D$ −126·1° in chloroform (c = 0·6) (Found: C, 42·3; H, 4·9; OMe, 34·2. $C_{15}H_{22}O_{14}$ requires C, 42·3; H, 5·2; OMe, 36·4%). *Tetracarbethoxy methylfructoside*, prepared by methylating tetracarbethoxy fructose (m. p. 118°) with Purdie's reagents, did not crystallise and showed $[\alpha]_D$ − 90·9° in acetone (c = 1·2) (Found: C, 47·1; H, 6·1. $C_{19}H_{30}O_{14}$ requires C, 47·3; H, 6·2%).

The authors are indebted to the Armstrong College Research Fund for financial assistance, which they acknowledge with gratitude.

UNIVERSITY OF DURHAM, ARMSTRONG COLLEGE,
NEWCASTLE-ON-TYNE. [*Received, April 9th*, 1927.]