CXX.—*The Constitution of the Disaccharides. Part X. Maltose.**

By CONRAD J. ASTLEY COOPER, WALTER NORMAN HAWORTH, and STANLEY PEAT.

THE investigation of the structure of maltose by Haworth and Leitch (J., 1919, **115**, 809) was one of the earliest of those undertaken in the disaccharide series. In the interval which has elapsed, greater familiarity with the properties and mode of identification of the partly methylated glucoses, and particularly of the trimethyl glucoses, has been gained.

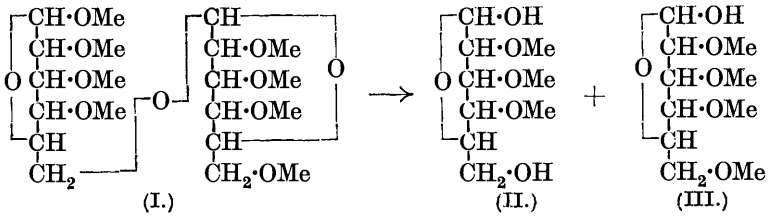
During a research, which will shortly be published, on the constitution of Ling and Nanji's *iso*maltose (J., 1923, **123**, 2666), certain irregularities were revealed which led us to suspect the accuracy of the formula previously applied to maltose. Consequently, the study of the latter sugar has been again undertaken during the past 18 months, with results which seem to require a modification of Fischer's formula for maltose, which was supported by the work of Haworth and Leitch.

In the earlier paper, the structural formula which appeared to represent maltose showed the linking of the two hexoses as occurring through the primary alcohol residue of one hexose with the reducing group of the second. The experimental data on which this conclusion was based were dependent on the recognition of the structure of the trimethyl glucose (II) obtained, along with tetramethyl glucose (III), by hydrolysis of heptamethyl methylmaltoside (I). In these formulæ the revised structure for normal glucose is used (Charlton, Haworth, and Peat, this vol., p. 89); consequently the older 2 : 3 : 5-trimethyl glucose is now written as 2 : 3 : 4-trimethyl glucose.

The facts available at that time pointed to the non-identity of this specimen of trimethyl glucose, which was a liquid, with crystalline 2 : 3 : 6-trimethyl glucose, which was isolated as a hydrolysis product of methylated cellobiose (Haworth and Hirst, J., 1921, **119**,

* Almost the whole of the experimental results given in this paper were obtained during the early part of 1925, but publication was held over for the inclusion of other confirmatory details. A private communication from Sir James Irvine was received on February 28th, 1926, intimating, but without experimental details, that he had communicated a paper to the Society announcing the isolation of 2 : 3 : 6-trimethyl glucose as a hydrolysis product of methylated maltose. In the circumstances, we consider it is advisable now to submit our results for publication, inasmuch as they may serve to confirm and supplement those obtained by Irvine and his collaborators, whose priority we acknowledge.

193). Moreover, the oxidation of the trimethyl glucose derived from methylated maltose led to the isolation of what was considered to be a trimethyl saccharolactone (IV), and for these reasons, since the primary alcohol residue had apparently undergone oxidation to a carboxyl group without loss of a methoxyl residue, the specimen of trimethyl glucose was considered to have three methoxyl residues in the 2 : 3 : 4-positions, as shown in formula (III).



(I.) (II.) (III.)

In a new series of experiments, the whole of the early work was repeated, and gave identical analytical results for the oxidation product of the trimethyl glucose. The method of isolating the trimethyl glucose was then modified, and instead of separating the hydrolysis products of methylated maltose by distillation, the aqueous solution containing the methylated hexoses was repeatedly extracted with chloroform, which entirely removed tetramethyl glucose as the normal crystalline variety (2 : 3 : 4 : 6).

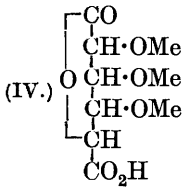
Remaining in the aqueous solution was the trimethyl glucose, and this was recovered by evaporation followed by extraction. The extracted syrup spontaneously crystallised, and yielded about 6% of the total in the form of the readily identifiable 2 : 3 : 6-trimethyl glucose. This was similar in all respects to the specimen previously isolated both from methylated cellobiose and from methylated lactose. Moreover, the remaining syrup appeared to consist of the β-form of this normal sugar, and probably contained also α- and β-forms of the corresponding γ-sugar, into which the normal variety appears to pass somewhat readily owing to the presence of a free hydroxyl group in the γ-position in the chain. Possibly owing to the latter consideration, crystalline 2 : 3 : 6-trimethyl glucose cannot be isolated in quantity.

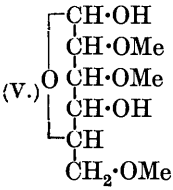
An alternative interpretation to that given in the earlier paper by Haworth and Leitch can now be offered, inasmuch as, accepting the trimethyl glucose as in reality 2 : 3 : 6-trimethyl glucose (V), this could pass on oxidation to dimethyl saccharolactone (VI). Under the experimental conditions described by Haworth and Leitch, the oxidation product from the trimethyl sugar was digested with ethyl alcohol for the purpose of removing traces of water, and it would appear to have undergone partial transformation

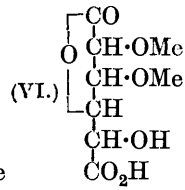
into the ethyl ester of the dimethyl saccharolactone. The analytical data previously quoted are given in column 1, and those of dimethyl saccharolactone (VI) and its ethyl ester (VII) in columns 2 and 3. The mean of the latter two results, given in column 4, will be seen to be closely similar to the analytical data previously interpreted under column 1 as indicating the constitution of the product as that of a trimethyl saccharolactone.

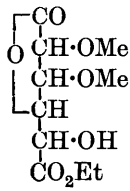
	1.	2.	3.	4.
C	46·03	43·6	48·4	46·0
H	6·26	5·45	6·46	5·95
OMe	35·9	28·2	37·5	32·85

In order to test this explanation, we have again oxidised the liquid portion of the trimethyl glucose and submitted this to esterification with ethyl alcohol containing hydrogen chloride. The main fraction isolated from this treatment distilled at 110—115°/0·03 mm. and gave titration results which corresponded to those required for compound (VII).

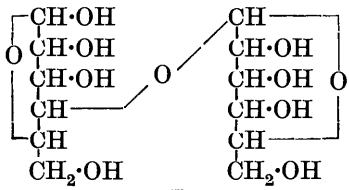
(IV.) 

(V.) 

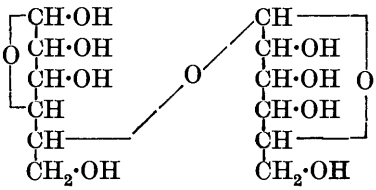
(VI.) 

(VII.) 

The valuable method of identifying 2 : 3 : 4-trimethyl glucose through its crystalline β-glucoside (Irvine and Oldham, J., 1921, **119**, 1758) was not known at the time when the maltose paper was published and consequently we were unable then to apply this method of diagnosis. It seems clear, however, that 2 : 3 : 4-trimethyl glucose cannot be one of the hydrolysis products of methylated maltose, inasmuch as the specimen in our possession has since failed to satisfy those tests. The β-glucoside, when prepared, did not crystallise on keeping or on nucleation with specimens of 2 : 3 : 4-trimethyl β-methylglucoside which had been isolated for purposes of



(VIII.)



(IX.)

diagnosis during our work on the constitution of gentiobiose and of amygdalin biose. On the other hand, the isolation of crystalline

2 : 3 : 6-trimethyl glucose points to the necessity of revising the structural formula of maltose, to which is now given the constitution (VIII) or (IX). The formula (VIII) differs stereochemically but not structurally from that of cellobiose, since the latter is a glucose β-glucoside and maltose is a glucose α-glucoside.

The adjustment of the formula of maltose removes many outstanding anomalies as to the behaviour of starch.

EXPERIMENTAL.

Hydrolysis of Heptamethyl Methylmaltoside. Isolation of 2 : 3 : 6-*Trimethyl Glucose and* 2 : 3 : 4 : 6-*Tetramethyl Glucose.*—A specimen of heptamethyl methylmaltoside (39·5 g.) prepared as previously described by Haworth and Leitch (*loc. cit.*) (b. p. 201—203°/0·03 mm.) was hydrolysed by digesting with 5% hydrochloric acid at 85° for 1½ hours and at 100° for a further period of 1½ hours. Thereafter the specific rotation of the solution remained constant, and the hydrolysis was complete. The neutralised solution was slightly concentrated under diminished pressure and extracted several times with large quantities of chloroform. The chloroform extract was dried and evaporated; the residual syrup crystallised almost immediately, yielding pure 2 : 3 : 4 : 6-tetramethyl glucose (16·5 g.).

The residual aqueous solution was completely evaporated under diminished pressure and gave a syrup (15 g.) which, on keeping for several weeks, partly crystallised. These crystals (m. p. 106—117°) were drained on porous tile, and purified by solution in dry ether, from which small, colourless needles separated in three fractions : (a) m. p. 105—111°; (b) 108—115°; (c) 102—109°. Further recrystallisation gave crystals (1·25 g.), m. p. 110—116°, which, in admixture with a specimen of 2 : 3 : 6-trimethyl glucose derived from methylated lactose (Haworth and Leitch), showed no depression of melting point. It showed in methyl alcohol ($c = 1·73$) $[\alpha]_D$ +102·6° after 15 minutes, changing to 70·2° after 12 hours, and, after catalysis, to 67·5° (Found : C, 48·4; H, 8·3; OMe, 40·4. Calc., C, 48·6; H, 8·1; OMe, 41·9%).

The uncrystallisable syrup from which the above crystals had been obtained was oxidised by digestion with nitric acid (*d* 1·2), heating to 80° until brown fumes began to be evolved, and thereafter at 70° for 5½ hours. After being cooled and tested for the presence of free sugar, the solution was again heated for a short period until the whole of the sugar was oxidised. The nitric acid was then removed by distillation under diminished pressure at 35°, water being constantly added during this operation. Finally, the whole of the water was evaporated, and the syrupy residue dissolved in ethyl alcohol containing 2% of hydrogen chloride. This solution

was boiled for 8 hours in order to complete the esterification, and the product was isolated in the usual manner. The methoxyl and ester groups were determined by the Zeisel method, calculating both OMe and OEt in terms of OMe, and showed 40·6%. The ester was then distilled, the first portion being collected at 88—95°/0·03 mm., but the main portion, the analysis of which is given below, distilled at 110—115°/0·03 mm. (Found : OR, 39·3. Calc. for the ethyl ester of dimethyl saccharolactone, $C_{10}H_{16}O_7$, 37·5%).

Titration. 0·1108 G. required 4·7 c.c. of *N*/10-sodium hydroxide in the cold, and on heating in a water-bath with excess of the alkali for 20 minutes, a total of 8·81 c.c. of *N*/10-sodium hydroxide was required. Calculated for the ethyl ester of dimethyl saccharolactone, $C_{10}H_{16}O_7$, 8·92 c.c., and for the trimethyl saccharolactone, $C_9H_{14}O_7$, 9·46 c.c. Hydrolysis of this ester gave dimethyl saccharolactone (Found : OMe, 27·8. Calc. : OMe, 28·2%).

On another occasion, the whole of the work described in the paper by Haworth and Leitch (*loc. cit.*) on the constitution of maltose was repeated in every detail, and the lactone derived from the oxidation of trimethyl glucose was titrated and gave the following results : 0·0979 g. required 8·37 c.c. of *N*/10-sodium hydroxide. Calculated for trimethyl saccharolactone, $C_9H_{14}O_7$, 8·33 c.c. In the earlier paper, a small typographical error appeared in the account given of the titration results, and the above re-determination was therefore carried out. This anomaly is explained in the introduction.

The authors express their thanks to the Department of Scientific and Industrial Research for the award of a grant to one of them.

UNIVERSITY OF DURHAM, ARMSTRONG COLLEGE, NEWCASTLE-ON-TYNE.
UNIVERSITY OF BIRMINGHAM, EDGBASTON.

[*Received, March 5th,* 1926.]