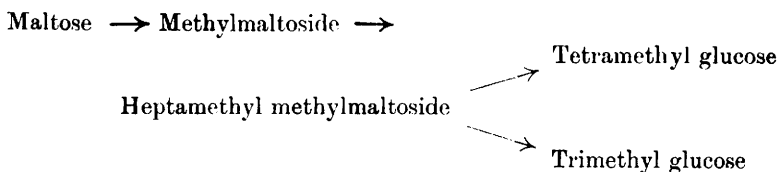


XLIX.—*The Constitution of Maltose. A New Example of Degradation in the Sugar Group.*

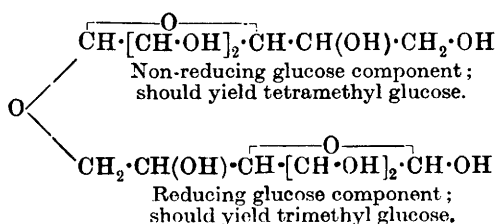
By JAMES COLQUHOUN IRVINE and JAMES SCOTT DICK.

In the following paper are described the principal results obtained in an investigation undertaken some years ago with the object of determining the constitution of maltose. The standard process was adopted of complete methylation of the disaccharide, followed by identification of the two alkylated sugars produced on hydrolysis, and the series of reactions as originally planned may be represented by the following synopsis:

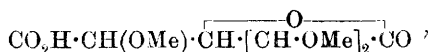


Although the above scheme has not been fully realised, it has been possible to confirm and supplement the earlier results of Purdie and Irvine (T., 1905, **87**, 1022), who showed that the non-reducing glucose component of maltose possesses the butylene-oxide structure, and thus yields crystalline tetramethyl glucose as one product of the above reactions.

This result establishes the constitution of one half of the disaccharide molecule, but, owing to an unexpected degradation of maltose encountered in the course of the work, we have been unable to isolate the trimethyl glucose which should be formed as a second hydrolysis product from a fully methylated maltoside. On the basis of the accepted constitution of maltose, the operation of the series of reactions should give, in addition to tetramethyl glucose, the butylene-oxide form of trimethyl glucose described by Purdie and Bridgett (T., 1903, **83**, 1037). This is shown below:



The identification of the particular form of trimethyl glucose to be expected is, however, difficult in view of the failure of this sugar to give crystalline derivatives, and accordingly, as a necessary preliminary to the present research, we re-examined the compound and determined its physical constants as standards of comparison. In addition, the constitution provisionally assigned to the sugar has been confirmed by a study of its decomposition products. When oxidised drastically by means of nitric acid, the essential product proved to be the monolactone of trimethyl-saccharic acid,



a result which confirms the view that the primary alcohol group in the parent sugar is unsubstituted.

The data thus accumulated proved, however, of little service in the present research, which developed an unexpected but interesting complexity. In preparing the necessary methylmaltoside, we adopted the method described by Mills (*Chem. News*, 1912, **106**, 165), in which hepta-acetyliodomaltose is converted into the corresponding acetylated methylmaltoside and the acyl groups are removed by hydrolysis. In the light of subsequent events, this proved to be an unfortunate decision. The various reactions appeared to proceed normally, but, on applying the silver oxide process to the " β -methylmaltoside," we obtained, after three methylations followed by vacuum distillation, a colourless syrup which gave on analysis by Zeisel's method figures agreeing closely with those required for a *hexamethyl methylmaltoside*. In the belief that the methylation was incomplete, further treatments with the alkylating mixture were carried out, but this had no effect on the composition. As a second preparation gave precisely the same result, although the silver oxide reaction was repeated five times, and this was followed by two further methylations, one by means of methyl sulphate and the other by diazomethane, we were forced reluctantly to the conclusion that steric hindrance had interfered completely with the methylation of one hydroxyl group of the maltose molecule.

The results of combustions were indecisive, and the correct interpretation was forthcoming only when the supposed hexamethyl methylmaltoside was hydrolysed, and the two sugars thus produced were separated by distillation in the high vacuum of the Gaede pump. As already mentioned, crystalline tetramethyl glucose was readily obtained as the fraction of lower boiling point, but the remaining product distilled only with the greatest difficulty under

a pressure of 0.1 mm., and could not be induced to crystallise. Examination showed this viscous syrup to be a reducing sugar and to possess the composition of a *dimethyl pentose*, so that clear evidence was thus obtained that, at some stage of the successive reactions, degradation of the maltose molecule had taken place to give derivatives of a sugar containing eleven carbon atoms in the chain. Owing to the close coincidence in the calculated compositions of a highly methylated methylmaltoside and a hexamethyl methylglucopentoside, it was impossible to detect this degradation before hydrolysis, and, owing to the unexpected nature of the result, it was necessary to obtain confirmatory evidence. The dimethyl pentose was therefore converted successively into the corresponding dimethyl methylpentoside and trimethyl methylpentoside, and each compound gave on analysis figures which agree closely with the above explanation. Further, the values found for the specific rotations of these compounds agree with the idea that they are derivatives of arabinose, and the corresponding nomenclature is accordingly employed in the experimental part.

There is little doubt that the degradation took place during the decomposition of maltose octa-acetate by means of hydrogen iodide, and is due to a species of reduction which is unusual in the sugar group. No doubt such a reaction, when once commenced, would be progressive, but in the twelve experiments conducted by us, the change was approximately arrested at a stage when the main product consisted of a derivative of a C_{11} sugar. The maltose originally used was of high purity, and the octa-acetate prepared from it also conformed to accepted standards. On the other hand, the supposed "hepta-acetyl methylmaltoside," obtained after reaction with hydrogen iodide followed by treatment with methyl alcohol, was abnormal. Although apparently a definite chemical individual, we were unable by any process of crystallisation to raise the melting point above $115-117^{\circ}$, whereas the recorded values are higher (Fischer and Armstrong, $121-122^{\circ}$, $125-126^{\circ}$; Königs and Knorr, $128-129^{\circ}$). Fischer has, however, remarked on the difficulty in obtaining this compound pure, and as the method of preparation adopted by us might lead to the production of non-separable α - and β -forms showing a lower melting point, there was no reason at the time to doubt the nature of the compound.

The interruption of our collaboration, due to the War, has prevented us from studying the degradation of sugars by means of hydrogen iodide on more general lines, but the subject is evidently important, as the possibility is opened out of degrading maltose in an acid system and comparing the results with those already

obtained by regulated oxidation in alkaline solution (Lewis and Buckborough, *J. Amer. Chem. Soc.*, 1914, **36**, 2385).

Meanwhile, in a separate research, the results of which will be communicated at an early date, the complete structure of maltose has been established by a method free from the complications now described.

EXPERIMENTAL.

Preparation of Maltose Octa-acetate.

As the preparation of this compound in a pure condition presents considerable difficulty, an account may be given of the method which in our experience proved the most satisfactory.

Pure maltose was acetylated by means of acetic anhydride and sodium acetate in the manner described by Herzfeld (*Annalen*, 1883, **220**, 200), but the reaction was continued for thirty minutes, after which the hot syrup was poured into cold water. On stirring vigorously, the product solidified, and the disintegrated solid was collected, dissolved in alcohol, and the solution neutralised with barium carbonate. The filtered solution was then poured into water, and the solid acetate which separated was collected on a filter and thereafter dried in a vacuum. On extracting the dry crystals repeatedly with a large excess of boiling ether, the impurities remained undissolved, and on removal of the solvents from the united extracts, the acetate was obtained in good yield. One recrystallisation from hot alcohol was then sufficient to give the pure compound melting at 157°.

Action of Hydrogen Iodide on Maltose Octa-acetate.

Sixty grams of the acetate, in portions of 5 grams, were treated in methylene chloride solution with carefully purified hydrogen iodide, as described by Mills (*loc. cit.*). The excess of the gas and the solvent were removed in a high vacuum, and the residual syrup was at once dissolved in dry methyl alcohol, and the solution shaken with silver carbonate until free from iodine. On concentration of the filtrate, the product crystallised readily, but even after repeated crystallisation the melting point could not be raised above 117°.

The yields obtained in the twelve preparations varied considerably, and were in no case more than 60 per cent. of the theoretical amount. Apparently an important factor is to minimise the time during which the acetate is in contact with hydrogen iodide to less than thirty minutes, and to remove the excess of the gas as rapidly

as possible. Otherwise the amount of syrup formed is increased and the proportion of crystalline product seriously diminished.

The removal of the acetyl groups from the supposed hepta-acetyl methylmaltoside was effected in the usual way by shaking with aqueous barium hydroxide, the ultimate product being a glucosidic syrup, which proved to be methylglucoarabinoside. Throughout all the above reactions, the customary precautions were taken to prevent molecular rupture, and the operations were thus extremely tedious.

Methylation of Methylglucoarabinoside.

No details of this reaction need be given, as it was conducted precisely as described in earlier papers dealing with the methylation of glucosides by means of silver oxide and methyl iodide. After two alkylations in methyl-alcoholic solution, the product was freely soluble in methyl iodide, and consequently no extraneous solvent was required in the final methylations. The product, which was a clear, viscid syrup, was purified by fractionation in a high vacuum, and the following table shows that successive treatments did not increase the methoxyl content above a fixed maximum.

Number of methylations.	B. p.	n_D	Methoxyl.
4	188—190°/0.35 mm.	1.4692	50.34 per cent.
5	195°/0.1 mm.	1.4688	50.66 „
5	205—208°/0.4 mm.	1.4695	52.2, 50.79 per cent.
6	200—203°/0.4 mm.	1.4689	50.45 „

In a second preparation, otherwise duplicate, the treatment was extended by one methylation by means of methyl sulphate and sodium hydroxide, and finally by diazomethane in ethereal solution, but without alteration in the analytical figures or physical constants of the product. The mean of several consistent analyses gave:

C=52.11; H=8.21; OMe=50.9 per cent.

Heptamethyl methylmaltoside:

$C_{20}H_{38}O_{11}$ requires C=52.86; H=8.37; OMe=54.63 per cent.

Hexamethyl methylmaltoside:

$C_{19}H_{36}O_{11}$ requires C=51.81; H=8.18; OMe=49.3 per cent.

Hexamethyl methylglucoarabinoside:

$C_{18}H_{34}O_{10}$ requires C=52.68; H=8.29; OMe=52.9 per cent.

The results fail to discriminate between the alternatives, and the molecular weight, determined in benzene solution by the cryoscopic method, was equally inconclusive.

Found: 425.

$C_{19}H_{36}O_{11}$ requires 440; $C_{18}H_{34}O_{10}$ requires 410.

On the evidence yielded by hydrolysis, the compound was finally shown to be essentially hexamethyl methylglucoarabinoside ($C_{18}H_{34}O_{10}$).

The new glucoside is a viscid, colourless syrup freely soluble in organic solvents generally, but less so in water. Presumably the specimen examined would consist of both α - and β -forms, so that the specific rotations have only a qualitative significance, but, as is usually the case with methylated compounds possessing the glucose configuration, the activity was but little affected by the nature of the solvent.

Solvent.	c.	$[\alpha]_D^{20^\circ}$.
Water	4.875	+78.8°
Methyl alcohol	5.609	77.5
Ethyl alcohol.....	5.316	75.9
Acetone	5.103	76.9

Hydrolysis of Hexamethyl Methylglucoarabinoside.

Preliminary experiments showed that the double hydrolytic change of removing the glucosidic methyl group and liberating the two constituent aldoses was best effected by boiling a 5 per cent. solution of the above compound in 5 per cent. aqueous hydrochloric acid. This method was accordingly applied to 38 grams of the glucoside, boiling under reflux being continued until the rotation diminished to a constant value, which it did in thirty minutes. The acid was neutralised with barium carbonate, the filtered solution evaporated to dryness under diminished pressure, and the residue extracted with boiling alcohol. After removal of the alcohol, the residual syrup was dissolved in hot acetone, the solution being again filtered and evaporated. The mixed sugars produced in the hydrolysis were obtained in this way as a pale yellow syrup, and were separated by fractionation at the Gaede pump.

A definite first fraction, amounting to 40 per cent. of the total weight, was collected at $125^\circ/0.5$ mm. as a moderately mobile liquid, but the remainder of the material distilled only with the greatest difficulty, and presented the appearance of a glass. As much decomposition took place in the later stages of the distillation, no attempt was made, after the first preliminary trial, to distil this product, heating being continued only until the first fraction had been removed.

The more volatile sugar crystallised readily, and, after draining on porous porcelain and two recrystallisations from light petroleum,

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was identified as butylene-oxidic tetramethyl glucose melting at 85—87°. (Found: C=50·62; H=8·41; OMe=52·46. $C_{10}H_{20}O_6$ requires C=50·85; H=8·47; OMe=52·54 per cent.)

Mutarotation in alcohol: Initial $[\alpha]_D^{20} + 104·9^\circ \rightarrow$ Final 83·9°.

Identification of Dimethyl Arabinose.—The less volatile sugar solidified on cooling to a glass, and no crystallising medium could be found for the compound, as it is very readily soluble in water or organic solvents, with the exception of light petroleum. It reduces Fehling's solution readily, and is thus a reducing sugar, but gave only syrupy products when treated with aniline, hydroxylamine, or with phenylhydrazine and acetic acid. In approximately 5 per cent. solution, the compound was dextrorotatory:

Solvent.	$[\alpha]_D^{20}$
Water	+57·7°
Ethyl alcohol.....	50·6
Acetone	56·9

Before determining the activity or the analytical composition, the compound was further purified from traces of tetramethyl glucose by solution in dry ether and the addition of light petroleum, after which the syrupy precipitate was dried in a high vacuum.

The mean of three consistent analyses showed that the sugar was neither the di- nor the tri-methyl glucose expected.

Found: C=47·63; H=7·99; OMe=35·28.

Dimethyl arabinose:

$C_7H_{14}O_5$ requires C=47·19; H=7·86; OMe=34·83 per cent.

Dimethyl glucose:

$C_8H_{16}O_6$ requires C=46·13; H=7·73; OMe=29·8 per cent.

Trimethyl glucose:

$C_9H_{18}O_6$ requires C=48·63; H=8·15; OMe=41·9 per cent.

All the results, and more particularly the methoxyl content, point to the idea that the sugar is a dimethyl arabinose, but further identification was obtained by converting the compound into the corresponding methylpentoside by Fischer's method.

Dimethyl methylarabinoside proved to be a colourless syrup (b. p. 120°/0·1 mm., n_D 1·4620) devoid of action on Fehling's solution until hydrolysed.

Found: C=50·38; H=8·60; OMe=48·9.

$C_8H_{16}O_5$ requires C=50·00; H=8·33; OMe=48·5 per cent.

Further confirmation of the composition of the parent sugar was obtained by subjecting the above pentoside to the silver oxide reaction, so as to produce trimethyl methylarabinoside, which was

isolated as a colourless, mobile liquid (b. p. 94—96°/0.08 mm., n_D 1.4460).

Found: C=52.18; H=8.80; OMe=60.1, 60.8.

$C_9H_{18}O_5$ requires C=52.42; H=8.73; OMe=60.2 per cent.

The whole series of analytical results thus consistently supports the view that all the compounds examined are derivatives of a pentose, and not of a hexose. Considering their method of formation, they would consist of mixtures of α - and β -forms, and consequently specific rotations need not be quoted, but the fact that in each case the compounds are strongly dextrorotatory justifies the opinion that they are derived from arabinose, and this is embodied in the nomenclature used.

Trimethyl α -Methylglucoside and Trimethyl Glucose.

The above compounds are already known, but were re-examined for reasons stated in the introduction. Both substances are viscous syrups and yield no crystalline derivatives, so that their identification rests chiefly on the determination of their specific rotations. Unfortunately, the values found by different observers show considerable variation, a fact which may be explained by the difficulty encountered in fractionating syrups of high boiling point under the vacua given by an ordinary water pump, and accordingly we conducted our final distillations under the highly diminished pressure of the Gaede pump.

Fifty grams of α -methylglucoside were dissolved in methyl alcohol and methylated by means of silver oxide (150 grams) and methyl iodide (183 grams), exactly as described by Purdie and Bridgett (*loc. cit.*). After two alkylations, the product was isolated in the usual way and subjected to systematic fractionation, as a result of which 29.5 grams of pure material were obtained after six distillations. The syrup boiled at 160—161°/10 mm., showed n_D 1.4606, and gave $[\alpha]_D^{20} +134.6^\circ$ in absolute alcohol, a value which is not far removed from the specific rotation quoted by Purdie and Irvine (T., 1903, 83, 1021).

On hydrolysis with aqueous hydrochloric acid, the glucoside was converted into trimethyl glucose, the sugar being isolated in the customary manner, and purified by repeated distillations which were continued after satisfactory analytical figures were obtained. The final boiling point recorded was 152—155°/0.02 mm., but the refractive indices and specific rotations shown by the product of different preparations fluctuated widely, although the parent glucoside employed was apparently identical. The

extent of this variation is shown in the two extreme cases quoted below.

In the first preparation, the trimethyl methylglucoside used showed n_D 1.4606 and $[\alpha]_D^{20} + 134.6^\circ$ in methyl alcohol, whilst in the second the corresponding values were 1.4596 and 132.4 . The trimethyl glucose obtained from these two sources showed:

	Preparation I.	Preparation II.
n_D	1.4780	1.4768
$[\alpha]_D^{20}$ in water	+48.6°	+60.7°
$[\alpha]_D$ in methyl alcohol	48.3	65.3
$[\alpha]_D$ in acetone	46.2	58.8

In view of these results, there can be little doubt that the sugar and the glucoside from which it was prepared were mixtures of isomerides, and the identification of $\beta\gamma\xi$ -trimethyl glucose must in the meantime depend on oxidation processes.

Oxidation of Trimethyl Glucose.

3.5 Grams of the sugar were dissolved in 50 c.c. of nitric acid (D 1.7), and the solution was heated to 80° in order to start the oxidation. Thereafter, the mixture was kept at 65° for three hours, then diluted with water, and evaporated to a syrup under diminished pressure. The process of dilution with water and subsequent evaporation was repeated four times, and was followed by three similar treatments, in which alcohol was used as the diluent. As the syrupy product darkened rapidly at 120° , no attempt was made to distil the compound, which was prepared for analysis by heating at $60^\circ/0.3$ mm. until constant in weight. Analysis showed the substance to be the monolactone of trimethylsaccharic acid.

Found: C=46.07; H=6.33; OMe=37.2.

$C_9H_{14}O_7$ requires C=46.13; H=6.02; OMe=39.7 per cent.

When dissolved in alcohol and rapidly titrated with $N/10$ -sodium hydroxide, the first neutralisation corresponded with the presence of one carboxyl group, and thereafter the compound behaved as a typical lactone on further titration. The lactonic structure was confirmed by the fact that in absolute alcohol the specific rotation remained practically constant, but diminished to a permanent value when aqueous alcohol was used as solvent.

Solvent.	Initial $[\alpha]_D^{20}$.		Final $[\alpha]_D$.
Absolute alcohol	+41.5°	→	+43.0° in 48 hours.
50 per cent. alcohol	43.2	→	24.0 „ „

We desire to express our indebtedness to the Carnegie Trust for a Research Scholarship which enabled one of us to take part in the work, and also to Miss E. S. Steele, who completed the research when our collaboration was interrupted.

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