CXIX.—*The Constitution of Maltose.*

By JAMES COLQUHOUN IRVINE and IAN MACLEOD ARMSTRONG BLACK.

A CONSIDERABLE section of the work conducted in this laboratory on the constitution of polysaccharides has been withheld from publication for some years owing to the fact that the results could not be readily explained. As these discordant features accumulated, it became increasingly evident that current views regarding the structure of maltose required revision and that it was necessary to

study the problem anew. This we have done and, as our results differ fundamentally from those upon which the accepted structure for the disaccharide is based, it is desirable to review the whole situation.

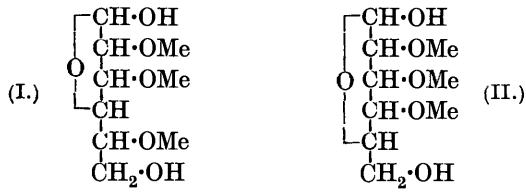
The first attempt to solve the constitution of maltose by means of methylation was made by Purdie and Irvine (J., 1905, **87**, 1022), who applied the silver oxide reaction directly to the free sugar. Although the alkylation was complicated by oxidation of the reducing group, the decisive result emerged that, on hydrolysis of the product, crystalline tetramethyl glucose was produced. This revealed the structure of one-half of the maltose molecule which, on the basis of the amylene-oxide formula for glucose,* becomes :

$$\underbrace{CH_2(OH){\cdot}CH{\cdot}CH(OH){\cdot}CH(OH){\cdot}CH(OH){\cdot}CH}_{O}{-}O{-}\text{Reducing glucose residue.}$$

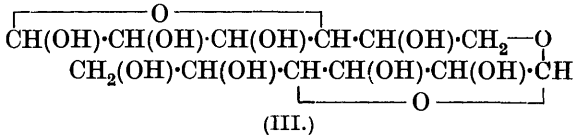
An attempt was subsequently made by Irvine and Dick (J., 1919, **115**, 593) to determine the position through which the second glucose residue is attached, the scheme involving the complete methylation of methylmaltoside and the identification of the scission products. In this case an experimental obstacle intervened, it being found that the method employed to prepare methylmaltoside was accompanied by degradation of the sugar so that one of the hydrolytic products finally obtained consisted of a methylated pentose. The research was, however, of some value as, once more, crystalline tetramethyl glucose was isolated, thereby confirming the earlier result of Purdie and Irvine. Subsequently, Haworth and Leitch (J., 1919, **115**, 809) applied the methyl sulphate reaction to maltose in two successive stages, the first being designed to convert the sugar into methylmaltoside, which was partly methylated in the second stage and thereafter fully alkylated. Hydrolysis of this product yielded two methylated glucoses, one of which, as was to be expected, was tetramethyl glucose. The object of the research was, however, to ascertain the structure of the *reducing* hexose residue in maltose, so that greater importance must be attached to the constitution of the remaining scission product, *viz.*, trimethyl glucose. The sugar isolated by Haworth and Leitch was a syrup and was stated by them to be the liquid variety of trimethyl glucose in which the terminal $-CH_2{\cdot}OH$ group is unsubstituted. As originally formulated, this sugar was described as 2 : 3 : 5-trimethyl

* The amylene-oxide formula for glucose is applied in this paper only tentatively and is restricted to derivatives which are known to be convertible into crystalline tetramethyl glucose. The results now contributed show that it is inadvisable to go further.

glucose (I), but adopting meanwhile the amylene-oxide structure, it may be termed 2 : 3 : 4-trimethyl glucose (II).

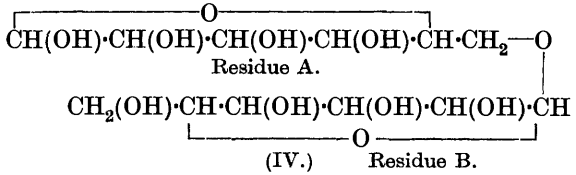


Irrespective of the oxygen-ring, the essential point is that the formation of such a sugar implies that the two hexose residues in the disaccharide are coupled through a terminal hydroxyl group. On this basis, Haworth and Leitch ascribed the following structure to maltose and applied, by analogy, a similar constitution to melibiose :



(III.)

This formula has remained in use for the past seven years, but was modified recently (Charlton, Haworth, and Peat, this vol., p. 89) by the incorporation of an amylene-oxide linkage in each glucose residue, giving the structure :



(IV.)

Evidently the constitution as given above is valid only if each half of the molecule gives rise to the appropriate methylated glucose. With regard to residue B, this was already known from the results of earlier workers, and the additional experimental evidence contributed by Haworth and Leitch consisted in the isolation and identification of the trimethyl glucose derived from residue A. Considering the fundamental structural issues involved (which are by no means confined to maltose), it is of the utmost importance to know that the trimethyl glucose is actually what it was described to be. Our results, unfortunately, show that this is not the case. The trimethyl glucose obtained by us from maltose is the crystalline 2 : 3 : 6-isomeride, and not, as stated by Haworth and Leitch, the liquid 2 : 3 : 4-variety. The erroneous conclusion to which the latter workers came is in no way concerned with the position of the oxygen

ring in glucose or with a difference in the interpretation of results, but is attributable to failure to identify correctly the sugar actually formed. It is regrettable that correction should have been so long delayed, particularly as the constitutional formulæ of other disaccharides and of the polysaccharides based on glucose become involved in the fundamental error.

The evidence upon which Haworth and Leitch identified and ascribed a structure to the trimethyl glucose they obtained from maltose may be discussed. The sugar failed to solidify and was separated from tetramethyl glucose by distillation, a process of doubtful utility in any case where the presence of 2 : 3 : 4-trimethyl glucose might be expected. No crystalline derivative was prepared and the bulk of the material was subjected to oxidation by nitric acid, the product thus formed being described as a trimethyl saccharolactone since it corresponded in composition with such a compound. Inquiry into the particular method of oxidation employed has, however, shown that it is untrustworthy. We have ascertained that unchanged sugar may persist along with oxidation products and, in addition, the removal of nitric acid by evaporation with alcohol results in partial esterification of the oxidation acids. In consequence, the analytical results obtained on *undistilled* products are subject to serious errors. For example, a methyl group may be removed by oxidation from the terminal 6-position of the sugar chain, but an ethyl group may enter the carboxyl position, thus introducing compensation into the methoxyl determinations. We have encountered all of the above complications and may cite the oxidation of monomethyl glucose by nitric acid as a conspicuous, but by no means unique, example of a complex reaction which leads to a mixture of products displaying fortuitously the properties and composition of a simple lactone. This accounts for our recent practice in isolating oxidation products in the form of volatile esters or of crystalline derivatives.

Turning to other properties of the trimethyl glucose described by Haworth and Leitch, it may be mentioned that the specific rotations of the compound did not agree with those determined by previous workers (Irvine and Dick, *loc. cit.*) and failed to reveal the characteristic depression shown after distillation. Information was, in fact, available showing that it is impossible to identify 2 : 3 : 4-trimethyl glucose by observation of the activity of distilled specimens, as the value of the specific rotation may vary as much as 20° to 30° owing to the partial transformation of the dextrorotatory sugar into its lævorotatory anhydride. This irregularity was encountered so far back as 1903 and was again emphasised by Irvine and Oldham (J., 1921, **119**, 1754).

Consideration of the whole situation shows that the claims of Haworth and Leitch regarding the trimethyl glucose they obtained from maltose rested upon insecure experimental evidence which has not been supplemented as knowledge of methylated sugars increased. There can be no doubt that the material they described as the liquid form of trimethyl glucose was an impure specimen of the 2 : 3 : 6-isomeride, which failed to crystallise owing to the experimental treatment to which it had been subjected. In this connexion, Irvine and Hirst (J., 1922, **121**, 1214) state " the capacity of this sugar (2 : 3 : 6-trimethyl glucose) to separate in the solid form is seriously affected by impurities and seems to be inhibited by thorough drying so that, on distillation, a viscous syrup is obtained which solidifies only after several weeks. Even gentle warming above the melting point is sufficient to impair crystallisation." The above statement, taken in conjunction with our experience of oxidations by means of nitric acid, shows that it is hazardous, without the most exhaustive confirmation, to claim that any preparation of a trimethyl glucose which fails to crystallise is the 2 : 3 : 4-isomeride.

In overturning a result upon which so many other constitutional formulæ depend, it has been necessary to exclude sources of error so far as they can be foreseen and to repeat the operations several times and by independent workers. Reference is made in the experimental part to some of the precautions adopted and to variations in the procedure. These fall under three main heads: (1) confirmation of the purity and uniformity of the maltose used, (2) variations in the method of methylation, (3) alternative methods of isolating the scission products. We employed three distinct samples of maltose, one of which was made in the laboratory during the War and was certified as conforming to bacteriological standards. With regard to the process of methylation, we followed in the first instance exactly the method described by Haworth and Leitch, applying the methyl sulphate reaction to the free sugar. In other experiments, methyl sulphate was used only until the product was soluble in chloroform, the methylation being completed by the silver oxide reaction alone. Despite these experimental variations, the same result was obtained, the product on isolation being a viscous syrup showing the properties ascribed by Haworth and Leitch to heptamethyl methylmaltoside.

It may be mentioned, however, that the methoxyl and carbon values determined on this material were consistently low, and that satisfactory analytical figures were obtained only when the initial material consisted of crystalline methylmaltoside. The hydrolysis proceeded normally, the liberated sugars being separated by extrac-

tion of an aqueous solution with chloroform. By this means it was possible to effect a sharp separation of the tetramethyl and trimethyl glucoses without distillation or heating above the melting points of these compounds. In all the experiments, both sugars crystallised and proved to be respectively 2 : 3 : 4 : 6-tetramethyl glucose and 2 : 3 : 6-trimethyl glucose. As a precautionary measure, we examined all the hydrolysis products to ascertain if any 2 : 3 : 4-trimethyl glucose was present, but no trace of this sugar could be detected.

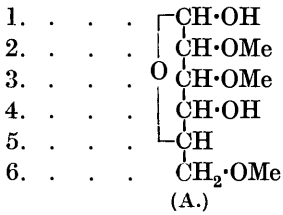
In order to place our procedure beyond question, we have duplicated the entire research, using pure β-methylmaltoside as the starting material. In this case also, the methylation was conducted in two ways, using either the silver oxide method or the methyl sulphate reaction throughout. Here again the same result was obtained, irrespective of the method employed, the hydrolysis of the compound giving, as before, crystalline tetramethyl glucose together with crystalline 2 : 3 : 6-trimethyl glucose free from the liquid isomeride. Finally, for the purposes of the present investigation, Irvine and Oldham prepared 2 : 3 : 4-trimethyl glucose by synthetical operations designed to leave the terminal CH_2·OH group unsubstituted (J., 1925, **127**, 2729). The product was entirely different from the isomeride obtained from maltose.

Considering the precautions adopted and the results of collateral investigations designed to test sources of error, we are convinced that maltose cannot be formulated in either of the ways suggested by Haworth. The necessity for correction is not limited to the single case of maltose, but extends to all constitutional schemes in which the maltose structure is either directly or indirectly involved. For example, with the displacement of maltose from the position it has hitherto occupied in the structural classification of the disaccharides, the following constitutional relationships must be again regarded as conjectural: (1) maltose and cellobiose, (2) maltose and gentiobiose, (3) lactose and melibiose (Haworth and Leitch, *loc. cit.*; J., 1918, **113**, 188; Haworth and Hirst, J., 1921, **119**, 193; Haworth and Wylam, J., 1923, **123**, 3120).

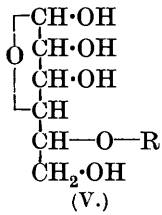
Further, speculations on the structure of *iso*maltose and of the molecular unit of starch, which have naturally been founded on a constitutional formula for maltose, lose their significance, a conclusion foreshadowed by results obtained in this laboratory on the methylation of starch and of the polyamyloses.

It would be premature, even with the additional information now available, to speculate as to the alterations in disaccharide formulæ which are now necessary, and discussion is limited to some general considerations. The question arises as to whether methylation

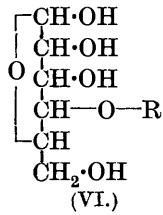
alters the linkage of one sugar residue with another, but this has already engaged our attention (Irvine and Oldham, J., 1925, **127**, 2910), although the argument that maltose and cellobiose give rise to different methylated sugars no longer holds. There remains an analysis of how far conclusions as to structure are logically valid when based on the formation of 2 : 3 : 6-trimethyl glucose. This sugar, formulated as an amylene-oxide, may be represented as (A) and on first inspection it might appear that all disaccharides which yield this compound must have the glucose residues attached through position 4. But inspection will show that the number of diglucoses which qualify for this mode of linkage is now larger than stereochemical considerations accommodate. The situation thus created is disconcerting, but is greatly simplified when it is recognised that 2 : 3 : 6-trimethyl glucose is capable of reacting as a γ-sugar, this property of the compound having been already pointed out (Irvine and Hirst, *loc. cit.*). It follows that the production of 2 : 3 : 6-trimethyl glucose is not absolutely diagnostic in discriminating between positions 4 and 5 as the point of union of two glucose residues. Thus, if we imagine two disaccharides to be constituted as under (V and VI), where R represents the non-reducing hexose residue,



(A.)

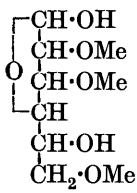


(V.)



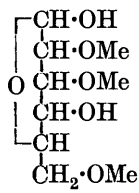
(VI.)

only the compound corresponding to (VI) would yield the stable form of trimethyl glucose directly. The other could, however, do so indirectly, giving in the first place :



Unstable Type.

which transposes to



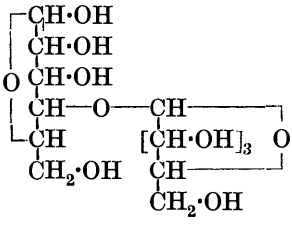
Stable Type.

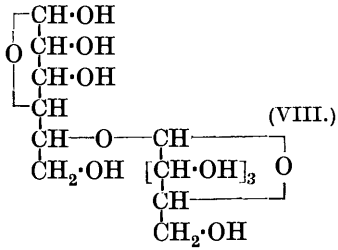
The possibility thus revealed invests all such constitutional studies with precisely the same uncertainty as is encountered in the hydrolysis of sucrose and inulin. Evidently the disaccharides must be studied afresh in the light of the possibility that γ-oxidic or other

linkages may be present in one or other of the constituent sugars. These considerations have been made the subject of other investigations now in progress in this laboratory.

According to the evidence now submitted, maltose may be formulated either as:

(VII.)





(VIII.)

The methylation process does not discriminate between these alternatives, one of which must represent cellobiose and *iso*cellobiose, whilst the other must be reserved for maltose together with, presumably, *iso*maltose. The conversion of methylmaltoside into β-methylglucoside appears to favour the allocation of formula (VII) to maltose but, on the other hand, the degradation of maltose is more easily explained in terms of formula (VIII). Work is in progress to decide between the above alternatives.

The results now contributed serve to emphasise a view formerly expressed (Irvine, J., 1923, **123**, 898) that no claim for finality can be made regarding the constitution of sugars and that each successive modification represents only a stage in knowledge.

Experimental.

Methylation of Maltose.—In order to economise description, it may be stated that each method of alkylation now described was applied to three distinct specimens of maltose. Two of these were obtained from trustworthy manufacturing firms and were selected as they displayed the correct melting point and specific rotation for the disaccharide. The third specimen was prepared in this laboratory during the War and was subjected, before use, to a special bacteriological examination. It was presumably identical with the material used by Haworth and Leitch. The descriptions of the methylation now given apply therefore to six distinct preparations, and the results quoted are typical.

Method I. The directions given by Haworth and Leitch (*loc. cit.*, pp. 813—814) were adhered to in every detail. After three methylations by means of methyl sulphate, the product extractable with chloroform weighed 27·5 g. (from 30 g. of maltose) and contained 50·5% of methoxyl. On distillation, 19·5 g. of a viscous syrup were

obtained (b. p. 189—191°/0·2 mm.; n_D 1·4685), but it may be noted that a small fraction of lower boiling point was also collected and that a viscous residue remained undistilled. The main fraction, on redistillation, boiled at 190°/0·2 mm. and showed $[\alpha]_D$ in alcohol + 91·1° for $c = 1·15$; $[\alpha]_D$ in acetone + 92·1° for $c = 1·256$; OMe, 50·4%; n_D 1·4706. After another methylation, the product was separated on distillation into three portions, and, although the boiling point showed no variation, the second fraction (11·2 g.) was selected as being in best agreement with the constants quoted by Haworth and Leitch for heptamethyl methylmaltoside.

The methoxyl content was nevertheless slightly low, but purification was effected by solution in light petroleum and extraction with water. A small amount of discoloured syrup was retained in the hydrocarbon solvent, and the main product, when recovered from the water, was entirely decolorised by boiling in chloroform solution with norit. Average yield, 10 g. per 30 g. of maltose used. Found: C, 52·3; H, 8·6; OMe, 52·7. Calc. for heptamethyl methylmaltoside, $C_{12}H_{14}O_3(OMe)_8$, C, 52·9; H, 8·4; OMe, 54·6%; n_D 1·4691; $[\alpha]_D$ in acetone + 90·6° for $c = 1·16$. The maltose provided by manufacturing firms gave results corresponding closely with those described above, although the final yield of methylated maltoside was invariably smaller. The same tendency for the methoxyl value to be low was again observed, successive preparations showing OMe, 52·0 and 52·4, in place of the calculated value 54·6%.

Method II. The initial stages in the methylation were conducted as before and the product soluble in chloroform was isolated. Thereafter only the silver oxide method was applied, the following being an account of a typical case. 40 G. of the partly methylated maltoside were alkylated as usual with methyl iodide (6 mols.) and silver oxide (3 mols.), the treatment being continued for 8 hours. The yield of distilled material amounted to 32 g., of which 22 g. were collected at the boiling point of heptamethyl methylmaltoside. The undistilled residue was rejected and the distilled material was again methylated and fractionated. Finally, the middle fraction was redistilled and purified by solution in light petroleum and extraction with water as already described.

The heptamethyl methylmaltoside thus isolated was identical with that obtained by Method I and gave the same hydrolysis products, but the methoxyl content was again low (OMe, 52%) and the refractive index was 1·4700 in place of 1·4691.

Hydrolysis of Heptamethyl Methylmaltoside.—Method A. In studying this reaction the preparations of the alkylated maltoside obtained from different specimens of maltose were kept apart and treated separately; identical results were, however, obtained in each case.

The maltoside was hydrolysed by heating with 5% aqueous hydrochloric acid as described by Haworth and Leitch, but a variation was introduced into the method of separating the sugars, the acid liquor being extracted six times with chloroform. The syrup isolated from the chloroform solution crystallised at once and consisted of tetramethyl glucose.

The sugar remaining in the aqueous liquor was recovered in the usual manner and converted into the corresponding methylglucoside by boiling with methyl alcohol containing 1% of hydrogen chloride until the solution was devoid of reducing action. After rendering alkaline by the addition of sodium bicarbonate, the alcohol was removed and the residue taken up in water. On extracting six times with chloroform, the trimethyl methylglucoside passed into solution in the chloroform, from which it was recovered and purified by distillation at 145°/0·6 mm. This treatment removed traces of impurity and the glucoside was then rehydrolysed with 5% aqueous hydrochloric acid. On isolation of the product in the usual manner, the trimethyl glucose was obtained as a viscous syrup which slowly crystallised in the manner characteristic of 2 : 3 : 6-trimethyl glucose. The sugar was recrystallised from ether and identified as afterwards described.

In order to secure control evidence, the above operations were conducted in lots of 10 g., a typical result being that 10·3 g. of heptamethyl methylmaltoside gave 4·7 g. of crystalline tetramethyl glucose and 4·7 g. of syrupy trimethyl glucose. The latter, in turn, yielded 3·6 g. of distilled trimethyl methylglucoside, from which 3·3 g. of the corresponding sugar were obtained.

Method B. The hydrolysis of heptamethyl methylmaltoside was in this case conducted under conditions which would convert the liberated sugars into the corresponding methylglucosides. This was effected by boiling with excess of methyl alcohol containing 1% of hydrogen chloride, it being found that, in the course of 7 hours' treatment, the specific rotation, which had gradually diminished, attained a constant value. Boiling was continued for an additional period of 5 hours, after which the acid was neutralised and the solvent alcohol removed. The residue was then dissolved in water and the solution extracted repeatedly with chloroform, a syrup being obtained on evaporating the latter solvent. This syrup was a mixture of tetramethyl and trimethyl methylglucosides which was purified from traces of extraneous products by distillation under diminished pressure. The total distillate was thereafter hydrolysed in the usual manner by means of aqueous hydrochloric acid and the two sugars thus formed were separated by extraction with chloroform as described in Method A. The results were as before, crystal-

line tetramethyl glucose being isolated from the chloroform solution and the aqueous liquor retaining trimethyl glucose. This was isolated initially as a syrup which crystallised on keeping. In this particular instance, the solidification of the sugar was complete only after an interval of 3 weeks owing, it would appear, to the presence of a small proportion of a very viscous syrup which was less soluble in ether and had a smaller methoxyl content than trimethyl glucose. The crystallisation of the sugar was delayed by cooling and proceeded more satisfactorily at room temperature.

Examination of the Hydrolysis Sugars.—Identification of 2 : 3 : 4 : 6-*tetramethyl glucose.* The identification of the tetramethyl glucose presented no difficulty. All the specimens were recrystallised three times from light petroleum. The composition, melting point, mixed melting point, and mutarotation determined on the product agreed exactly with the accepted standards for 2 : 3 : 4 : 6-tetramethyl glucose.

Identification of 2 : 3 : 6-*trimethyl glucose.* In the hydrolysis experiments already described, the trimethyl glucose was obtained as a crystalline mass which still retained a small quantity of a viscous syrup. The material was thoroughly incorporated with dry ether containing a little acetone, and the crop of crystals removed by filtration. On evaporation of the filtrate and extraction of the residue with ether any non-crystallisable syrup was left undissolved, while the extract gave further crops of crystalline sugar. In one instance, when the proportion of adhering syrup was larger than usual, it was removed by draining on porcelain, from which it was recovered and examined, with negative results, for 2 : 3 : 4-trimethyl glucose. Each preparation of the sugar was purified by recrystallisation from ether containing a small proportion of low-boiling petroleum. In this way, the compound was obtained in characteristic long needles melting at 113—114° and showing no depression of the melting point when mixed with a standard specimen of 2 : 3 : 6-trimethyl glucose (Found: OMe, 41·2. Calc., 41·9%). When dissolved in water the sugar displayed downward mutarotation, giving the equilibrium value $[\alpha]_D^{20°}$ + 70·9°, the accepted permanent specific rotation for 2 : 3 : 6-trimethyl glucose being +70·5°. The results quoted are typical of those obtained with all the specimens examined.

Preparation of Methylmaltoside.—In order to attain greater accuracy, the reactions of methylation and hydrolysis were duplicated using crystalline methylmaltoside as the starting material. As a number of interesting features were encountered in the preparation of methylmaltoside, these are referred to now, together with such practical details as we have found to be advantageous.

Stage I. The preparation of octa-acetyl maltose proceeds most satisfactorily when not more than 30 g. of maltose are used in each experiment. In successive preparations 300 g. of the sugar were converted into the acetate, each experiment yielding on an average 20 g. of product which had been recrystallised from alcohol until the m. p. was 158—159°.

Stage II. Trial experiments showed that the action of hydrogen bromide on octa-acetyl maltose gives the best results when carried out on small quantities of the order of 2 g. This may be increased to a maximum of 10 g. but, with larger quantities, degradation of the disaccharide takes place and serious difficulties are introduced into the purification of the acetylated methylmaltoside. By tedious repetition of the typical experiment now described, 250 g. of the octa-acetate were converted into hepta-acetyl methylmaltoside. 2 G. of octa-acetyl maltose were dissolved in 50 c.c. of a mixture consisting of glacial acetic acid saturated with hydrogen bromide (10%), of ether (15%), and of benzene (75%). The use of this particular mixture of solvents secures a permanently clear solution which enables the reaction to be followed by reliable polarimetric readings. The rotation of the solution came to a constant value in about 12 hours, the final specific rotation, recalculated for the change of concentration, ranging between + 184° and + 190°. The solution was washed twice with water and dried over anhydrous sodium sulphate, the solvent being thereafter removed. The residual syrup was dried in a vacuum at a temperature not exceeding 55°, a process which was accompanied by vigorous frothing.

Stage III. The bromo-derivative was dissolved by shaking with anhydrous methyl alcohol in the presence of silver carbonate, mixing being conducted on a mechanical shaker until a test sample of the solution was free from bromine. At this stage crystals of the product usually separated and consequently both the silver residues and the filtrate were extracted with hot chloroform. On removal of the solvent, hepta-acetyl methylmaltoside remained as a syrup which crystallised readily and was purified from absolute alcohol. In the course of 10 parallel preparations it was found that, as a rule, three crystallisations from alcohol gave a product melting at 124—125°, but, by repeating the crystallisation, this value could be raised to 128—129° (Found: C, 49·8; H, 5·9; OMe, 4·5. Calc., C, 49·8; H, 5·8; OMe, 4·8%. $[\alpha]_D$ in chloroform + 53° for $c = 1·5$). This melting point is identical with that quoted by Koenigs and Knorr, who prepared the compound from the corresponding nitrate. The loss sustained in these recrystallisations is considerable, as only about 40% of the original material is obtained in the pure condition.

In addition, a second crystalline product was isolated in amounts which varied in different preparations and it may be noted that when this substance was present in large proportion it was impossible to separate it from hepta-acetyl methylmaltoside by ordinary fractional crystallisation. Normally, this by-product was deposited from the mother-liquors, accumulated in the course of recrystallising hepta-acetyl methylmaltoside, when kept in a cool place. After recrystallisation from alcohol the compound melted at 145—146°, and showed $[\alpha]_D$ in chloroform + 69·1° for $c = 1·5$ (Found: OMe, 5·2; $CH_3·CO_2H$, 63·3. Calc. for $C_{24}H_{34}O_{16}$, OMe, 5·4; $CH_3·CO_2H$, 62·3%). The examination in detail of this compound will form the subject of a later communication.

Stage IV. Hepta-acetyl methylmaltoside, in quantities of about 40 g., was dissolved in a large excess of absolute alcohol saturated with dry ammonia. After 2 days, the rotation of the solution became constant and thereafter the solvent was removed under diminished pressure. The viscous syrup then remaining was dissolved in the minimum amount of alcohol and the methylmaltoside precipitated by the addition of small quantities of a mixture of chloroform and ether. The product was thereafter repeatedly recrystallised from a mixture of alcohol and ethyl acetate—a process which, if wasteful, is necessary before the maximum melting point of 110—111° is attained. Average yield, 9·5 g. In this condition, methylmaltoside contained 1 molecule of combined water (Found: OMe, 8·3; H_2O, 4·9. Calc. for $C_{13}H_{24}O_{11},H_2O$, OMe, 8·3; H_2O, 4·8%).

The following observations were made on a specimen dried over phosphoric anhydride at 100°/15 mm.: C, 43·8; H, 7·0. Calc. for $C_{13}H_{24}O_{11}$, C, 43·8; H, 6·75%. $[\alpha]_D$ in alcohol + 63·5° for $c = 1$; in water, + 83·9° for $c = 1$.

Methylation of Methylmaltoside.—This methylation was carried out by the silver oxide reaction in a manner parallel with that employed in the case of methylglucoside. In the first three methylations it was necessary to use methyl alcohol as an extraneous solvent, but thereafter the material was freely soluble in methyl iodide alone. After the sixth methylation, the refractive index was 1·4689 and the methoxyl content 50·1%. Two additional methylations failed to alter n_D, although the methoxyl content had increased to 52·3%. On distillation in a high vacuum, no lower-boiling distillate was obtained and the material distilled sharply at the boiling point of heptamethyl methylmaltoside (Found: n_D, 1·4662; yield, 76%; C, 52·7; H, 8·45; OMe, 54·1. Calc. for $C_{20}H_{38}O_{11}$, C, 52·9; H, 8·4; OMe, 54·6%).

Solvent.	c.	$[\alpha]_D$.
Water	0·508	+88·1°
Alcohol	0·562	81·9
Chloroform	0·557	78·9
Acetone	0·577	78·1

Hydrolysis of Heptamethyl Methylmaltoside.—A 4·5% solution of the compound in 5% aqueous hydrochloric acid was boiled until the rotation, which at first diminished, increased to a constant value. Judging from the initial polarimetric reading, it would appear that hydrolysis commenced in the cold.

Time.	($l = 1$).	α.	$[\alpha]_D$.
Start		+3·11°	+69·3°
15 mins'. boiling		2·68	59·6
1 hour's	,,	2·85	63·4
$2\frac{3}{4}$,,	,,	3·27	72·3 constant.

After neutralising the solution with barium carbonate it was decolorised with norit and extracted six times with chloroform. The extract gave crystalline tetramethyl glucose (yield, 91% of the theoretical amount). Trimethyl glucose was recovered from the aqueous liquor by evaporation and extraction of the residue with acetone. Removal of this solvent left a syrup which was taken up in ether containing a trace of acetone and treated as already described. The trimethyl glucose crystallised rapidly, solidification beginning spontaneously in a few hours (yield, 87% of the theoretical amount).

Tetramethyl glucose. After two recrystallisations, m. p. 93—95°; $[\alpha]_D$ in absolute alcohol + 112·1° (initial) $\longrightarrow$ 83·4° (constant).

Trimethyl glucose. After two recrystallisations, m. p. 113—114°; mixed m. p. 113—114°; permanent specific rotation in water + 70·2°; OMe, 41·6%. All the above determinations agree exactly with the standard values for 2 : 3 : 6-trimethyl glucose and further confirmation was obtained by converting the sugar into the corresponding β-methylglucoside. This proved to be identical with the trimethyl methylglucoside obtained from cellulose; m. p. 57·5°; mixed m. p. 57°; C, 50·6; H, 8·4; OMe, 51·9. Calc., C, 50·8; H, 8·5; OMe, 52·5%. The specific rotation in methyl alcohol for $c = 1$ was − 29·3°.

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