CCXIX.—*The Methylation of Cellulose. Part II.*
Hydrolysis of Methylated Cellulose.

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THE methylation of fibrous cellulose by the agency of sodium hydroxide and methyl sulphate, with the formation of products the composition of which may be represented by the simple empirical formulæ $C_{12}H_{19}O_9 \cdot OMe$ and $C_6H_9O_4 \cdot OMe$, has been

described in a previous communication (T., 1913, **103**, 1735); it was there pointed out that, notwithstanding the apparent constancy in composition of the substances formed in several independent series of experiments carried out under slightly varied conditions, the methylated products are nevertheless not necessarily chemical individuals. The results now communicated of additional experiments on the methylation of cellulose, and of a study of the hydrolytic decomposition of the methylated cellulose, tend to confirm the view that the latter substance is not chemically homogeneous. It is, however, important to notice that the expectation that the products of hydrolysis of the methylated cellulose would prove to be methylated glucoses has been justified; the further investigation of these methylated sugars which is now in progress will, it is hoped, afford definite evidence regarding the manner of linkage of the glucose residues in the cellulose molecule.

The well-marked stages formerly observed on the first and second treatments of the cellulosic material with the methylating reagents, which corresponded respectively with the formulæ $C_{12}H_{19}O_9 \cdot OMe$ and $C_6H_9O_4 \cdot OMe$, were not encountered on a repetition of the experiments with a larger quantity of material. In the following table a comparison is made of the amounts of methoxyl in the products from each successive treatment in one of the original series of experiments described in the former paper (I) with those in the products at the corresponding stages in a newer series (II), the details of which are given in the experimental part of this communication :

Concentration of sodium hydroxide.	Percentage of methoxyl after				
	1st	2nd	3rd	4th	5th treatments
*I. 15—18 grams per 100 c.c. ...	8.5	19.7	23.3	25.5	24.6
II. 17 ,, ,, 	5.3	11.5	14.0	18.7	20.7

The divergences between the methoxyl contents at corresponding stages in the two series, due perhaps to the somewhat different concentrations of the alkali and to the differences in the quantities of material undergoing treatment, clearly indicate that the agreement previously observed between simple formulæ and the composition of the methylated cellulose is fortuitous; a study of the products of the hydrolytic decomposition of methylated cellulose points to the same conclusion.

The yields at each stage of series II in the foregoing table indicated that but little of the methylated cellulose had dissolved in the wash-water, but, on repeating the process for a sixth time, a considerable quantity of material passed into solution. This may

* The percentages of sodium hydroxide quoted in the original paper are approximate and refer to grams per 100 c.c. of solution. In the later experiments the concentrations have been accurately determined.

perhaps be due to the fact that a much more concentrated solution of sodium hydroxide was employed. Both portions of the product from this final treatment—the part which remained undissolved and the part which dissolved—contained approximately the same proportion of methoxyl; it is therefore assumed, meantime, throughout the following discussion, that both possessed the same constitution.

The hydrolysis of the methylated cellulose was carried out on the undissolved portion from the final treatment, which contained about 25 per cent. of methoxyl, and was effected by the use of very concentrated aqueous hydrochloric acid, according to the method employed by Willstätter and Zechmeister for the hydrolysis of cellulose (*Ber.*, 1913, **46**, 2401). The process, which proved highly efficient, and was unaccompanied by any evidences of profound decomposition, yielded a mixture of methylated hexoses, which were separated by the methods described in the experimental part. A trimethyl hexose was obtained in the crystalline state, and there is little doubt that this compound is a true methylated glucose, since it displays practically identical specific rotation in all ordinary solvents, and this property, as already pointed out by Irvine and Hogg (this vol., p. 1386), is characteristic of the glucose configuration. The various hydrolytic products isolated may thus be classified as follows:

(1) An amorphous monomethyl glucose, or mixture of monomethyl glucoses.

(2) An amorphous dimethyl glucose, or mixture of dimethyl glucoses.

(3) A crystalline trimethyl glucose.

(4) A trace of crystalline matter which, in crystalline form and range of solubility, resembled tetramethyl glucose.

No glucose was isolated, but indications were obtained of its presence or of the presence of an unmethylated product.

In considering the significance of these products of hydrolysis, it is legitimate at this stage to leave almost out of account the possible occurrence of tetramethyl glucose, since the trace of this substance suspected to be present would have its presence explained by the assumption of even a very small degree of degradation during the operations of methylation. At the same time, it is conceivable that tetramethyl glucose may be a normal hydrolysis product of methylated cellulose, and that its origin may be traced to the existence in the cellulose complex of terminal glucose residues linked to the remainder of the molecule through the reducing group. The possibility presents itself that cellulose may consist essentially of an open chain of condensed glucose residues.

Although no very precise estimate can be made at present of the relative quantities of the various products of hydrolysis, it is probable that the amounts of dimethyl and trimethyl glucoses were nearly the same; the weight of trimethyl glucose separated in the crystalline form was approximately 10 per cent. of the weight of the crude product of hydrolysis, and the presence of more trimethyl glucose was recognised by conversion of the residual mixed sugars into the corresponding methylglucosides, which were fractionated by distillation under diminished pressure. The comparative ease with which trimethyl glucose crystallises from that portion of the hydrolysis product which possesses the solubilities characteristic of a trimethyl glucose seems to indicate that only one trimethyl glucose is present, and therefore that the cellulose molecule is symmetrical. On this basis, it would be expected that a methylated cellulose which possesses the formula $C_6H_9O_4 \cdot OMe$ should yield on hydrolysis monomethyl glucose, and that alone; even without assuming the symmetry of the cellulose molecule, it is probable that a monomethyl glucose or mixture of monomethyl glucoses would be obtained from a methylated cellulose represented by the above formula. A methylated cellulose of the formula $C_{12}H_{17}O_7(OMe)_3$ would contain 25.4 per cent. of methoxyl, which is approximately the percentage in the sample of methylated cellulose hydrolysed in these experiments; it might therefore be expected, unless the linkages of the glucose residues in the cellulose molecule are to a high degree unsymmetrical, that if the methylation occurred uniformly with intermediate formation of a definite compound, $C_6H_9O_4 \cdot OMe$, the methylated cellulose, which contains about 25 per cent. of methoxyl, should yield on hydrolysis nearly equal quantities of monomethyl and dimethyl glucose, and but little or none of a more highly methylated sugar; since this is not in accordance with the fact, it must be concluded, especially since there is an indication of the presence of glucose in the product of hydrolysis, that, notwithstanding the care taken in attempting to ensure uniform impregnation of the cellulosic material with the solution of alkali and with methyl sulphate, the methylation did not occur uniformly, and that the agreement between simple formulæ and the composition of the methylated cellulose was accidental.

The occurrence of a trimethyl glucose as essentially the most highly methylated glucose derived from methylated cellulose is of importance, since it is in harmony with the view that the proportion of free hydroxyl groups to every six carbon atoms of cellulose is three; the possible occurrence, already referred to, of terminal glucose residues containing four unsubstituted hydroxyl groups would, in the presumably large cellulose molecule, cause only a

negligible increase in the ratio of hydroxyl groups to carbon atoms. It has not yet been ascertained whether the crystalline trimethyl glucose isolated is the only one present, nor has its constitution been completely determined; it does not form an osazone, a fact which indicates the replacement by methoxyl of the hydroxyl group adjacent to the reducing group. Leaving out of consideration the dimethyl methylglucosides, there are four possible trimethyl glucoses, each of which may exist in the α - and the β -form:

The allocation of formula I to the trimethyl glucose derived from methylated cellulose is excluded, since a methylated glucose represented by this formula would be able to form an osazone. The sugar of this constitution has already been prepared by Irvine and Scott (T., 1913, **103**, 564), and by Irvine and Macdonald (unpublished result), and differs in properties from that under discussion. A trimethyl glucose of the constitution represented by formula II has been prepared by Irvine and Dick (unpublished), and likewise differs in properties from that derived from cellulose. There remain, therefore, formulæ III and IV, a discrimination between which has not yet been attempted.

The amorphous monomethyl and dimethyl glucoses were separated by conversion of the residual syrup, from which the trimethyl glucose was extracted into a mixture of methylglucosides, which were separated by the action of solvents and by distillation. The methylglucosides were then hydrolysed. Neither of the sugars appears to be identical with methyl glucoses already known. Both form osazones. It is very probable that each is a mixture, for, even on the assumption that only one trimethyl glucose (counting the α - and β -form as one) can be obtained from methylated cellulose, the possibility occurs of three monomethyl and three dimethyl glucoses being liberated on hydrolysis as derivatives of the incompletely methylated glucose residues of the cellulose molecule. Again, if the glucose residues in cellulose are not symmetrically linked, the liberation of more than one trimethyl glucose, and of a correspondingly greater number of monomethyl and dimethyl glucoses, would be expected on hydrolysis of the methylated cellulose. It is therefore not surprising that the amorphous mono-

methyl and dimethyl glucoses, although they gave good analytical figures, could not be obtained in the crystalline state, for, on the simplest assumption, each may be a mixture of three or, counting the α - and β -forms separately, of six isomeric substances, and they may be more complex mixtures.

It remains to notice the evidence for the occurrence of glucose in the product of hydrolysis. That portion of the syrup obtained on hydrolysis which was least soluble in acetone dissolved readily and completely in methyl alcohol, so that it cannot have contained an appreciable quantity of glucose, unless (as may have been the case) the solubility of any glucose present was greatly modified by the presence of other substances. One portion of this fraction contained about half the percentage of methoxyl that would be present in a monomethyl glucose; this seemed to indicate the presence of a disaccharide, but the results of molecular-weight determinations and the percentages of hydrogen and carbon (determined in the purified, but still apparently impure, substance, a small quantity only of which was available) were not in agreement with the composition of such a compound. From the corresponding fraction derived from another portion of the same sample of methylated cellulose, a substance of approximately the same methoxyl content as monomethyl glucose was separated. It seems probable, therefore, that the product of hydrolysis contained some uncombined glucose. These results are quoted at this stage as, in utilising Willstätter and Zechmeister's method of hydrolysis, we have not ignored the possibility that, under the condensing influence of the concentrated acid used, a certain amount of auto-condensation may have taken place in the liberated sugars.

The research is being extended in order to complete the methylation of cellulose and to ascertain the constitution of the methylated sugars formed on hydrolysis.

EXPERIMENTAL.

Methylation.

The methylated cellulose which was subjected to hydrolysis was prepared by impregnating cotton wool (1 equivalent $C_6H_{10}O_5$) with a solution of sodium hydroxide (2 mols.), and adding methyl sulphate in portions to the mixture until the alkaline reaction disappeared; this required about one and a-half times the quantity of methyl sulphate calculated to react with the sodium hydroxide present. The mixture became warm during the reaction, and the methylated cellulose was then washed and dried. The product from five similar consecutive treatments, in which the solution of sodium hydroxide employed contained 17 grams per 100 c.c., was

finally (sixth treatment) soaked for a week under diminished pressure in a more concentrated solution of sodium hydroxide (38·3 grams in 100 c.c.), and then treated with sufficient methyl sulphate to destroy the alkaline reaction; this required four times the calculated quantity of methyl sulphate. In the table of quantitative details which follows, the initial weight in each case (except the first) is the quantity used of the product from the immediately preceding treatment; the final weight is that of the washed and dried product:

Concentration of the sodium hydroxide solution = 17 grams in 100 c.c.	First treatment :	103 grams of cotton wool gave 101 grams. 0·2023 gave 0·0808 AgI. OMe=5·28 per cent.
	Second treatment :	99·5 grams gave 95 grams. 0·3130 gave 0·2719 AgI. OMe=11·48 per cent.
	Third treatment :	92 grams gave 86 grams. 0·2980 gave 0·3153 AgI. OMe=13·98 per cent.
	Fourth treatment :	83 grams gave 79 grams. 0·3082 gave 0·4374 AgI. OMe=18·74 per cent.
	Fifth treatment :	74 grams gave 68 grams. 0·2719 gave 0·4258 AgI. OMe=20·69 per cent.
	Sixth treatment :	Concentration of the sodium hydroxide solution = 38·3 grams in 100 c.c.

The methylation was carried out on two separate portions each of which was treated similarly : 65 grams gave 45·6 grams.

(i) 0·2274 gave 0·4111 AgI. OMe=23·89 per cent.
0·1655 gave 0·2986 CO₂ and 0·1042 H₂O.
C=49·20 ; H=7·04 per cent.

(ii) 0·2315 gave 0·4550 AgI. OMe=25·97 per cent.

The combined filtrates and washings from the sixth treatment were neutralised and evaporated on the water-bath; while the solution remained dilute, a gelatinous substance separated from the hot solution, but redissolved when the solution cooled. When the solution became more concentrated, part of the gelatinous precipitate remained undissolved in the cold solution, but redissolved when the salts present were removed by washing with water. A small portion was separated and analysed:

0·1884 gave 0·3376 AgI. OMe=23·68 per cent.

Hydrolysis.

The methylated cellulose hydrolysed was the final product from the above operations, and contained 23·89—25·97 per cent. of methoxyl. It gelatinised when added at 0° to an aqueous solution of hydrogen chloride which had been saturated at that temperature, and dissolved in a few hours, giving a nearly colourless solution, which afterwards turned somewhat brown. The quantities used in three experiments were: (1) 12 grams of methylated cellulose and 260 c.c. of the solution of hydrochloric acid; (2) 15 grams of methylated cellulose and 650 c.c. of hydrochloric acid;

(3) 15 grams of methylated cellulose and 780 c.c. of hydrochloric acid. In each case the mixture of methylated cellulose and hydrochloric acid was allowed to remain for five to six hours at 0° , and then for twenty hours at the atmospheric temperature in a closed vessel. A current of air was now drawn through the liquid to remove part of the hydrochloric acid, and the solution then diluted. After polarimetric observations had shown that no further change was occurring, the bulk of the water and hydrochloric acid was removed by distillation under diminished pressure; the residue was diluted with water, neutralised with silver carbonate, and, after filtration, shaken with animal charcoal to remove traces of colloidal silver. The filtered solution was concentrated under diminished pressure, and yielded a nearly colourless syrup of almost exactly the same weight as the original material.

This syrup was extracted first by boiling with ether, and then by boiling repeatedly with acetone. The ethereal extract contained merely a trace of dissolved matter. The acetone extract contained trimethyl glucose, dimethyl glucose, and monomethyl glucose; it was from this fraction, also, that the trace of crystalline matter suspected to be tetramethyl glucose was separated. The residues from the extraction with ether and acetone dissolved readily in methyl alcohol; this fraction appeared to contain monomethyl glucose, and possibly glucose. It should be pointed out that the solubilities of these sugars, or rather, perhaps, the ease with which they dissolve, are greatly modified when they occur together in a mixture. Thus trimethyl glucose, which could not be extracted by ether from the crude product of hydrolysis, was found to dissolve quite readily in ether when it had been separated from the other sugars present in the acetone extract.

Acetone Extract.—The solution in acetone was concentrated, and, on cooling, part of the dissolved substance was precipitated. The precipitated syrup was again extracted with acetone, and by repetitions of these operations the portion most soluble in acetone was collected; it remained as a pale yellow, very viscous syrup when the acetone was removed by distillation. A molecular-weight determination by the cryoscopic method in water showed that it consisted essentially of monosaccharides:

0.3713 gram in 8.098 grams of water gave $\Delta t = 0.39^{\circ}$. M.W. = 218.

Trimethyl Glucose.—This was separated from that part of the product of hydrolysis which was most soluble in acetone by adding ether to its solution in acetone. This precipitated the bulk of the dissolved matter. The supernatant liquid was decanted, the solvents removed by distillation, and the residue was redissolved in

acetone. The same cycle of operations was then repeated several times until the syrup left after distillation of the mixture and ether crystallised on keeping. The crystals were drained on a porous plate, and after several recrystallisations from ether, trimethyl glucose was obtained pure in needle-shaped crystals, melting at 110° . (Found, C=48.40; H=8.08; OMe=41.29. $C_9H_{18}O_6$ requires C=48.62; H=8.17; OMe=41.90 per cent.)

The compound at this stage was essentially the α -form. After it had been washed several times with ether it gave a maximum initial rotation:

0.1424 gram dissolved in 10 c.c. of acetone gave in a 1-dcm. tube:

	$\alpha_{D,20}$	$[\alpha]_{D,20}$
Initial.....	+1.44°	101.12°
Final	+0.99°	69.52°

0.2578 gram dissolved in 10 c.c. of methyl alcohol gave in a 1-dcm. tube:

	$\alpha_{D,20}$	$[\alpha]_{D,20}$
Initial.....	+2.68°	103.96°
Final	+1.74°	67.49°

As the spontaneous changes were exceedingly slow, the equilibrium values were obtained after catalysis with a trace of sodium hydroxide. The readings were made at room temperature.

The β -form has not been isolated; it appears to be more soluble in ether than the α -form.

The ethereal mother liquors from the crystallisation of the trimethyl glucose were precipitated with light petroleum, the supernatant liquid was decanted, and the solvents were removed from it by distillation. By redissolving the residue in ether and repeating the operations just described, a trace of a crystalline substance was obtained which was soluble in light petroleum, and had the characteristic appearance of tetramethyl glucose.

Dimethyl Glucose and Monomethyl Glucose.—The syrup soluble in acetone, from which trimethyl glucose had been extracted, was further worked up so as to separate the more soluble portion which, it was presumed, would contain the bulk of the dimethyl glucose. 6.2 Grams of this syrup were heated in a sealed tube with 80 c.c. of a 0.25 per cent. solution of hydrogen chloride in methyl alcohol for thirty-two hours, after which time the liquid no longer reduced Fehling's solution. The solution of methylglucosides was then diluted with water, neutralised with silver carbonate, and filtered; traces of silver still present were removed by warming the solution gently with animal charcoal. 5.7 Grams of a viscid, opaque, pale yellow syrup were left behind when the water was removed by

distillation under diminished pressure. The syrup was extracted repeatedly by boiling with ether. The residue from this extraction (about 2 grams) was boiled for forty-five minutes with 50 c.c. of a 5 per cent. aqueous solution of hydrogen chloride. The solution was then neutralised with silver carbonate, filtered, shaken with charcoal, and again filtered. After removal of the water, the residue was extracted with acetone, which removed very little substance, then with absolute ethyl alcohol. The material extracted by ethyl alcohol was dried in a vacuum at 60° , when it formed a hard glass, which gave analytical figures for monomethyl glucose. (Found, $C=43.12$; $H=7.29$; $OMe=17.09$. $C_7H_{14}O_6$ requires $C=43.27$; $H=7.27$; $OMe=15.99$ per cent.)

0.3027 gram dissolved in 10 c.c. of methyl alcohol gave in a 1-dcm. tube $\alpha_D + 1.92^{\circ}$, whence $[\alpha]_D 63.4^{\circ}$.

The yellow, viscous liquid left behind when the ether was distilled from the ethereal extract obtained from the mixture of glucosides was distilled under diminished pressure. The first portion of the distillate (2.03 grams) was a colourless, viscous liquid (b. p. $141^{\circ}/0.21$ mm.). Its methoxyl content showed it to be a mixture of trimethyl and dimethyl glucosides:

0.1359 gave 0.4956 AgI. $OMe=48.18$.

$C_9H_{18}O_6$ requires $OMe=41.90$; $C_{10}H_{20}O_6$ requires $OMe=52.55$ per cent.

0.2982 gram dissolved in 10 c.c. of methyl alcohol gave in a 1-dcm. tube $\alpha_D + 1.39^{\circ}$, whence $[\alpha]_D 46.61^{\circ}$.

The second fraction was, when cold, a colourless, transparent glass (b. p. $143^{\circ}/0.03$ mm.). The methoxyl content showed it to be dimethyl methylglucoside. (Found, $OMe=40.57$. $C_9H_{18}O_6$ requires $OMe=41.90$ per cent.)

0.2330 gram dissolved in 10 c.c. of methyl alcohol gave in a 1-dcm. tube $\alpha_D + 1.87^{\circ}$, whence $[\alpha]_D 80.26^{\circ}$.

The remainder of the second fraction was hydrolysed by boiling it for fifty minutes with 100 c.c. of a 5 per cent. aqueous solution of hydrogen chloride. The solution was neutralised with barium carbonate, the filtrate concentrated on the water-bath, and the residue dried in a vacuum at 60° and extracted with acetone; the dissolved material was dried in a vacuum, again at 60° , and again extracted with acetone. Addition of a small quantity of ether precipitated any barium chloride still present. The dried syrup finally obtained was analysed, and found to be dimethyl glucose. (Found, $C=46.68$; $H=7.89$; $OMe=31.26$. $C_8H_{16}O_6$ requires $C=46.13$; $H=7.75$; $OMe=29.81$ per cent.)

0.3908 gram dissolved in 10 c.c. of methyl alcohol gave in a 1-dcm. tube $\alpha_D + 2.65^{\circ}$, whence $[\alpha]_D + 67.8^{\circ}$.

The residue in the flask after distillation of the dimethylglucoside was a clear, brown glass—presumably monomethyl methylglucoside, but it has not yet been examined.

Residue Undissolved by Acetone.—The experimental results for this portion are given in some detail, in order to indicate the grounds for the surmise that glucose is present. The residue dissolved completely in methyl alcohol, except for a trace of colouring matter. In the case of one of the portions of methylated cellulose hydrolysed, ether was added to the solution of this residue in methyl alcohol; the precipitate, after having been dried, was redissolved in methyl alcohol and precipitated with acetone, when it was obtained as a soft, amorphous material, which hardened when it had been washed several times with acetone:

0.1736 gave 0.2722 CO_2 and 0.0988 H_2O . $\text{C}=42.77$; $\text{H}=6.37$.

0.1830 „ 0.2870 CO_2 „ 0.1075 H_2O . $\text{C}=42.77$; $\text{H}=6.57$.

0.2320 „ 0.1390 AgI. $\text{OMe}=7.92$.

The molecular weight was determined by the ebullioscopic method in ethyl alcohol and by the cryoscopic method in water:

0.2676 gram in 15.02 grams of ethyl alcohol gave Δt 0.11° .

M.W.=186.

0.3772 gram in 22.88 grams of water gave Δt -0.115° . M.W.=267.

A disaccharide, $\text{C}_{13}\text{H}_{24}\text{O}_{11}$, would require $\text{C}=43.80$; $\text{H}=6.79$; $\text{OMe}=8.71$ per cent. M.W.=356.

The substance was further purified by repeating several times the solution in methyl alcohol and precipitation with acetone. When dried in a vacuum at 40° it became slightly brown, and melted at 160 – 165° :

0.1256 gave 0.0501 AgI. $\text{OMe}=5.27$.

0.1398 gram in 7.99 grams of water gave Δt -0.215° . M.W.=151.5.

The residue insoluble in acetone from the hydrolysis of another portion of the same sample of methylated cellulose was extracted repeatedly by boiling with ethyl alcohol, and the extracts were worked up so as to collect the part most soluble in ethyl alcohol. This was obtained finally as a white substance, which separated from solution in ethyl alcohol in what appeared to be a crystalline powder; when this was examined under the high power of a microscope, however, it was found to consist of minute, amorphous particles. The methoxyl content pointed to its being monomethyl glucose:

0.1291 gave 0.1278 AgI. $\text{OMe}=13.08$.

$\text{C}_7\text{H}_{14}\text{O}_6$ requires $\text{OMe}=15.98$ per cent.

It thus appears that that portion of the product of hydrolysis

which is nearly insoluble in acetone, but soluble in methyl alcohol, and contains only half the percentage of methoxyl which would be present in a monomethyl glucose, yields a fraction which approximates in composition to a monomethyl glucose; the remainder may be glucose.

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