4. One of the azo compounds, 2',4'-dinitro-4-hydroxy-2,3,5,6-tetramethylazobenzene, exists in two polymorphic crystalline forms. One is an orange powder and the other forms deep red prisms.

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[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY, LAWRENCE COLLEGE]

Factors Involved in the Methylation of Cellulose Acetate and of Cellulose Dissolved in Trimethylbenzylammonium Hydroxide

BY GERALD G. JOHNSTON[1]

Although it is comparatively easy with a few operations to arrive at a degree of methylation which approaches that of trimethyl cellulose, it is very difficult to reach the theoretical value unless special methods, more or less indirect in nature, are employed.

One such method was based upon the idea that acetylation would activate the otherwise tardily reacting hydroxyl groups and consisted of acetylating cellulose, or partly methylated cellulose, prior to alkylation.[2] In this way Heuser and Hiemer[2] obtained for cellulose regenerated from viscose a methoxyl content of 45.42% (theory, 45.57%) while the principle of the method has since been applied with varying success by Haworth and other investigators.[3] Methylation was also greatly facilitated with short chain cellulosic material.[2] More recently, Karrer and Escher[4] have called attention to the observation that the theoretical methoxyl value for trimethyl cellulose can only be obtained with cellulose degraded to a certain extent. They suggest that either steric hindrances or ring formation between individual chains could prevent an occasional hydroxyl group from becoming methylated unless it was made accessible by pretreatments involving hydrolysis or oxidation. If, however, degradation is allowed to proceed further, the number of end groups of the chains will increase, *i. e.*, more and more hydroxyl groups in the 4-position become available for methylation. Calculation shows that a shortening of the chain of a degree of polymerization of 1500 to 150 and 50 would increase the total methoxyl content by 0.11 and 0.43%, respectively. For this reason, the methoxyl content of highly degraded trimethyl cellulose may even exceed the theoretical value.[4]

In order to establish the relationship between methoxyl content and degree of polymerization more definitely, a series of cellulose acetates of decreasing degree of polymerization was prepared and subsequently methylated. Included in this series were two commercial cellulose acetates whose degree of polymerization ranged between the laboratory products of the higher and lower values.

These acetates were prepared from bleached cotton linters[5] as described below. The combined acetic acid content was determined according to the method of Murray, Staud and Gray.[6]

1. **Fibrous secondary acetate** was prepared by the method of Hess and Ljubitsch.[7] After 25 days at room temperature the product had a combined acetic acid content of 48.00%.

Hess and Ljubitsch's method was shown by Staudinger and Eilers[8] to leave the glycosidic linkings of the cellulose chains unattacked and, accordingly, to yield an acetate which, in contrast to secondary acetates of similar combined acetic acid content, is insoluble in acetone as well as in other solvents generally used for viscosity measurements, as, for example, dioxane and *m*-cresol. The acetate prepared in this study showed the same behavior.

2. **Fibrous triacetate** was prepared by the method of Böhringer and Söhne as described by Dorée and Healey[9] with acetic anhydride dissolved in toluene and with perchloric acid and sulfur dioxide as catalysts. After ten hours the combined acetic acid content was 61.5%. The product was soluble in chloroform and insoluble in acetone.

3. **Non-fibrous triacetate** was prepared by the method of Barnett[10] with acetic anhydride and with chlorine and sulfur dioxide combined as a catalyst. The combined acetic acid content was 62.4% (theoretical for triacetate 62.55%).

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(1) Chemist, Waldorf Paper Products Co., St. Paul, Minnesota. A portion of a thesis submitted in partial fulfillment of the requirements of the Institute of Paper Chemistry for the degree of Doctor of Philosophy from Lawrence College, Appleton, Wisconsin, June, 1940; carried out under the direction of E. Heuser.

(2) Heuser and Hiemer, *Cellulosechem.*, **6**, 101, 125 (1925).

(3) Haworth, Hirst and Thomas, *J. Chem. Soc.*, 821 (1931).

(4) Karrer and Escher, *Helv. Chim. Acta*, **19**, 1192 (1936).

(5) Supplied through the courtesy of the Hercules Powder Company.

(6) Murray, Staud and Gray, *Ind. Eng. Chem., Anal. Ed.*, **3**, 269 (1931).

(7) Hess and Ljubitsch, *Ber.*, **61**, 1460 (1928).

(8) Staudinger and Eilers, *ibid.*, **68**, 1611 (1935).

(9) Dorée and Healey, *J. Textile Inst.*, **29**, T27 (1938).

(10) Barnett, *J. Soc. Chem. Ind.*, **40**, 253 (1921).

4 and 5. The two commercial secondary acetates,[11] nos. 4 and 5 had 56.0 and 54.2% combined acetic acid content.

6 and 7. Non-fibrous secondary acetates were prepared according to Barnett's method as described by Haworth and Machemer.[12]

These acetates were not completely soluble in acetone. Difficulties in filtering the still turbid solution of the acetone-soluble portion were overcome by adding "High-flow" filter aid (Johns-Manville Sales Corporation) to the solution and covering the filter paper in a Büchner funnel with 3 mm. of the same material. The clear solution was atomized into ice-cold water and the precipitate thus obtained was washed and air dried.

The combined acetic acid contents of products 6 and 7 were 43.3 and 57.2%.

The seven acetates, including a sample of the original cotton linters, were subjected to a single standard methylation according to the procedure of Haworth, Hirst and Thomas.[8]

The methoxyl content was determined according to the method of Vieböck and Schwappach.[13]

The degree of polymerization of the acetates, with the exception of the fibrous secondary acetate (no. 1) which was insoluble, and of some of the methylated products, was determined by ascertaining their specific viscosity in *m*-cresol and converting the latter into molecular weight according to Staudinger's equation. For acetylated cellulose[14] a K_m value of 8×10^{-4} and for methylated cellulose[15] a K_m value of 12.5×10^{-4} was used.

The degree of polymerization of the cotton linters was determined by measuring the viscosity in cuprammonium solution. The value of the K_m constant used in this case[16] was 5×10^{-4}. The viscosities were determined in an Ostwald type viscosimeter. The degrees of polymerization (D. P.) in this investigation refer to cellulose. They are obtained by converting the values found for the derivatives into cellulose values and dividing the latter by 162.

The results are presented in Table I.

It is seen from the data that the methoxyl content of the methylated product increases as the degree of polymerization decreases.

TABLE I

DEGREE OF POLYMERIZATION AND METHOXYL CONTENT OF CELLULOSE ACETATES AND COTTON LINTERS

No.		Degree of polymerization	Methoxyl content
1	Fibrous secondary acetate, Hess and Ljubitsch	..	18.0
2	Fibrous triacetate, Böhringer and Söhne	666	21.0
3	Non-fibrous triacetate, Barnett	234	32.8
4	Commercial secondary acetate I, non-fibrous	160	44.7
5	Commercial secondary acetate II, non-fibrous	140	44.5
6	Laboratory secondary acetate I, non-fibrous, Haworth and Machemer	141	43.3
7	Laboratory secondary acetate II, non-fibrous, Haworth and Machemer	131	44.65
8	Bleached cotton linters	1500	34.6

The degree of polymerization of the first product may safely be assumed to be only a little lower than that of the original cotton linters. Bletzinger[17] has determined the molecular weight of a cellulose acetate which had been prepared by the same method, by ascertaining its specific viscosity in cuprammonium solution in which, as Staudinger and Daumiller[18] have shown, the acetate is completely saponified. Bletzinger found for an acetate of 25.0% acetyl content a degree of polymerization of 1325, whereas the original cellulosic material (bleached paper rag stock) showed a value of 1432.

In none of the experiments had the methoxyl content of trimethylcellulose (45.57%) been reached. Repeated methylation did not change this result. A sample of methylcellulose (44.65% methoxyl) obtained from acetate no. 6 was remethylated once under the conditions used in the first operation and yielded a product with 44.75% methoxyl. A sample of methylcellulose (43.30% methoxyl) obtained from acetate no. 7 was remethylated three times and yielded products with 44.0% methoxyl after the first, and 44.5% after the second and third remethylation. Likewise, remethylation of methylcellulose (44.7% methoxyl) obtained from acetate no. 4 increased the methoxyl content only to 44.8%.

Barsha and Hibbert[19] have tried to overcome the difficulties encountered in effecting complete methylation by dissolving the partially methylated product in chloroform, reprecipitating into petroleum ether and subsequent remethylation of the precipitate suspended in acetone. However, their best result (obtained with wood pulp) was 44.63% methoxyl, that is, not better than those reported here. In fact, when Barsha and Hibbert's procedure was applied to a sample of methylcellulose which contained 44.75% methoxyl (the remethylated product obtained from acetate no. 6), its methoxyl content remained unchanged.

(11) Supplied through the courtesy of E. I. du Pont de Nemours & Company.

(12) Haworth and Machemer, *J. Chem. Soc.*, 2270 (1932).

(13) Vieböck and Schwappach, *Ber.*, **63**, 2818 (1930).

(14) Staudinger and Eilers, *ibid.*, **68**, 1611 (1935).

(15) Staudinger and Reinecke, *Ann.*, **535**, 147 (1938).

(16) Staudinger and Mohr, *Ber.*, **70**, 2296, 2309 (1937).

(17) Unpublished work at The Institute of Paper Chemistry.

(18) Staudinger and Daumiller, *Ann.*, **529**, 219, 220–223 (1937).

(19) Barsha and Hibbert, THIS JOURNAL, **58**, 1006 (1936).

The methoxyl contents obtained here fall below those which were obtained by Haworth, Hirst and Thomas,[3] or by Haworth and Machemer,[12] whereas they are the same as, or higher than, those which were obtained by other investigators[20] who have applied Haworth and co-workers' procedure.

None of the investigators who have closely approached the theoretical value have ascertained the degree of polymerization of their acetates, but it is probable that it was rather low. Likewise, there seems to be no doubt that the theoretical value which Freudenberg and Boppel[21] obtained by remethylating a premethylated product with sodium metal dissolved in liquid ammonia and methyl iodide was due to a decrease of chain length during the remethylation.[22]

In further attempts to reach the theoretical value, two methylcellulose preparations (44.5 and 43.5% CH_3O) were reacetylated and the resulting acetyl-methylcellulose products (their combined acetic acid contents being 1.7 and 2.3%, respectively) were subjected to remethylation. This procedure resulted in 45.3 and 45.0% methoxyl.

When the degree of polymerization of these two preparations was determined, it was found to have dropped considerably; for Product I, to 30, and for Product II, to 50. Thus, it is clear that the higher methoxyl contents could be obtained only by far-reaching degradation. The question whether this degradation occurred during reacetylation or remethylation must remain undecided, since erratic results were encountered with the products obtained after the various operations. In some cases, the degree of polymerization of the acetates remained practically unchanged on methylation or was slightly lower; in most of the cases, however, an increase in the degree of polymerization was observed to have occurred. A satisfactory explanation cannot be given without further study. In the light of previous experience, it is probable that the far greater part of the degradation occurred during acetylation. This conclusion seems to be confirmed by the data presented in Table II which, however, are given with reservation.

TABLE II

DEGREE OF POLYMERIZATION ON REACETYLATION AND REMETHYLATION

Original methyl cellulose		After reacetylation		After remethylation	
I[a]	II	I	II	I	II
228	258	17	61	30	50

[a] The acetate from which this product was obtained showed a D. P. of 140 (product 5 of Table I).

When comparing the methoxyl content of the first three products of Table I with the methoxyl content of the original (unacetylated) cotton linters (34.6%), some doubt arose as to whether acetylation may still be regarded as a means of activation of the hydroxyl groups of cellulose, for then we would expect the acetylated materials to yield the higher values.

That the methoxyl contents of the products which resulted from the acetates 4, 5, 6, and 7 were considerably higher than those of the others is due, apart from the influence of the lowered degree of polymerization, to the fact that these acetates were methylated while in solution.

This conclusion is further substantiated by the result of an experiment in which the same acetate (no. 6, Table I) was methylated in acetone in one case and without being dissolved in the other.

Whereas, with methylation of the acetate in solution, a methoxyl content of 44.8% was obtained, the acetate which had not been dissolved showed only 27.6% methoxyl.

The influence which the physical form of the acetate thus exerts upon the degree of substitution is also seen from results obtained by methylation of acetates which had been converted into finely divided precipitates, in comparison with the same products which were used in the form of a dry powder or of a dry fibrous material.

Samples of the non-fibrous triacetate (Product 3, Table I) and the fibrous triacetate (Product 2, Table I) were methylated according to standard procedure, the former suspended in acetone and the latter after the water had been displaced by alcohol and the alcohol by acetone. In addition, samples of the same acetates were dissolved in chloroform and precipitated from their solution with petroleum ether. The precipitates were centrifuged, washed with petroleum ether and acetone and worked into a smooth paste in a mortar while acetone was gradually added. The fine, milky suspension thus obtained was subjected to methylation. Whereas the triacetate in the form of a dry powder and the fibrous triacetate showed 32.8 and 21.0%, the precipitates showed 40.8 and 37.0% methoxyl.

The results reported so far seem to show that two factors are instrumental in accomplishing a

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(20) Hess, Abel, Schön and Komarewsky, *Cellulosechem.*, **16**, 69 (1935); Karrer and Escher, *Helv. Chim. Acta*, **19**, 1192 (1936); Wolfrom, Sowden and Lassettre, THIS JOURNAL, **61**, 1072 (1939).

(21) Freudenberg and Boppel, *Ber.*, **70**, 1542 (1937).

(22) Freudenberg, Boppel and Meyer-Delius, *Naturwissenschaften*, **26**, 123 (1938); *C. A.*, **32**, 5655 (1938).

high degree of substitution. The degree of polymerization of the cellulosic material has to be appreciably low and the conditions of methylation have to be such that homogeneity of reaction is assured.

However, when such conditions were obtained by subjecting a solution of the acetate to methylation, the best methoxyl content still remained about 1% short of the theoretical value. This result is surprising, for one would expect both the covered and the uncovered hydroxyl groups of partially acetylated cellulose dissolved in acetone to be equally accessible to the methylating agents.

Because of this unexpected result it appeared desirable to investigate the process of methylation more closely in the hope of being able to discover those factors which seem to disturb the homogeneity of the reaction.

The process of methylation was followed by determining the methoxyl content of samples taken at intervals.

The results obtained with acetate number 4, Table I, with subsequent methylation according to standard procedure are presented in Table III.

TABLE III

RATE OF METHYLATION OF CELLULOSE ACETATE DISSOLVED IN ACETONE

Reaction time, min.	10	30	50	100
Methoxyl, %	1.10	14.60	44.60	44.80

The data show that the rate of methylation is rather slow up to thirty minutes; the main reaction obviously occurs between thirty and fifty minutes, after which it increases only very slowly. This course of the reaction was unusual, since all cellulose reactions show a faster rate in the beginning, and indicated that some particular factor had prevented the reaction from taking the normal course.

The rate of deacetylation could not be determined with certainty in this experiment because, with the method used, the possibility existed that the acetyl groups which at the beginning of the reaction were probably still present in the material in solution, were subject to saponification while the samples were being prepared for analysis.

However, visual observation of the various phases of the process of methylation suggested a way of determining the approximate rate of deacetylation. At the same time this observation supplied a satisfactory explanation for the anomaly of the course of the reaction.

As soon as the sodium hydroxide solution and the dimethyl sulfate were added to the acetone solution of the acetate, small globules were formed. Evidently these globules consisted of concentrated sodium hydroxide solution surrounded by very thin films of methylcellulose. These globules were not broken up by stirring. However, after about thirty to forty minutes had elapsed, the mixture acquired the appearance of an "emulsion," and the globules gradually disappeared. This condition was evidently due to a precipitation of the cellulose derivative in finely divided form.

It could be shown in an orienting experiment that it was possible to separate the globules from the solution by filtration without breaking them up to any great extent. The alkali content of the globules revealed that scarcely any of it had been consumed by the acetate; as a matter of fact, analysis of the filtrate showed that the majority of the acetyl groups were still in combination with the cellulose.

To a solution of a secondary acetate in acetone was added a given volume of aqueous sodium hydroxide of the same concentration as used for methylation. The globules formed were carefully filtered over filter paper and analyzed for their alkali content by titration; 99.2% of the alkali added to the acetone solution was recovered. From the filtrate, the acetate was isolated as described above. Its combined acetic acid content was found to be 55.8 against 56.0% in the original acetate.

The technique of separating the globules from the solution was then utilized in the following experiment, in which the rate of deacetylation and of methylation were determined simultaneously. In addition, the thin films which surrounded the globules were collected and also analyzed for their acetyl and methoxyl content. This material amounted to only about 10% of the weight of the acetate.

Individual portions of a secondary acetate (Product 4, Table I) dissolved in acetone were methylated according to standard procedure for twenty, thirty, and forty minutes. At the end of each period the reaction mixture was carefully filtered on alkali-resistant filter paper, the globules surrounded by the solid material being retained. The latter was freed of alkali by washing with hot water, and air-dried. Whereas the filtrates after twenty and thirty minutes were water-clear, the filtrate after forty minutes was turbid. The globules had started to break up in the reaction mixture before filtering which made it difficult to ensure complete separation of the globules from the solution with this sample. Consequently, the film material from this experiment was somewhat contaminated with methylcellulose which had precipitated in the reaction mixture.

The acetone solution was precipitated into cold water and the precipitate washed with cold water and air-dried. Both solid materials, thus isolated, were analyzed for methoxyl and combined acetic acid.

The results are presented in Table IV and Fig. 1.

TABLE IV

RATE OF DEACETYLATION AND METHYLATION OF CELLULOSE ACETATE DISSOLVED IN ACETONE

Time of reaction, min.	0	20	30	30	40
Methoxyl, %, acetone-soluble portion	..	0.91	1.45	2.20	40.20
Combined acetic acid, %, acetone-soluble portion	56.0	54.8	53.3	51.0	0.0
Methoxyl, %, acetone-insoluble portion	..	20.1	35.5	..	44.2

The combined acetic acid content of the insoluble portion was zero in all cases. Obviously, the more intimate contact between the alkali of the globules and the films surrounding them causes the acetyl groups to be easily saponified. This process is likely to continue during the time the film material is being freed of alkali by washing.

The figures in Table IV and curve A (acetone-soluble portion) in Fig. 1 again show that very little methylation takes place up to a time of thirty minutes. Thereafter, the rate of methylation increases rapidly. Accordingly, the rate of deacetylation is very slow up to thirty minutes (curve B) but increases rapidly between thirty and forty minutes.

The rate of methylation deduced from the analysis of the acetone-insoluble portions (curve C) approaches the normal course of cellulose reactions as would be expected from the more intimate contact between the reactants.

The rates of methylation and deacetylation of the acetone-soluble portion appear to be in direct relation to the physical phenomena observed. At the beginning of the reaction most of the acetate remains in solution but, owing to globulation of the sodium hydroxide, it fails to establish sufficient contact with the alkali. Consequently, very little methylation can take place. For the same reason, the acetyl groups are saponified only to a small extent. However, as soon as the product of reaction has acquired a certain methoxyl content, which is the case after about thirty minutes, it becomes insoluble in acetone and tends to precipitate from the solution. This phenomenon causes the globules to break. As a result, contact between the reactants is established, and both the rate of methylation and that of deacetylation increase rapidly.

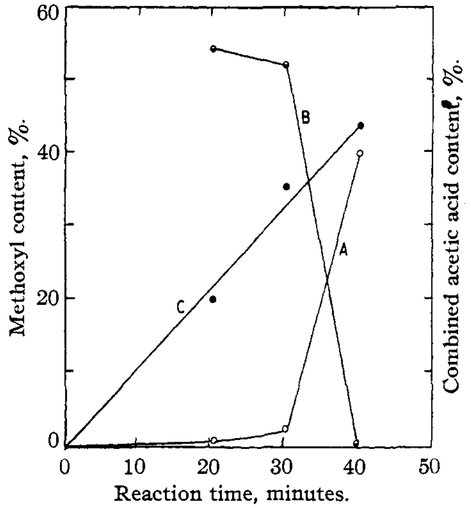

Fig. 1.—Rate of methylation and deacetylation of cellulose acetate in acetone; A, methoxyl in acetone-soluble portion; B, combined acetic acid content in acetone-soluble portion; C, methoxyl in acetone-insoluble portion.

The results of these experiments seem to indicate that the benefit of allowing the reaction to take place on the cellulosic material in a homogeneous system is not actually realized, because the main reaction occurs on the precipitate and, thus, in a heterogeneous system. Although precipitation coincides with a period of more intimate contact between the cellulose (now in the form of a partially methylated acetate) and the alkali, which simultaneously increases the rates of deacetylation and methylation, the reaction gradually slows down before the theoretical methoxyl content is reached.

But even with the drawbacks peculiar to the method here applied, conditions are more favorable than when cellulose in fibrous form is subjected to methylation. Although in the latter case the reactants are in intimate contact from the start, the system remains essentially heterogeneous throughout. Obviously, with the cellulosic material present in the form of a finely subdivided precipitate, the system becomes less heterogeneous, and this difference seems to explain, at least in part, why (with one methylating operation) cellulose acetate dissolved in acetone yields the higher methoxyl content.

It is conceivable that, if both intimate contact from the start and favorable physical form could be combined, the method for methylating cellulose acetate could be much improved. If globulation could be prevented, a greater part of the reaction would take place in the homogeneous system. However, much less concentrated alkali (which forms no globules) cannot be used. Attempts to break up the globules by mechanical means or with the aid of wetting agents were not successful.

It was thought, therefore, that such a combination of favorable conditions as mentioned above could be brought about by allowing cellulose dissolved in a quaternary ammonium base to react with dimethyl sulfate.

The method of Bock[23] was followed although the object of this investigator was to introduce the smallest quantity of methyl which would result in a still water-soluble derivative.

For most of the experiments a commercial wood-pulp cellulose dissolved in 40% trimethylbenzylammonium hydroxide (Triton B[24]; the solution contained about 4% cellulose) was used. The cellulose regenerated from this solution with dilute hydrochloric acid had a degree of polymerization of 164—*i. e.*, a figure which was quite comparable with that of the secondary acetate used in previous experiments (Product 4, Table I). In order to increase the swelling action of the base upon the cellulosic material and possibly the rate of reaction, the temperature was gradually lowered.

To a measured portion of the cellulose solution, which had been made sufficiently alkaline with an excess of trimethylbenzylammonium hydroxide, the necessary quantity of dimethyl sulfate was added gradually over a period of two hours while the solution was stirred continuously. At the end of this period the mixture was allowed to stand overnight. The temperature during the two-hour period and thereafter was varied from 25 to −20 to −30°. At the end of the two-hour period (in certain cases somewhat later), the reaction product precipitated. At the end of the overnight period it was filtered on a Büchner funnel, washed with hot water and acetone and dried in the vacuum desiccator.

For comparison, a secondary acetate (Product 4, Table I) was dissolved in trimethylbenzylammonium hydroxide, methylated at a temperature of −2 to 5° and isolated as methylcellulose in the same way as described above. All products were analyzed for methoxyl content.

The results obtained with wood pulp as the cellulosic material are listed in Table V.

It is seen from these data that lower temperature favors the reaction, although practically nothing seemed to be gained by going outside the range of −2 to 5°.

TABLE V

METHYLATION OF CELLULOSE DISSOLVED IN TRIMETHYLBENZYLAMMONIUM HYDROXIDE AT DIFFERENT TEMPERATURES

Temp., °C.	25	10 to 20	−2 to +5	−20 to −30
Methoxyl, %	39.3	42.9	43.3	43.5

The best methoxyl content obtained by this technique was 43.5%. Incidentally, this figure seems to represent the highest value ever obtained by only one methylation operation and with cellulose which had not been converted into a derivative, although it must be kept in mind that the methylated product originated from a cellulosic material of rather low degree of polymerization (164).

Remethylation of the product having 39.3% methoxyl content (Table V) raised the methoxyl content to 40.6%. On the assumption that the same increase would have been realized by remethylation of the product with 43.5% methoxyl content the results of the two different methods may be regarded as being practically the same.

No better results were obtained with the acetate dissolved in trimethylbenzylammonium hydroxide. The methoxyl content was found to be only 42.7%. This value falls below that which was obtainable with cellulose as such dissolved in the base. The result thus seems to support the view previously expressed—namely, that any activation of hydroxyl groups by acetylation is not reflected in a faster rate of methylation; it seems to be counterbalanced by adverse influences.

The beneficial effect expected from a technique by which the cellulosic material was subjected to methylation while being dissolved and by which intimate contact between the reactants was established from the start did thus not materialize. Obviously, it is the conditions prevailing during the second phase of the reaction which are of essential influence upon the final result. In all cases, the product of reaction precipitates from the solution after a certain methoxyl content has been reached—with cellulose dissolved in quaternary ammonium base this was found to be about 32%—so that the rest of the reaction takes place on a precipitate, that is, under less favorable conditions, an initially homogeneous system having changed into a heterogeneous one.

This change is the result of a gradual transition of the originally lyophilic cellulose into a lyophobic cellulose derivative. This transition ought

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(23) Bock, *Ind. Eng. Chem.*, **29**, 985 (1937).

(24) Supplied through the courtesy of Röhm and Haas Company.

to favor the strengthening of the cohesive forces which are active between the individual chain molecules of the micellar system so that, as with proceeding methylation the lyophobic character of the product of reaction becomes more pronounced, neither strong sodium hydroxide nor even such a powerful swelling agent as the quaternary ammonium base is capable of overcoming these forces and thus of opening the path for further methyl groups to enter. As a matter of fact, it has been known for some time[25] that dimethylcellulose has almost entirely lost its ability to swell in sodium hydroxide solution, and it is only by lowering the temperature considerably that some of the original swelling ability of the cellulose may be restored, but obviously not sufficiently for enabling the reaction to become complete.

This deduction also may be stated in terms of the presence of, still somewhat hypothetical,[26] hydrogen bonds. On the assumption that hydrogen bridges exist in cellulose between the hydrogen atoms of the hydroxyl groups, which are attached to the glucose residues, and are operative in lateral direction between individual chain molecules, the methylation of fibrous cellulose may be interpreted to proceed as follows.

In the presence of strong caustic soda solution cellulose swells to such an extent that the intramicellar spaces are widened. This and the simultaneous formation of alkali cellulose may be assumed to result in the cleavage of hydrogen bridges between inter- and intramicellar hydroxyl groups so that the interaction between the latter and methyl groups can take place. However, with increasing methoxyl content, the product of reaction loses more and more of its ability to swell, and hydrogen bonds between remaining free hydroxyl groups are restored. Due to lack of swelling these bonds are no longer accessible to alkali, and further methylation is inhibited.

In the cases of cellulose acetate dissolved in acetone and of cellulose dissolved in trimethylbenzylammonium hydroxide, we are dealing with individual micelles (or chain bundles) or even with individual chain molecules, both being easily accessible to the methylating agents. As a result, the hydrogen bonds between the hydroxyl groups of cellulose or between the unacetylated groups of cellulose acetate are broken (if they have not already been broken on dissolving in acetone). Provided sufficient contact between the reactants is established, methylation proceeds at a relatively fast rate. However, when a certain methoxyl content has been reached, the lyophobic character of the product of reaction becomes predominant and causes it to be thrown out of solution. This precipitation results in a restoration of hydrogen bonds between the unreacted hydroxyl groups which makes the system resistant to alkali, and thus prevents the methylating agents from gaining access to the remaining hydrogen bridges. The reaction comes to a standstill.

In the light of these interpretations it would appear that the problem could be solved if it were possible to find a solvent or solvent mixture whose polarity would be balanced by that of the product of reaction so that the latter, uninfluenced by the increasing degree of substitution, would remain in solution indefinitely. Such a solvent is not easily found, because it must be resistant to methylation.

Against the interpretation based upon the assumption of hydrogen bonds one might argue that it requires relatively little energy for breaking such bonds and that the forces which counteract the introduction of the last small quantity of methyl into cellulose must be considerably stronger.

The existence of such stronger bonds has been made probable for starch by Brawn, Hirst and Young.[27] These investigators seem to have some evidence of the existence of covalences between the reducing hydroxyl groups (in the 1-position) of one starch chain molecule and a hydroxyl group in the 6-position of an adjacent chain. Such primary valency bonds which were found to be less resistant to hydrolysis than the 1–4 glycosidic linkings between the glucose residues of the individual chains may also be assumed to exist in cellulose.[28] Definite proof of their existence would confirm the view expressed by Karrer and Escher[9] discussed earlier in this paper and thus offer a more satisfactory explanation of the difficulty encountered in the complete etherification of cellulose.

Summary

1. Cellulose acetates of different degrees of polymerization were prepared according to various methods and methylated according to a

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(25) Heuser and Schuster, *Cellulosechem.*, **7**, 29 (1926).

(26) Ellis and Bath, THIS JOURNAL, **62**, 2859 (1940).

(27) Brawn, Hirst and Young, *Trans. Faraday Soc.*, **36**, 880 (1940).

(28) Haworth, *J. Soc. Chem. Ind.*, **58**, 917 (1939).

standard procedure. The methoxyl content obtained in one methylating operation increases with decreasing degree of polymerization. However, the highest methoxyl content still remains by about 1% below the theoretical value for trimethylcellulose.

2. This result is not changed by repeated remethylation. It is only on reacetylation followed by remethylation that the theoretical value is more closely approached. However, the preparations thus obtained are the derivatives of considerably degraded cellulose.

3. Acetylation of cellulose as a step preparatory to methylation is of no beneficial effect unless the acetate is dissolved in acetone.

4. The influence of the physical form in which the acetate is brought into contact with the methylating agents is also shown by the fact that acetates converted into finely divided precipitates yield a considerably higher methoxyl content than the same acetates used in their fibrous form or as a dry powder.

5. The rates of methylation and deacetylation are determined and are found to be initially slow, in spite of the fact that the acetate is in solution, the reason being that the strong sodium hydroxide solution does not mix sufficiently with the acetone solution. When the methoxyl content has reached a certain value, the product of reaction starts to precipitate and establishes contact with the alkali. This contact causes the rates of methylation and deacetylation to increase rapidly. However, after 44 to 45% methoxyl have been introduced the rate of methylation slows down considerably without the theoretical value of 45.57% being reached.

6. Methylation of cellulose and cellulose acetate dissolved in a quaternary ammonium base follows the normal course of cellulose reactions, since contact between the reactants exists from the start. But even in these cases the product of reactions precipitate after a certain methoxyl content has been reached, and the reaction comes practically to a standstill when the reaction product possesses about 43% methoxyl. The highest methoxyl content is obtained only at low temperature.

7. In the light of the gradual transition of the initially lyophilic cellulose into a lyophobic derivative, which is accompanied by a change from a homogeneous into a heterogeneous system, an attempt is made to explain the failure to introduce the theoretical quantity of methoxyl by the activity of cohesive forces which might consist either of hydrogen bonds or of covalences operative between remaining free hydroxyl groups of adjacent chain molecules.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Structure of the Cori Ester

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The naturally occurring hexose phosphates are of great biological interest. One of the most significant of these substances is the hexose monophosphate isolated from frog muscle in the form of its barium (amorphous) and brucine (crystalline) salts by Cori and Cori.[1] This hexose phosphate has been designated the Cori ester. Cori and Cori[2] demonstrated that this ester was the main product when glycogen underwent phosphorolysis with an enzyme (phosphorylase) isolated from rabbit muscle. The reversibility of this enzymic system to produce a polysaccharide was demonstrated by Schäffner and Specht[3] and by others,[4] using glycogen and phosphorylases isolated from yeast, muscle and liver.

In the vegetable world, Hanes[5] has demonstrated the widespread occurrence in leaves, roots, fruits and tubers, of a phosphorylase capable of converting starch to the Cori ester and of resynthesizing the latter to a polysaccharide by reversal of the enzymic reaction.

With other enzymic systems, sometimes termed phosphoglucomutases, the Cori ester, whether

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[1] C. F. Cori and Gerty T. Cori, *Proc. Soc. Exptl. Biol. Med.*, **34**, 702 (1936).

[2] C. F. Cori and Gerty T. Cori, *ibid.*, **36**, 119 (1937).

[3] A. Schäffner and H. Specht, *Naturwissenschaften*, **26**, 494 (1938).

[4] C. F. Cori, G. Schmidt and Gerty T. Cori, *Science*, **89**, 464 (1939); *J. Biol. Chem.*, **129**, 629 (1939); W. Kiessling, *Biochem. Z.*, **302**, 50 (1939); P. Ostern, D. Herbert and E. Holmes, *Biochem. J.*, **33**, 1858 (1939).

[5] C. S. Hanes, (a) *Proc. Roy. Soc.* (London), **B128**, 421 (1940); (b) **B129**, 174 (1940).