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CHLORINATION OF CELLULOSE WITH METHANESULPHONYL CHLORIDE IN *N,N*-DIMETHYLFORMAMIDE AND CHLORAL

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ABSTRACT

Treatment of hardwood dissolving sulphate pulp with *N,N*-dimethylformamide, chloral, and methanesulphonyl chloride at 75° effected rapid and selective chlorination, initially at the primary positions. When most of the primary hydroxyl groups had been replaced, reaction occurred at HO-3 to give 3,6-dichloro-3,6-dideoxy-D-allose residues. 4,6-Dichloro-4,6-dideoxy-D-galactose residues, derived from non-reducing end-groups were detected only in highly chlorinated cellulose. The degradation of cellulose during chlorination was investigated by gel-permeation chromatography.

INTRODUCTION

The direct preparation of chlorodeoxycellulose from cellulose has been effected by using thionyl chloride[1–4], methanesulphonyl chloride[5,6], chlorodimethyliminium chloride[7], and phosphoryl chloride[8]. Except in the earlier work[1,2], *N,N*-dimethylformamide was used as the reaction medium, because it is involved in the formation of reactive intermediates ($Me_2\overset{+}{N}=CHR\ Cl^-$, R = Cl, OMs) and minimises cellulose degradation by binding liberated hydrogen chloride as the dimethyl chloroformiminium salt[3] ($Me_2\overset{+}{N}=CHCl\ Cl^-$).

Chlorination of cellulose in *N,N*-dimethylformamide is a heterogeneous reaction. Cellulose samples may be made more accessible to chlorinating reagents by mercerization[1,3–5], regeneration[6], or pre-swelling[8], in order to prepare chlorodeoxycellulose with a high chlorine content. A high degree of substitution (d.s. 0.83) was obtained by using[6] cellulose regenerated from cupriethylenediamine and mesyl chloride–*N,N*-dimethylformamide. However, the chlorine contents of chlorodeoxycelluloses previously prepared without significant coloration and degradation were generally far less than 19.6% (d.s., 1).

Other solvent systems used for cellulose are pyridine–chloral[9], *N,N*-dimethylformamide–chloral[10], *N,N*-dimethylformamide–dinitrogen tetroxide[10], amines–sulphur dioxide[11], and *N,N*-dimethylformamide–nitrosyl chloride[12]. Recently, Nakao[13] reported that a highly chlorinated cellulose (d.s., 2.8) can be prepared by

treating cellulose with thionyl chloride in *N,N*-dimethylformamide–chloral. We were thereby prompted to study, and now report on, the homogeneous chlorination of cellulose in this solvent system.

RESULTS AND DISCUSSION

Hardwood dissolving sulphate pulp (L-DKP), which dissolves faster than does linter cellulose in *N,N*-dimethylformamide–chloral, was variously treated with mesyl chloride at 75°. As shown in Fig. 1, the chlorine content of the product increased rapidly up to 16% (d.s., 0.8) during 1 h and then slowly up to 24% (d.s., 1.3) during 48 h. The initial rate of chlorination is higher than that reported for heterogeneous chlorination. Products with a chlorine content of ~16% were soluble in water, whereas those with chlorine contents of ~20% were insoluble. Chlorination for longer than 2 h caused slight coloration of the product. The d.s. value finally attained was the same as the highest value (d.s., 1.3) previously reported for a powdery product of heterogeneous chlorination[1].

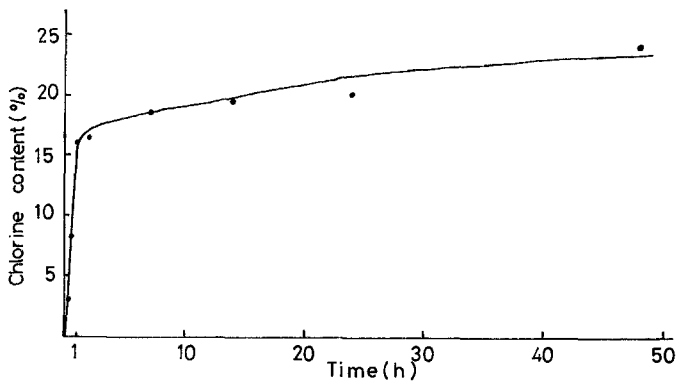


Fig. 1. Change in chlorine content of hardwood dissolving sulphate pulp with time of chlorination at 75° [mesyl chloride (15 ml/g of cellulose), *N,N*-dimethylformamide (100 ml), and chloral (10 g/g of cellulose)].

Chlorodeoxycelluloses were hydrolysed in 72% sulphuric acid after deformylation with aqueous sodium carbonate[6], and the products were analysed as trimethylsilyl derivatives by g.l.c. and g.l.c.–m.s. (Fig. 2). Glucose gave two peaks corresponding to the α and β anomers, whereas 6-chloro-6-deoxyglucose and 3,6-dichloro-3,6-dideoxyallose each gave only one. Two very small peaks of 4,6-dichloro-4,6-dideoxygalactose were detected only in the hydrolysates of highly chlorinated cellulose (Cl, 24.3%), suggesting the cleavage of glycosidic bonds and the exposure of non-reducing end-groups on prolonged chlorination. The formation of two dichlorodideoxy sugar residues has been observed[14] on chlorination of methyl β-D-maltoside with mesyl chloride–*N,N*-dimethylformamide, but has not been found hitherto for

cellulose. The alditol acetate method[15] could not be used for g.l.c. of chlorinated sugars, because treatment with sodium borohydride caused dehalogenation.

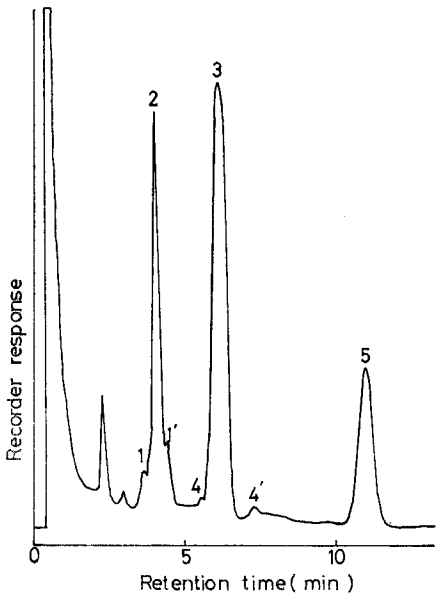


Fig. 2. G.l.c. (SE-30; 220°; helium flow-rate, 32.5 ml/min) of trimethylsilyl derivatives from the hydrolysis of highly chlorinated cellulose (Cl, 24.3%); 1 and 1′, 4,6-dichloro-4,6-dideoxy-α- and -β-D-galactose; 2, 3,6-dichloro-3,6-dideoxy-D-allose; 3, 6-chloro-6-deoxy-D-glucose; 4 and 4′, α- and β-D-glucose; 5, inositol.

The relation between the chlorine content of the chlorodeoxycellulose and the sugar yields therefrom, shown in Fig. 3, indicates that chlorination initially occurs selectively at C-6 to yield 6-chloro-6-deoxyglucose residues and that, after almost all of the primary hydroxyl groups have been replaced, reaction occurs at HO-3 to yield 3,6-dichloro-3,6-dideoxyallose residues. By analogy with the reaction of disaccharides[14], chlorination of the non-reducing end-groups of cellulose should occur at C-3 or at C-4, with the resulting 4,6-dichloro-4,6-dideoxy-D-galactose and 3,6-dichloro-3,6-dideoxy-D-allose residues being resistant to further chlorination, probably for steric reasons.

Cellulose becomes soluble in *N,N*-dimethylformamide after the addition of chloral (>3 mol per hydroxyl group)[10], probably because of hemiacetal formation[9,16]. After 15 min of reaction with mesyl chloride at 75°, precipitation of polymer begins, suggesting that the hemiacetal linkage may be cleaved by the hydrogen chloride produced from the mesyl chloride, and cellulose is regenerated. The following facts also indicate the liberation of free hydroxyl groups. The 3,6-dichloro-3,6-dideoxy-allose and 4,6-dichloro-4,6-dideoxygalactose residues formed in the above reaction are also formed from methyl β-maltoside in the absence of chloral[14]. Chlorination of

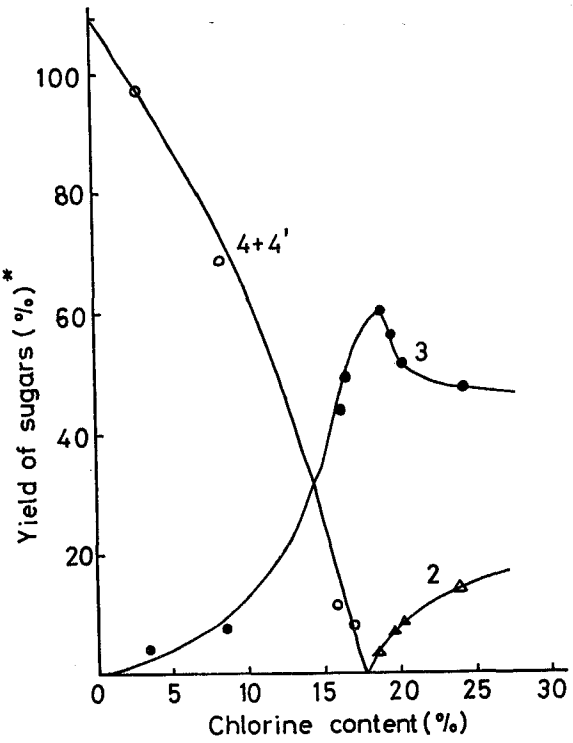


Fig. 3. Relation between chlorine content of chlorodeoxycellulose and yields of constituent sugars; 4+4′, α- and β-D-glucose; 3,6-chloro-6-deoxy-D-glucose; 2, 3,6-dichloro-3,6-dideoxy-D-allose. *Based on weight of chlorodeoxycellulose.

cellulose with mesyl chloride in the presence or absence of chloral produces formic ester groups.

Cellulose regenerated from *N*,*N*-dimethylformamide–chloral in the reaction medium is amorphous and accessible to the reagents, and redissolves after facile chlorination. On the other hand, cellulose suspended in *N*,*N*-dimethylformamide remains insoluble during chlorination.

Formation of stable linkages between cellulose and chloral during chlorination is negligible, otherwise glucose residues would be significantly present in the products with d.s. values >1 (Cl, 19.6% in Fig. 3), and dichloro sugar residues would not be detected in the products of d.s. slightly higher than 1.0.

The solubility of chlorodeoxycellulose in 72% sulphuric acid decreased with increase of chlorine content. Therefore, prior to hydrolysis, chlorodeoxycellulose was soaked in 72% sulphuric acid for 2–36 h depending on its solubility. The soaking time affected the sugar yields. Slightly chlorinated cellulose (Cl, 3%), when soaked in 72% sulphuric acid for 2 h followed by treatment with boiling 8% acid for 2 h, gave glucose and 6-chloro-6-deoxyglucose in an almost quantitative yield (Fig. 3). On the other

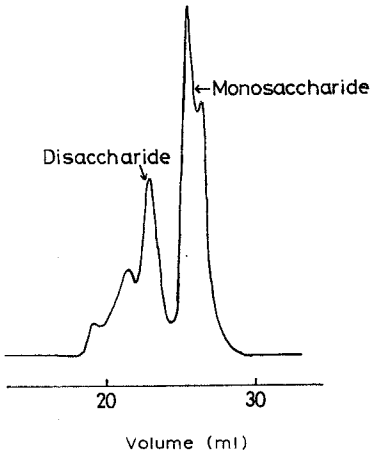


Fig. 4. Gel-permeation chromatogram (μStyragel 100 Å, tetrahydrofuran at 1 ml/min and 23°, detection by refraction index) for the acetylated products of hydrolysis of highly chlorinated cellulose (Cl, 24.3%).

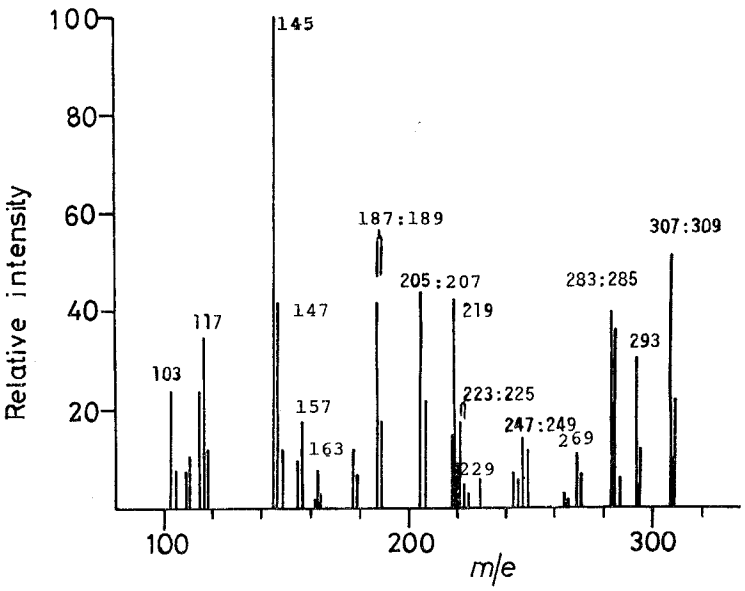
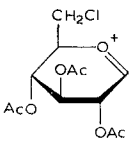


Fig. 5. Mass spectrum of the disaccharide acetate fraction isolated from the hydrolysate of highly chlorinated cellulose (Cl, 24.3%).

hand, when L-DKP was soaked for 36 h before hydrolysis, the yield of glucose was 50%. Under similar conditions of hydrolysis, methyl 6-chloro-6-deoxy-β-D-glucopyranoside gave 90% of 6-chloro-6-deoxy-D-glucose. Clearly, the liberated glucose is further degraded on prolonged treatment with acid. However, the low total yield of sugars from highly chlorinated cellulose, which was subjected to soaking for 36 h before hydrolysis, cannot be explained by the degradation of glucose, because it contains few glucose residues.

The incorporation of chlorine substituents into the sugar moiety of methyl glycosides decreases the rate of hydrolysis[17]. In order to investigate the resistance of highly chlorinated cellulose to hydrolysis, a sample (Cl, 24.3%), after acid treatment, was acetylated and analysed by gel-permeation chromatography. Fig. 4 indicates the presence of disaccharides and higher oligosaccharides, in addition to monosaccharides. Thus, incomplete hydrolysis of chlorine-containing oligosaccharides, together with further degradation of liberated sugars, may explain the reason why the total yields of sugars in Fig. 3 are far less than 100%, except that from slightly chlorinated cellulose.

The acetylated disaccharide fraction was isolated and subjected to m.s. All ions, except those at *m/e* 295, 293, 221, and 219 (Fig. 5), could be explained by the presence of fragments **1–3** due to the cleavage of glycosidic bonds (*cf.* Ref. 14). Thus, the fraction was concluded to be composed of the three kinds of chlorine-containing sugar residues detected in the hydrolysates. The origin of ions at *m/e* 295, 293, 221, and 219 is not clear. No fragments indicating the presence of glucose residues could be detected.



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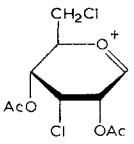

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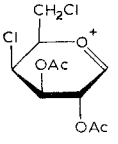

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An attempt to increase the yields of chlorodeoxy sugars from highly chlorinated cellulose (Cl, 24.3%) by the use of more vigorous conditions of hydrolysis was unsuccessful, because the yield of 6-chloro-6-deoxyglucose decreased, in contrast to the yield of 3,6-dichloro-3,6-dideoxyallose which increased.

Previous studies[1–7] on heterogeneous chlorination revealed that reaction is accompanied by some degradation of the cellulose, and therefore chlorination up to d.s. 1.0 could not be attained without significant loss of physical properties. For example, chlorodeoxycellulose prepared from linter cellulose by using thionyl chloride and pyridine was coloured and powdery, although it had a high chlorine content (d.s. 1.3)[1]. The change of molecular weight distribution determined by gel-permeation chromatography after nitration is shown in Fig. 6, and average molecular weights, calculated according to Chang's method[18], are given in the Experimental. Clearly.

the prolonged chlorination associated with sample 3 caused a decrease in molecular weight (*cf.* sample 2).

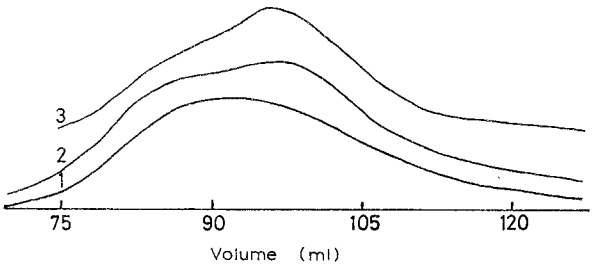

Fig. 6. Gel-permeation chromatogram (as nitrates on Styragel 3×10^5, 3×10^4, 3×10^3 Å, tetrahydrofuran at 1.5 ml/min and 22°, detection by refractive index) of cellulose (1) and chlorodeoxycellulose (Cl: 2, 16%; 3, 20%).

The molecular weight distribution curve (Fig. 6) of sample 2 has two peaks. Sample 2 was not significantly degraded, because the chlorination treatment was brief, and 4,6-dichloro-4,6-dideoxygalactose was not detected in its hydrolysate. Changes of molecular weight and conformation in solution, due to the replacement of hydroxyl groups by chlorine substituents, might account for the elution curve of sample 2.

Thus, chlorination of cellulose in *N*,*N*-dimethylformamide is a convenient procedure, as it avoids tedious pretreatment and leads to higher degrees of substitution and less degradation than the heterogeneous chlorination procedure previously reported.

EXPERIMENTAL

General methods. — Concentrations were carried out under diminished pressure below 45°. For g.l.c., a Model G-80 Yanagimoto instrument fitted with a flame-ionization detector was used, with glass columns (250×0.4 cm) containing 5% of SE-30 on Shimalite W (60–80 mesh) at 220°. For the g.l.c.–m.s., a Hitachi gas chromatograph 063 (equipped with the above column and connected to a Hitachi RMU-6L instrument) was used. Spectra were recorded at 70 eV.

Gel-permeation chromatography was performed with a Waters Gel Permeation Chromatograph Model 201. The molecular weight distribution of cellulose samples was measured on three pairs of Styragel columns (2 ft) in the porosity ranges 3×10^5, 3×10^4, and 3×10^3 Å, with tetrahydrofuran at 1.5 ml/min and 22°. Polystyrene standards supplied by Waters were used for calibration. For analysis of the acetates of the hydrolysates of highly chlorinated cellulose (Cl, 24.3%), four μStyragel columns (30 cm × 7 mm) of porosity 100 Å were used with a solvent flow-rate of 1 ml/min at 23°.

Analysis of chlorine was carried out by the titration method[19]: chloride ion produced by burning samples in an oxygen atmosphere was absorbed in water

containing hydrogen peroxide and titrated with mercuric perchlorate (diphenylcarbazone indicator).

Materials. — Hardwood dissolving sulphate pulp ($\overline{\text{d.p.}}_v$ 750), containing < 4% of xylose, was used as a cellulose sample. A pulp sheet was fluffed by a mixer. Reagent grade methanesulphonyl chloride, chloral, and *N*,*N*-dimethylformamide were stored over molecular sieves and used without further purification.

3,6-Dichloro-3,6-dideoxy-D-allose was prepared by hydrolysing its methyl glycoside[20] with 0.5M sulphuric acid for 8 h at 100°. Sulphate ions were then removed with barium hydroxide, and the syrupy product was eluted from silica gel with 3:1 ethyl acetate–chloroform. The appropriate fractions were collected and concentrated, and the residue was crystallised from aqueous methanol. The product had m.p. 142–144° (dec.), $[\alpha]_D$ −110° (*c* 0.45, water) (Found: C, 33.4; H, 4.58; Cl, 32.8. Calc. for $C_6H_{10}Cl_2O_4$: C, 33.2; H, 4.61; Cl, 32.7%).

6-Chloro-6-deoxy-D-glucose[21] and 4,6-dichloro-4,6-dideoxy-D-galactose[22] were also synthesized by hydrolysis of the corresponding methyl glycosides[20,23].

Fluffed cellulose (L-DKP, 5 g, dried overnight at 105°) was immersed in a mixture of *N*,*N*-dimethylformamide (500 ml) and chloral (50 g) at room temperature with occasional shaking. A clear, viscous solution was obtained in a week.

Chlorination of cellulose. — Methanesulphonyl chloride (5 ml) was added dropwise to a stirred cellulose solution (50 ml), and the mixture was stirred at 75°. At intervals, a sample was poured into ice–water, and the precipitate was processed as described by Horton *et al.*[6]. The yields of chlorinated products were approximately equal to the weights of cellulose used.

Hydrolysis of chlorodeoxycellulose. — Dispersions of chlorodeoxycellulose (20–30 mg) in 72% sulphuric acid (1 ml) were kept at room temperature with occasional stirring until dissolution was complete (2–36 h); each solution was then diluted with water (20 ml), boiled under reflux for 2 h, cooled, neutralized with saturated aqueous barium hydroxide, and centrifuged. The supernatant solution was concentrated to a thick syrup.

The syrup was trimethylsilylated[24], and the products were analysed by g.l.c.–m.s. Each peak in Fig. 2 was identified by comparing the retention time and mass spectrum with those of authentic samples. Quantification was effected by using *myo*-inositol as the internal standard. Reaction at 80° was required to convert *myo*-inositol, which is poorly soluble in pyridine, into its trimethylsilyl derivative[25].

Detection of oligosaccharides in the hydrolysates of highly chlorinated cellulose. — Chlorodeoxycellulose (Cl, 24.3%; 130 mg) was hydrolysed as described above. The resulting syrupy product was treated for 4 h with a boiling mixture (1:1) of pyridine and acetic anhydride, and the product mixture was then isolated in the conventional manner and subjected to gel-permeation chromatography (Fig. 4). The two large peaks were assigned to monosaccharides and disaccharides on the basis of coincidence of their elution volumes with those of glucose penta-acetate and cellobiose octa-acetate.

D.p. of chlorodeoxycellulose. — The molecular weight distribution of cellulose derivatives was measured by gel-permeation chromatography after nitration with

fuming nitric acid and phosphorus pentoxide[26]. The number-average molecular weight ($\overline{M}_n$) and weight-average molecular weight ($\overline{M}_w$), calculated according to the procedure of Chang[18], were as follows:

Sample	*Reaction time (h)*	$\bar{M}_n$	$\bar{M}_w$	$\bar{M}_w/\bar{M}_n$
1	0	15,700	109,000	7.0
2	1	15,800	109,000	6.9
3	24	13,800	85,500	6.2

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