FACILE PREPARATION OF DEOXYIODOCELLULOSE AND ITS CONVERSION INTO 5,6-CELLULOSENE

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ABSTRACT

Treatment of 6-chloro-6-deoxycellulose with sodium iodide in 2,5hexanedione gave 6-deoxy-6-iodocellulose; >80% of the chlorine atoms were replaced. 6-Deoxy-6-iodo-D-glucose was identified by g.l.c.-m.s. in hydrolyzates of deoxyiodocellulose. Acetylated 6-deoxy-6-iodocellulose was converted almost quantitatively into 5,6-cellulosene acetate, which was characterized by hydrolyzing the product and converting the resultant dicarbonyl sugar into an isopropylidene acetal **10**. The changes of molecular-weight distribution during iodination and dehydroiodination were investigated by gel-permeation chromatography.

INTRODUCTION

6-Deoxy-6-iodocellulose is an important and versatile intermediate for synthesis of other cellulose derivatives. Iodination of cellulose is usually effected by heating cellulose 6-p-toluenesulfonate with sodium iodide. However, tosylation is usually conducted heterogeneously, and therefore the reaction is very slow, and tosylation occurs not only at O-6 but also at O-2 and O-31. "5,6-Cellulosene", the product of elimination of hydrogen halide is a potentially useful cellulose derivative. Dimitrov *et al.*² prepared 5,6-cellulosene derivatives by treating cellulose iodo-p-toluenesulfonate and cellulose iodonitrate with potassium hydroxide in methanol. Under these dehydroiodination conditions, however, the number of double bonds in the 5,6-cellulosene derivatives was only 0.4 per glucose residue, and 3,6-anhydro-D-glucose residues were also formed. Recently, the reaction of deoxyhalo sugars with 1,8-diazabicyclo[5,4,0]undec-7-ene(DBU) in N,N-dimethylformamide was reported to give unsaturated derivatives in high yields^{3,4}.

The previous report⁵ showed that treatment of cellulose with methanesulfonyl chloride in N,N-dimethylformamide and chloral gave 6-chloro-6-deoxycellulose having d.s. ~1.0. The present paper describes the preparation of deoxyiodocellulose from chlorodeoxycellulose and its conversion into 5,6cellulosene.

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RESULTS AND DISCUSSION

Conversion of chlorodeoxycellulose into deoxyiodocellulose. — Acetylated 6chloro-6-deoxycellulose (3, d.s. 1.0) and 6-chloro-6-deoxycellulose (2, d.s. 1.0) were treated with sodium iodide in 2,5-hexanedione at 120° for various periods of time. As shown in Table I, the chlorine was almost completely replaced by iodine after 8 h. The heterogeneous reaction of 2 introduced almost the same amount of iodide as the corresponding homogeneous reaction, indicating that the iodination of 2 proceeded in the same manner as that of cellulose p-toluenesulfonate¹. When N,N-dimethylformamide was used as the reaction solvent, the replacement of chlorine by iodine was incomplete (Table I).

Treatment of acetylated deoxyiodocellulose with a catalytic amount of sodium methoxide at 4° caused dehalogenation to give 3,6-anhydro-D-glucose residues. Consequently, acetylated deoxyiodocellulose was hydrolyzed in 72% sulfuric acid without previous O-deacetylation.

The hydrolyzate was analyzed after trimethylsilylation by g.l.c.-m.s. (Fig. 1). 6-Deoxy-6-iodo-D-glucose gave two peaks, corresponding to the α and β anomers. A small peak for 6-chloro-6-deoxy-D-glucose was detected. Two peaks for D-glucose were detected, suggesting that deiodination of deoxyiodoglucose residue occurred during iodination, because the starting 6-chloro-6-deoxycellulose contained <2% of unchanged D-glucose residues, as indicated in Table I. The detector response for deoxyiodo sugars was about one fourth of that of glucose.

The incorporation of halogen and acetyl substituents into the glucosyl residues decreased the rate of hydrolysis and the solubility in 72% sulfuric $acid^{5,6}$. Therefore, prior to hydrolysis by dilute acid, deoxyiodocellulose samples were

TABLE I

EFFECT OF SOLVENT AND REACTION TIME ON CONVERSION OF CHLORODEOXYCELLULOSE INTO DEOXYIODOCELLULOSE

Chlorodeoxy- celluiose samples	Solvent	Reaction ^a time (h)	Cl (%)	I (%)	Acetyl (%)	Relative ratio of constituent sugars in deoxyiodocellulose		
						D-Glc	6-Cl-D- Glc	6-I-D- Glc
Acetylated chlorodeoxy			12.5	_	29.0	0.01	0.99	0
cellulose	2,5-Hexane-	2	2.6	27.1	21.3	0.09	0.12	0.79
	dione	4	2.0	29 .1	21.7	0.09	0.04	0.87
		6	2.0	28.3	21.9	0.21	0.01	0.78
		8	1.6	28.0	19.5	0.20	0.01	0.78
Chlorodeoxy- cellulose			18.0			0.02	0.98	_
	2,5-Hexane- dione	2	5.5	30.3		0.06	0.19	0.75
	N, N-dimethyl-	4	5.9	26.2		0.13	0.35	0.53
	formamide	7	5.9	24.4		0.19	0.32	0.48
		16	5.6	17.8		0.33	0.29	0.38
		40	5.0	9.9		0.48	0.38	0.14

^aIodination was conducted by reacting 5% sodium iodide in 2,5-hexanedione or N,N-dimethylformamide with chlorodeoxycellulose samples of d.s. 1.0, using a bath ratio of 20 g solution/g of chlorodeoxycellulose. After cooling the solution to 20°, the products were poured into ice-water, washed with 0.1M sodium thiosulfate, dialyzed against water, and freeze-dried.



Fig. 1. G.l.c. (SE-30; 220°; N₂ flow-rate 40 mL/min) of trimethylsilyl derivatives from the hydrolyzate of acetylated deoxyiodocellulose (I, 27.1; Cl, 2.6%); 1 and 1', α - and β -D-glucose; 2, 6-chloro-6-deoxy-D-glucose; 3 and 3', 6-deoxy-6-iodo- α - and - β -D-glucose; and 4, myo-inositol.

soaked in 72% sulfuric acid for 24 h. When methyl 6-deoxy-6-iodo- α -D-glucopyranoside was soaked in 72% sulfuric acid for 24 h, diluted to 8% with water, and boiled under reflux for 2 h, the yield of 6-deoxy-6-iodo-D-glucose was 65%. Clearly, the 6-deoxy-6-iodo-D-glucose liberated is further degraded on prolonged treatment with acid. Under similar conditions, "hardwood dissolving sulfate" pulp (L-DKP) and methyl 6-chloro-6-deoxy- β -D-glucopyranoside gave 90% of D-glucose and 95% of 6-chloro-6-deoxy-D-glucose, respectively. Thus, the total yield of sugars from deoxyiodocellulose samples was <100%, usually 55–65%.

Conversion of 6-deoxy-6-iodocellulose into 5,6-cellulosene. — Preliminary experiments with methyl 2,3,4-tri-O-acetyl-6-deoxy-6-iodo- α -D-glucopyranoside as a model compound for the reaction with DBU in N,N-dimethylformamide indicated that the reaction time of 2 h at 50° was sufficient to eliminate iodine. Similar treatment of acetylated 6-deoxy-6-iodocellulose (4, d.s. 0.8) gave acetylated 5,6-cellulosene (7). The product contained a small amount of halogen (I, 2.2%); Cl, 3.0%). The O-deacetylated product was subjected to mild acid hydrolysis, and the product in the hydrolyzate was converted into an isopropylidene derivative that was analyzed by g.l.c.-m.s. Only one peak, for 6-deoxy-1,2-O-isopropylidene- α -Dxylo-hexofuranos-5-ulose (10) was detected, indicating that dehydrohalogenation had occurred between C-5 and C-6 to give the D-xylo-hex-5-enopyranose residue. An acid hydrolyzate of 5,6-cellulosene (8) was analyzed by l.c. 6-Deoxy-D-xylohexos-5-ulose (9) was predominant and 3,6-anhydro-D-glucose was not detected. Dehydrohalogenation of deoxyiodocellulose with DBU occurred almost quantitatively, as with disaccharide derivatives⁴. The number of double bonds calculated in the 5,6-cellulosene (8) from the yield of 6-deoxy-D-xylo-hexos-5-ulose (9) was 0.7 per glucose residues, which was higher than the previously reported value for dehydrohalogenation of cellulose iodo-p-toluenesulfonate and iodonitrate with potassium hydroxide in methanol².

The ¹³C-n.m.r. spectrum of the hydrolyzate from **8** showed mixtures of tautomers of 6-deoxy-D-xylo-hexos-5-ulose (**9**), namely 6-deoxy- α - and β -D-xylo-hexofuranos-5-ulose and a pyranose structure, (1R,5R)-6-deoxy-D-xylo-hexopyranos-5-ulose, as previously reported by Kiely *et al.*⁷ for the hydrolyzate of 6-deoxy-1,2-O-isopropyliden- α -D-xylo-hexo-furanos-5-ulose. Demonstration of the tautomeric structures of compound **9** by g.l.c.-m.s. was unsuccessful. (1R,5R)-6-Deoxy-D-xylo-hexopyranos-5-ulose was not detected among the trimethylsilyl derivatives of the hydrolyzate from **8**, probably because of the instability of this hemiacetal.

The ¹³C-n.m.r. spectrum of the product afforded additional evidence that the product was acetylated 5,6-cellulosene 7 (Fig. 2). The signals were assigned by comparison with those of 1,2,3,4-tetra-O-acetyl-6-deoxy- β -D-xylo-hex-5-eno-pyranose⁸ and methyl 2,3,4-tri-O-acetyl-6-deoxy- α -D-xylo-hex-5-enopyranoside. The peak at 151 p.p.m. is that of C-5, and the peak at 99 p.p.m. is due to C-1 and C-6.

The molecular-weight distribution during the modifications were monitored



Fig. 2. 13 C-N.m.r. spectrum of acetylated 5,6-cellulosene in (CD₃)₂SO at 50° (45° pulse, repetition time 3 s, 10,000 accumulations, concentration 20%).

by gel permeation chromatography and results are shown in Fig. 3. The molecularweight distribution curves of acetylated 6-deoxy-6-iodocellulose were similar to that of the chlorodeoxy derivative. The prolonged iodination did not cause a decrease in molecular weight [compare sample 2 (2 h reaction) and sample 3 (6 h reaction)]. The molecular-weight distribution curve of acetylated 5,6-cellulosene (7) was similar to that of the acetylated deoxyiodocellulose (4).



Fig. 3. Gel-permeation chromatogram (as acetates on two GMX columns, tetrahydrofuran at 1.0 mL/min and 42° , detection by refractive index) of chlorodeoxycellulose (3, 1), deoxyiodocellulose (4) [(2); reaction time of 2 h, (3); reaction time of 6 h], and 5,6-cellulosene (7, 4).

Thus, iodination of chlorodeoxycellulose acetate with sodium iodide in 2,5hexanedione is convenient as it leads to a higher degree of substitution by iodine and more-selective replacement by iodine than the procedure previously reported². Conversion of deoxyiodocellulose into 5,6-cellulosene may be effected almost quantitatively by treating deoxyiodocellulose with DBU.

EXPERIMENTAL

General methods. — Concentrations were performed under diminished pressure below 45°. Optical rotations were measured with an automatic polarimeter (JASCO model DIP-140). For g.l.c., a Model 163 Hitachi gas chromatograph fitted with a flame-ionization detector was used, with glass columns (300×0.4 cm) containing; A, 3% of SE-30 on Chromosorb W AW DMCS (80–100 mesh) at 220°; and B, Unisole F-200 (30–60 mesh) at 150°. G.l.c.-m.s. was performed with a Jeol JMS D-100 (20 eV) instrument. Gel-permeation chromatography was effected with a Toyo Soda Gel-Permeation Chromatograph Model HLC-802 UR. The molecularweight distribution was determined on two GMX columns with tetrahydrofuran at 1.0 mL/min and 42°. Polystyrene standards supplied by Waters and Toyo Soda were used for calibration. High-performance liquid chromatography (l.c.) was performed with a JASCO Tri Rotar liquid chromatograph and Shodex Sugar colums SP1010P and SP1010, with water at 0.6 mL/min at 80°.

Chlorine and iodine were determined titration. The determination of chloride ion was described in the previous paper⁵; iodide ion produced upon burning samples in oxygen was absorbed in water and subjected to iodometric titration⁹.

For n.m.r. spectroscopy, a Jeol FX-100 spectrometer (5-mm tubes) was used. The ¹³C-n.m.r. spectra (25.1 MHz) were obtained for solutions in $(CD_3)_2SO$ (cellulose derivatives) and D_2O (hydrolyzate of cellulosene), with internal Me₄Si and methanol, respectively.

Materials. — 6-Chloro-6-deoxycellulose (2, d.s. 1.0) was prepared by treating the cellulose (L-DKP) in *N*,*N*-dimethylformamide and chloral with methanesulfonyl chloride for 3 h at 70° (ref. 5). 6-Deoxy-6-iodo-D-glucose was prepared by hydrolyzing its methyl glycoside¹⁰ with 0.5M sulfuric acid for 8 h at 100°. Sulfate ions were removed with barium hydroxide, and the syrupy product was purified by column chromatography on silica gel with 45:5:3 ethyl acetate–ethanol–water as a solvent. The appropriate fractions were collected, evaporated, and the residue was crystallized from aqueous methanol. The product had m.p. 114.3–115.6, $[\alpha]_D$ +70.5° (c 0.99, water).

Anal. Calc. for C₆H₁₁IO₅: C, 24.8; H, 3.79; I, 43.8. Found: C, 25.04; H, 3.80; I, 43.9.

6-Deoxy-1,2-O-isopropylidene- α -D-xylo-hexofuranos-5-ulose (10) and 6-deoxy-D-xylo-hexos-5-ulose¹¹ (9) were also prepared by literature procedures.

Acetyl groups were determined by g.l.c. (column B) from the acetic acid liberated. The cellulose samples, dissolved in 4:1 dichloromethane-methanol, were

O-deacetylated with sodium methoxide, and the mixtures were treated with Amberlite IR-120 (H^+) ion-exchange resin to remove sodium ions. The amount of acetic acid was determined by g.l.c., using propanoic acid as the internal standard.

Iodination of chlorodeoxycellulose. — Samples of chlorodeoxycellulose (1 g) and sodium iodide (1 g) were dissolved in 20 mL of 2,5-hexanedione or N,N-dimethylformamide, and heated at 120° for the periods of time indicated in Table I. The product was poured into ice-water, and the precipitate was washed with 0.1M sodium thiosulfate solution, dialyzed against water for 16 h, filtered, and freeze-dried (yield 95%).

Hydrolysis of deoxyiodocellulose — Dispersions of deoxyiodocellulose samples (20–30 mg) in 72% sulfuric acid (1 mL) were kept at room temperature with occasional stirring for 24 h. Each solution was diluted with water (20 mL), boiled under reflux for 2 h, cooled, made neutral with saturated aqueous barium hydroxide, and centrifuged. The supernatant solution was concentrated to a thick syrup.

The syrup was trimethylsilylated, and the products were analyzed by g.l.c.m.s. using column A. Each peak in Fig. 1 was identified by comparing the retention time and the mass spectrum with those of authentic samples. Quantification was effected by using *myo*-inositol as the internal standard⁵.

Acetylated 5,6-cellulosene. — A solution of 6-deoxy-6-iodocellulose acetate (4, 0.5 g) in N,N-dimethylformamide (5 mL), containing DBU (0.5 mL) was stirred for 2 h at 50°. The product was poured into ice-water, and the precipitate was collected. The product was dialyzed against water for 16 h, filtered off, and freeze-dried (0.275 g, 90%).

5,6-Cellulosene (8). — Acetylated 5,6-cellulosene (7) was O-deacetylated with a catalytic amount of sodium methoxide for 4 h. The product was poured into ice-water and the precipitate was dialyzed against water for 16 h, filtered, and freeze-dried (yield 60%).

Hydrolysis of 5,6-cellulosene. — 5,6-Cellulosene (8) was hydrolyzed in 0.05M sulfuric acid for 2 h at 50°. The hydrolyzate was made neutral with saturated aqueous barium hydroxide, and centrifuged. The supernatant solution was concentrated to a thick syrup. The syrup was converted into the isopropylidene derivative as described by Kiely *et al.*⁷. A peak corresponding to compound **10** was identified by comparing the retention time and the mass spectrum with those of authentic sample.

Degree of polymerization of deoxyhalocellulose and 5,6-cellulosene acetates. — The molecular-weight distribution of cellulose samples was measured by gelpermeation chromatography.

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