6-Deoxy-6-hydrogenocelluose: Synthesis and Characterization of Cellulose with Reduced Functionality

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Abstract

Cellulose *p*-toluenesulfonic acid esters (TsCell) as well as TsCell peracetate were treated with sodium borohydride in aprotic-dipolar solvents aiming at the synthesis of 6-deoxy-cellulose derivatives. The nucleophilic displacement reaction is incomplete at a reaction temperature of 50 °C, while a sample free of sulfur was obtained at 100 °C provided that the primary hydroxyl groups were tosylated only. The solubility of the TsCell turned from aprotic-dipolar solvents to water after the reaction. The reaction is selective towards the primary position, while secondary Ts groups remained unaffected. The solubility of the samples is governed by the remaining substituents, namely Ts and acetyl moieties. The formation of the 6-deoxy moiety was evidenced by the presence of a signal at18 ppm in the ^{13}C-NMR spectrum, which is characteristic for the 6-deoxy moiety.

Keywords: *6-deoxy-cellulose, hydrogen bonds, NMR spectroscopy, nucleophilic displacement, reduction*

Introduction

Conversion of cellulose into various derivatives is conducted due to different reasons. A commercially very import process is the fiber spinning via cellulose xanthogenate, where cellulose is transformed to a relatively unstable derivative and regenerated after a shaping process [1]. A variety of cellulose derivatives is produced in different quantities for a huge number of applications [2-4]. All in all, the hydrogen bond system, which renders the cellulose insoluble in the typical organic solvents and in water is broken up to a certain extent and the polymers become soluble. In this regard, the influence of the type of substituent, its degree of substitution, and -very importantly- its distribution within the repeating unit and along the polymer chain on the macromolecular properties has been discovered [5-7].

The repeating unit of cellulose contains three hydroxyl groups of different reactivity. Thus, conversions typically lead to products with random functionalization pattern provided that the steric demand of the reagent applied is low. Using reagents with high steric demand affords products with exclusive functionalization of easily accessible hydroxyl groups within the repeating unit. Selective blocking of hydroxyl groups can be used to influence the hydrogen bond system [8]. Thus, the proton of the hydroxyl group has to be replaced by another moiety. In this regard, so-called deoxy-celluloses are an interesting class of substances because the hydroxyl group has been substituted completely. Except deoxy-celluloses bearing heteroatoms at position 6 of the repeating unit, conversions of the primary hydroxyls to methyl groups are scarcely described in the literature [9].

6-Deoxy-6-chloro celluloses can be obtained by reacting cellulose with sulphuryl chloride in *N,N*-dimethyl formamide (DMF) [10]. Highly selective bromination of cellulose using lithium bromide and *N*-bromosuccinimide has been described [11]. The halogen renders the adjacent carbon atom susceptible for nucleophilic displacement reactions. Cellulose derivatives bearing the deoxy group at position 3 have been prepared by reduction of 3-deoxy-6-*O*-trityl cellulose with tributyl tin [12]. It could be demonstrated that the enzymatic degradation of 6-deoxy-cellulose by cellulases from *Trichoderma viride* and *Aspergillus niger* is slower compared with cellulose but still faster than the degradation of 6-halogeno-6-deoxy-celluloses [13]. The preparation of 6-deoxy-celluloses comprises the introduction of a leaving group, e. g. 6-deoxy-6-halogeno or *p*-toluenesulfonic acid (Ts) ester, followed by conversion with a hydride donor, e. g., sodium borohydride [14-16]. Pyrolysis reactions of cellulose derivatives afforded products having complex structures, e. g., unsaturated functionalities in addition to deoxy moieties [17]. Cyanoethyl cellulose had been converted to deoxy-celluloses by reduction with sodium in liquid ammonia [18-20]. The treatment of 6-deoxy-6-azido cellulose bearing residual Ts groups bound to the secondary hydroxyl groups of the cellulose with lithium aluminum hydride was found to remove those Ts groups in addition to the intended reduction of the azide moieties without mentioning the presence of deoxy structures [21].

Because most of the studies on deoxy-cellulose derivatives had been published many decades ago, the structure characterization of the products is limited to the methods available to date. Therefore, we attempted to revisit the synthesis of 6-deoxy-cellulose and their characterization with modern techniques like NMR spectroscopy.

Experimental

Materials

Microcrystalline cellulose (Avicel®, Sigma Aldrich) was dried in vacuum at 105 °C over potassium hydroxide. Lithium chloride (Sigma Aldrich) was dried in vacuum at 150 °C over potassium hydroxide. *p*-Toluenesulfonic acid chloride (Sigma Aldrich), sodium borohydride, DMF (over molecular sieves, Sigma Aldrich) and *N,N*-dimethylacetamide (DMA, over molecular sieves, Sigma Aldrich) were used as received. Triethylamine (Sigma Aldrich) was distilled from calcium hydride prior to use.

Measurements

FTIR spectra were recorded on a Nicolet Avatar 370 DTGS spectrometer using the KBr technique. The ^{1}H- and ^{13}C-NMR spectra were acquired with Bruker Avance 400 (400 MHz) spectrometer in dimethyl sulfoxide (DMSO)-d_6 or in D_2O at 60 °C with a concentration of at least 5% (w/w) of polymer in solution using the solvent peak as internal reference. Elemental analysis (C, H, S content) was carried out using a Vario EL III (Elementaranalysensysteme Hanau, Germany). The chlorine content was determined according to Schöniger's method [22].

Methods

Synthesis of cellulose p-toluenesulfonic acid esters (TsCell)

Cellulose *p*-toluenesulfonic acid esters (samples **1a**, degree of substitution of Ts groups, DS_{Ts} 0.94, degree of substitution of 6-deoxy-6-chloro groups, DS_{Cl} 0.11 and **1b**, DS_{Ts} 2.11, DSCl 0.18) were prepared by conversion of cellulose dissolved in DMA/LiCl Ts chloride in the presence of triethylamine according to a previously published method [23]. Sample **1c**, DS_{Ts} 0.98 (DS_{Cl} not determined) is a peracetylated Ts cellulose [24].

Reaction of TsCell 1a with NaBH4, typical example

TsCell (5.0 g, 0.016 mol, sample **1a)** was added to 50 mL dry DMF under stirring until complete dissolution of the polymer occurred. Sodium borohydride (2,14 g, 0.057 mol, 3.5 mol/mol modified AGU) was added and the mixture was stirred for 24 h at 50 °C. Gelation occurred and the mixture was diluted with 25 mL DMF. Diluted HCl (15%) was added to the cooled mixture in order to destroy excess sodium borohydride followed by pouring the mixture into 1 L ethanol/water (90:10, v/v). The precipitated polymer was collected by filtration, washed 5 times with 200 mL ethanol/water (90:10, v/v) each, once with 200 mL ethanol, and dried in vacuum at 60 °C.

Yield: 2.7 g

Elemental analysis: 47.96% C, 5.84% H, 0.17% N, 0.31% S.

The polymer dissolved in DMA, DMSO, DMF, and *N*-methylpyrrolidone (NMP) but not in water.

^{13}C-NMR spectroscopy (DMSO-*d6*, ppm): 145.48, 130.54, 128.07 ($C_{aromatics,\,Ts}$), 103.4 (C1), 98.40 (C1'), 84.50, 79.90, 75.03, 74.37, 73.98, 70.61 (C2,3,4,5), 60.96 (C6, OH), 21.60 ($CH_{3,\,Ts}$), 18.07 ($C6_{Deoxy}$).

FTIR spectroscopy (KBr, cm^{-1}): 3524 ν OH (weak), 3010-3000 ν =CH, 2960, 2904 ν CH, CH_3, 1600 ring vibration, 1376 δ CH_3, ν_{as} SO_2, 1252 δ CH (branched alkane), 1119, 1098, 1054 ν C-O-C(AGU), 842 δ =CH (strong).

Results and Discussion

The conversion of TsCell (sample **1a-1c**) was carried out with sodium borohydride in dry DMF or DMSO at elevated temperatures (Figure 1, Table 1). Gelation of the system was observed during the reaction that indicated a change of solubility of the polymer. Quenching with diluted HCl and precipitation in ethanol/water (90:10, v/v) afforded the corresponding 6-deoxy-celluloses. The products were characterized by elemental analysis as well as by FTIR- and NMR spectroscopy.

The FTIR spectrum of sample **2a** (not shown) showed the typical signals of the cellulose backbone and the

Table 1: *Conditions for and results of the reaction of cellulose p-toluenesulfonic acid esters (TsCell) with sodium borohydride for 24 h.*

Conditions				Results										
TsCell[a]	Amount (g)	Solvent[b]	Temperature (°C)	Product	Yield (g)	Elemental analysis (%)				Solubility[b]				
						C	H	N	S	H_2O	DMA	DMF	DMSO	NMP
1a	5.0	DMF	50	**2a**	2.7	47.96	5.84	0.17	4.31	-	+	+	+	+
1a	5.0	DMF	100	**2b**	1.37	44.79	6.39	0.76	0	+	-	-	-	-
1b	1.8	DMSO	100	**2c**	0.95	44.97	4.79	0	11.08	-	+	+	+	+
1c	1.50	DMF	100	**2d**	1.03	44.48	6.37	0.86	0.64	-	+	+	+	+

[a] **1a**: Degree of substitution of Ts groups, DS_{Ts}, 0.94, degree of substitution of 6-deoxy-6-chloro groups, DS_{Cl}, 0.11; **1b** DS_{Ts} 2.11, DS_{Cl} 0.18; **1c** DS_{Ts} 0.98, DS_{Cl} not determined.

[b] *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), *N,N*-dimethylacetamide (DMA), *N*-methylpyrrolidone (NMP), soluble (+), insoluble

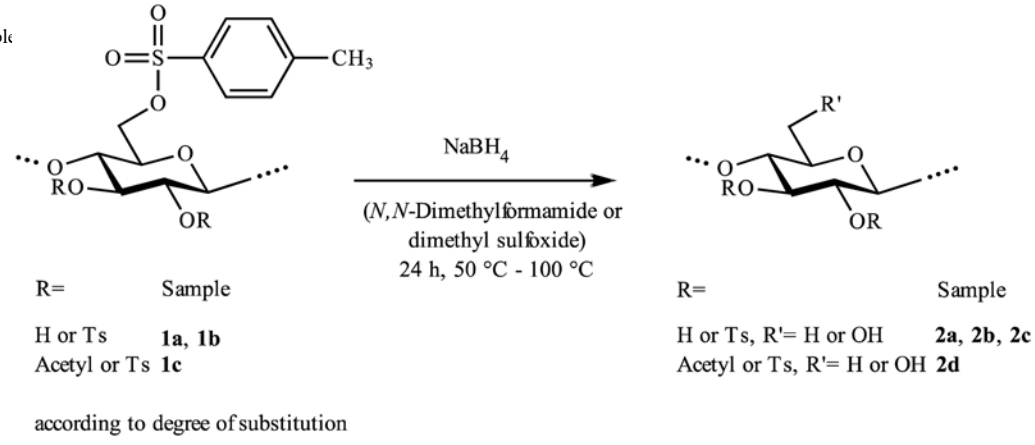

Figure 1: *Reaction scheme for the conversion of cellulose p-toluenesulfonic acid (Ts) ester with sodium borohydride.*

remaining Ts groups. Hydroxyl groups lead to a signal at 3524 cm^{-1}. Weak signals appearing in the range between 3000 cm^{-1} and 3100 cm^{-1} as well (=CH), a signal at 1600 cm^{-1} (ring vibration), 1497 cm^{-1} (ν_{as} SO_2), 1192 cm^{-1} (ν_s SO_2), 1376 cm^{-1} (δ CH_3), and 842 cm^{-1} (δ CH_3) were attributed to the Ts group. Moreover, a set of absorptions between 1054 cm^{-1} and 1120 cm^{-1} was assigned to the glycosidic bonds (ν C-O-C) of the polymer backbone. However, the FTIR spectroscopy did not give clear evidence for the presence of the intended 6-deoxy structure.

The elemental analysis indicated that the sulphur content of sample **2a** with 4.31% was below the sulphur content of Ts cellulose **1a** (9.73%). If the reduction took place at 100 °C, the sulphur practically disappeared

(sample **2b**). In case of higher DS_{Ts} of the starting material, some sulfur remained after the reaction with sodium borohydride (sample **2c**, 11.08% S after the reaction). This led to the conclusion that Ts groups bound to position 6 of the repeating unit had been replaced by hydrogen or by a hydroxyl group. As known, Ts groups attached to positions 2 and 3 are more stable and remain in the molecule (sample **2c**). This finding could also be observed by ^{13}C-NMR spectroscopy (Figure 2). The signal occurring in the spectra of all samples in the range around 18 ppm can be assigned to the 6-deoxy function (-CH_3) and agrees with the literature data on 6-deoxy-glucose [25]. The poor resolution of the DEPT135 NMR spectra of both samples did not allow reliable signal assignment. Nevertheless, all other structural features of the cellulose derivatives could be detected. In case of samples with low initial DS_{Ts} and high reaction temperature (samples **2b** and **2d**), the typical signals of the Ts moiety almost completely disappeared, which is in accordance with results of the elemental analysis. In case of samples synthesized at lower temperature (sample **2a**) and higher initial DS_{Ts}, signals at 21.5 ppm (methyl group of Ts, C8) and 128 ppm – 145 ppm (aromatic carbon atoms, C9,10,11,12) were detected. It must be pointed out that the intended nucleophilic displacement reaction of Ts by hydride ions apparently did not proceed completely. A signal in the range between 60 ppm and 61 ppm was clearly assigned as CH_2OH moiety, i. e. position 6 of the repeating group. Thus, hydrolytic cleavage of the Ts groups caused by traces of water or during workup instead of formation of deoxy moieties must also be considered. Moreover, a signal appearing at 45 ppm was detected in the ^{13}C-NMR spectrum of sample **2a** only. This chemical shift is characteristic for CH_2Cl, which is the result of a side-reaction occurring during the tosylation of cellulose. Obviously, the chlorine is acting as leaving group as well and is replaced by hydride or a hydroxyl group is formed during the reaction at 100 °C.

Only sample **2b** was found to be water-soluble and insoluble in organic solvents. All other samples retained their solubility in aprotic-dipolar media. It can be hypothesized that the influence of intermolecular hydrogen bond from/to OH group at

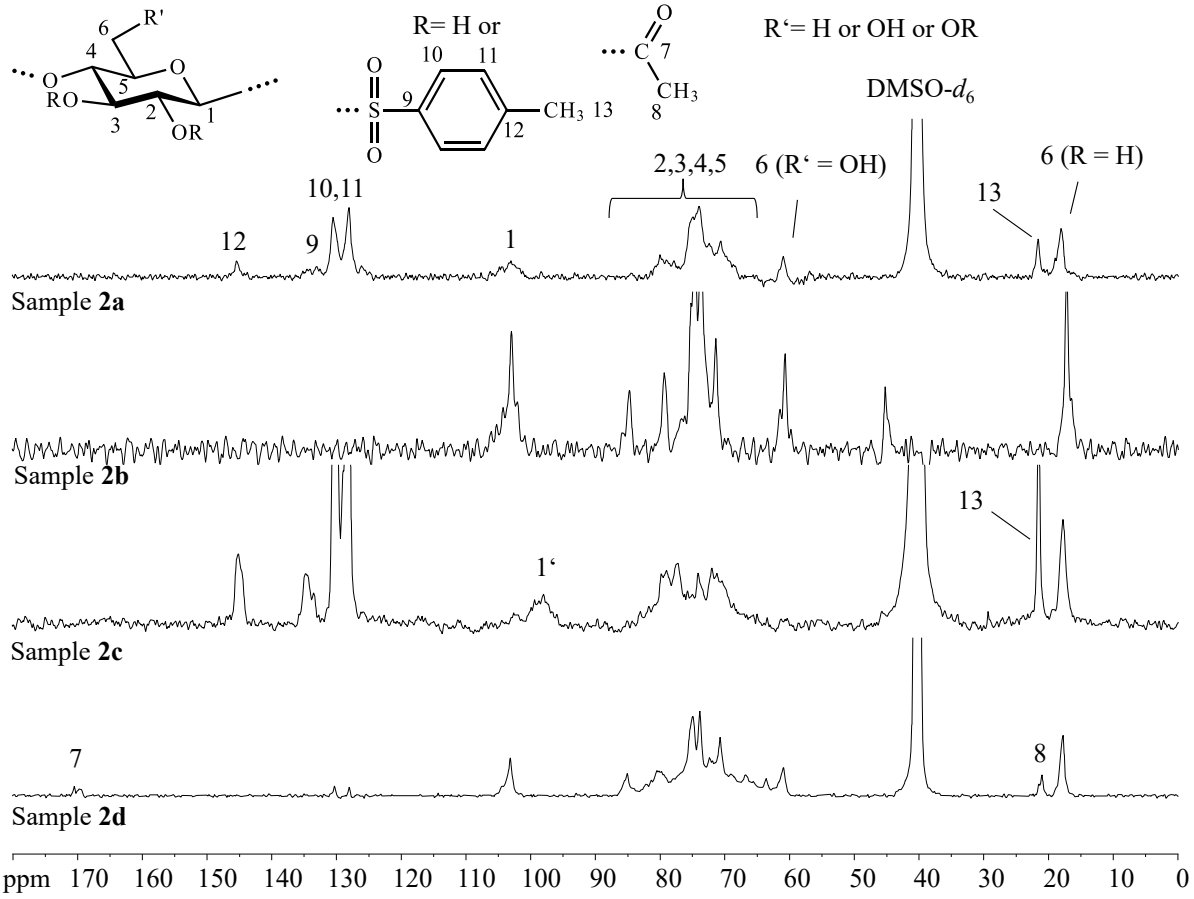

Figure 2: *^{13}C-NMR spectra of deoxy-cellulose derivatives obtained by reaction of cellulose-p-toluenesulfonic acid esters with sodium borohydride.*

position 6 is attenuated leading to solubilization of the polymer. On the contrary, the solubility of samples **2b-2c** in aprotic-dipolar solvents is governed by the nonpolar Ts groups and additional acetyl moieties in case of sample **2d**.

Conclusions

It could be demonstrated that 6-deoxy-celluloses can be prepared by treatment of Ts cellulose with hydride ions. The reaction occurs selectively at position 6 of the repeating unit. Thus, substituents bound to the secondary positions remained unaffected. The 6-deoxy group renders the polymer water soluble, which is a further proof of the importance of intermolecular hydrogen bonds for the dissolution behavior of cellulose. The cellulose derivatives with "reduced functionality" could be helpful in investigation of hydrogen bond-based phenomena.

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