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Pure Cellulose Nanoparticles from Trimethylsilyl Cellulose

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Summary: Silyl ethers of cellulose are promising derivatives of the biopolymer because they exhibit thermoplastic behavior at higher functionalization, may be applied as intermediate in subsequent reactions and have a high tendency to form defined supramolecular structures. Trimethylsilylation can be carried out by applying ionic liquids (ILs) such as 1-ethyl-3-methylimidazolium acetate (EMIMAc) as reaction medium. Pure trimethylsilyl cellulose (TMSC) can be efficiently synthesized with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) yielding products with degrees of substitution (DS) up to 2.89. During the synthesis of highly functionalized derivatives, precipitation of the TMSC occurred, which simplifies the recycling of the IL. The tendency of TMSC toward the formation of supermolecular structures was exploited for the formation of pure cellulose nanospheres by a simple dialysis process. FTIR spectroscopy confirmed the complete removal of the TMS functions during this process. Scanning electron microscopy, dynamic light scattering, atomic force microscopy, and particle size distribution analysis showed that cellulose particles with a size of 100 to 200 nm are accessible in this simple manner.

Keywords: hexamethyldisilazane; ionic liquids; nanoparticles; nanoprecipitation; trimethylsilyl cellulose

Introduction

Silylation of cellulose represents an attractive route for the preparation of soluble derivatives of the biomacromolecule and hence can significantly broaden the spectrum of applications. They are suitable for the homogenous chemical modification, for example, in controlled esterification reactions [1–3] leading to pure products after complete removal of the silyloxy moieties. Furthermore, the tendency of silylated celluloses towards the formation of supramolecular structures may open up new routes to design novel nano-scaled structures. Trimethylsilyl cellulose (TMSC) was applied for spinning cellulose fibers [4] by shaping and regeneration and for the preparation of ultrathin films of TMSC via LB techniques that could be even regenerated cellulose LB films.[5,6]

Silylation of cellulose is possible with trimethylsilyl chloride [7–9], N,O-bis(trimethyl-silyl)acetamide [10,11], and 1,1,1,3,3,3-hexamethyldisilazane (HMDS).[12–14] The heterogeneous conversion of cellulose, for example, in pyridine [7], gives TMSC with a degree of substitution (DS) up to 2.75. Attempts towards homogeneous silylation of cellulose in dimethyl sulfoxide/paraformaldehyde [15] and N,N-dimethyl acetamide (DMA)/LiCl [13,14] was achieved leading to almost fully functionalized derivatives. Although the silylation reactions confirmed the efficiency of homogeneous processes for the synthesis of well-soluble derivatives with adjusted DS values, they are not applicable in large scale because regeneration of the reaction media is difficult and time-consuming. Treatment with liquid ammonia was utilized for the

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activation of cellulose prior to the reaction.[12,16] Nevertheless, the cellulose is suspended and the reaction starts heterogeneously. Here it is difficult to control the product structure.[17]

Recently, it was found that ionic liquids (ILs) possess an enormous potential for chemical modification of polysaccharides. They dissolve cellulose easily without derivatization and degradation.[18,19] It was shown that ILs are appropriate reaction media for the homogeneous derivatization of cellulose.[20,21]

In this article, the synthesis of trimethylsilyl ethers of cellulose in the two ILs, 1-ethyl-3-methylimidazolium acetate (EMIMAc) and 1-butyl-3-methylimidazolioum chloride (BMIMCl) in comparison to DMA/LiCl is described. TMSC with various DS were synthesized and investigated concerning their self-assembly behavior by a controlled and slow exchange of the organic solvent from the polymer solution by dialysis. It was intended to prepare nanoparticles of TMSC that can be converted with HCl into pure cellulose particles. Such particles are valuable tools in biomedical applications as drug carrier, contrasting agents, or in material science, e.g., for surface modification.[22]

Experimental Part

Solvents and Reagents

Microcrystalline cellulose (Fluka, Avicel PH-101) dried at 105 °C for 2 h was used. *N,N*-dimethyl acetamide (DMA), tetrahydrofuran (THF), trimethylsilyl chloride, 1,1,1,3,3,3-hexa-methyldisilazane (HMDS) were supplied by Merck, Epichlorhydrin and FITC were supplied by Sigma-Aldrich, 1-butyl-3-methylimidazolium chloride (BMIMCl, BASF dry $\geq$ 99%, mp $\sim$ 70 °C), 1-ethyl-3-methylimidazolium acetate (EMIMAc, BASF quality $\geq$ 90%) and dimethyl sulfoxide (DMSO) supplied by Fluka were used without further purification.

Measurements

^{1}H NMR spectra were measured in DMSO-*d*6 or $CDCl_3$ (50 mg·mL^{-1}) with a Bruker Avance 250 spectrometer running at 250 MHz at room temperature. 16 scans were accumulated.

^{13}C NMR spectra were recorded in DMSO-*d*6 or $CDCl_3$ (100 mg·mL^{-1}) with a BRUKER AVANCE 250 or 400 spectrometer running at 63 or 101 MHz, at room temperature. From these spectra 10000-16000 scans were accumulated.

FTIR spectra were recorded on Nicolet Avatar 370 DTGS spectrometer with the KBr technique.

The elemental analysis was performed by CHNS 932 Analyzer (Leco).

The DS of the TMSC was calculated from the content of silicon determined gravimetrically as silicon dioxide after decomposition of the polymers with concentrated sulfuric acid according to McHard.[23] Alternatively, the DS values were determined by ^{1}H NMR spectroscopy after peracetylation of the silylated polymers.

The hydrodynamic diameter of the nanospheres was determined by dynamic light scattering (DLS) experiments with 0.1–0.2 wt% aqueous suspensions, using a He-Ne laser with a scattering angle of 173° (Malvern Zetasizer Nano ZS). Particle size distribution was determined by a particle size distribution analyzer (PLPSDA, Polymer Laboratories, Shropshire, UK) with a flow rate of 2.1 mL·min^{-1} and an injection volume of 20 μL operating at pH 7.

Atomic force microscopy (AFM) was carried out in the noncontact mode with a DualScope C-21 (DME) and silicon nitride tips (60.0 N·m^{-1}, 0.20 nN) to determine size and shape of the particles. The frequency applied was 280 kHz. For sample preparation, a stock solution of 1 mg·mL^{-1} was diluted to a concentration of 2 μg·mL^{-1}. Drops of this solution were deposited onto freshly cleaved mica, frozen at -18 °C and dried under vacuum (0,5 mbar) at ambient temperature using a lyophilizer CHRIST alpha 1–4.

For SEM images, a droplet of $\sim$0.2 mL was placed on a mica surface. The system was lyophilized for 6 h (see AFM) and sputtered with gold. The images were

obtained with SEM equipment LEO-1450 VP (LEO, Oberkochen, Germany) to determine size and shape of the particles.

Laser scanning microscopy (LSM) was carried out with a LSM 510 Meta (Zeiss) using laser excitation wavelengths of 488 nm for FITC and 633 nm for WGA.

The viscosity of the cellulose particle/water suspension (1 mg·mL^{-1}) was measured with a Rheostress 100, Haake, cone-plate rheometer at 25 °C.

Dissolution of Cellulose in IL

In case of BMIMCl the cellulose was mixed with the molten IL (~70 °C) and the temperature was increased to 80 °C afterwards. In case of EMIMAc the cellulose was added at ambient temperature. In both ILs an optically clear solution was obtained after stirring for 12 h.

Dissolution of Cellulose in DMA/LiCl

Cellulose (0.4 g, 2.47 mmol AGU) were suspended in 16 mL N,N-dimethyl acetamide (DMA) and stirred at 150 °C for 1 h. After the slurry was allowed to cool to 100 °C, 1.2 g of anhydrous LiCl were added. The cellulose dissolved completely during cooling to room temperature under constant stirring.

Synthesis of Trimethylsilyl Cellulose in IL (Typical Procedure)

Different AGU/HMDS molar ratios and ILs were investigated. The reaction conditions and results are listed in Table 1.

A cellulose/EMIMAc solution (0.5 g cellulose, 3.086 mmol AGU in 4.5 g EMIMAc) was mixed with HMDS (1.92 mL, 9.259 mmol) and allowed to react for 1 h at 80 °C. After the reaction, the mixture was cooled to room temperature and the product was isolated by precipitation into isopropyl alcohol (200 mL). After washing with isopropyl alcohol (200 mL), the product was dried under vacuum at 60 °C yielding pure TMSC (**1**).

Yield: 1.02 g (93.6%, sample **1**). DS_{Si} (determined by ^{1}H NMR spectroscopy after peracetylation): 2.67. Elemental Analysis: Found C 48.6, H 9.3, N 0.0. IR (KBr): 3500 ν(OH), 2957, 2904 ν(CH), 1243 ν(Si-C), 1036 δ(Si-O), 878, 839, 752 cm^{-1} ν(Si-C). ^{13}C NMR (DMSO-*d*6): $\delta = 0.0$–2.0 (C-7), 60.8–103.0 ppm (C-1 to C-6). ^{1}H NMR (DMSO-*d*6): $\delta = 0.0$ (H-7), 3.4–5.2 ppm (H-1 to H-6).

Synthesis of Trimethylsilyl Cellulose in DMA/LiCl (Typical Procedure)

Different AGU/HMDS molar ratios were investigated. The reaction conditions and results are listed in Table 1.

To a solution of cellulose in DMA/LiCl, containing 0.4 g of cellulose (2.47 mmol AGU), 0.6 g HMDS (3.72 mmol) and 0.021 g trimethylsilyl chloride (0.19 mmol) were added. After the reaction for 1 h at 80 °C, the mixture was cooled to room temperature and the product was isolated by precipitation into deionized water (200 mL). After filtration, the product was dried under vacuum at 60 °C yielding pure TMSC (**9**).

Yield: 0.86 g (91.1%, sample **9**). DS_{Si} (determined gravimetrically as silicon dioxide): 2.17. Elemental Analysis: Found C 46.7, H 8.7, N 0.0. IR (KBr): 3489 ν(OH), 2960, 2904 ν(CH), 1254 δ(Si-C), 1047 ν(Si-O), 880, 840, 751 cm^{-1} ν(Si-C).

Peracetylation (Typical Procedure for Sample Preparation to Determine the DS by ^{1}H NMR Spectroscopy)

A mixture of pyridine (1 mL) and acetic acid anhydride (1 mL) was added to 50 mg of TMSC. The reaction mixture was stirred for 3 h at 45 °C, cooled to room temperature and stirred overnight. After 3 h stirring at 45 °C and cooling to room temperature again, the product was isolated by precipitation into isopropyl alcohol (50 mL). The product was reprecipitated from chloroform into isopropyl alcohol (50 mL), filtered, washed with isopropyl alcohol (50 mL) three times and dried under vacuum at 60 °C (**1**).

Yield: 0.52 mg (98%, sample **1**). $DS_{Si} = 2.67$, $DS_{Prop} = 0.33$ (determined by ^{1}H NMR spectroscopy). FTIR (KBr): no ν(OH), 2957, 2904 ν(CH), 1757 ν(C=O

Table 1.
Reaction conditions (solvent and molar ratio of reactants) and properties of the reaction products (DS and solubility) for the trimethylsilylation of cellulose in ionic liquids or DMA/LiCl (1 h, 80 °C).

Reaction Conditions		Product				
	Molar Ratio[a]			Solubility[f]		
Solvent	AGU/HMDS/TMSCl	DS[b]	No.	DMSO	DMA	THF
EMIMAc	1 / 3 / 0	2.67 [c]	**1**	−	−	−
EMIMAc	1 / 5 / 0	2.73 [c]	**2**	−	−	+
EMIMAc	1 / 8 / 0	2.85 [c]	**3**	−	−	+
BMIMCl	1 / 3 / 0	- [d]	**4**	−	−	−
BMIMCl	1 / 5 / 0	- [d]	**5**	−	−	−
BMIMCl	1 / 8 / 0	1.85 [c]	**6**	+	+	+
DMA/LiCl	1 / 1 / 0.1	0.52 [e]	**7**	+	+	−
DMA/LiCl	1 / 1.5 / 0.1	1.35 [e]	**8**	+	+	−
DMA/LiCl	1 / 2 / 0.1	2.17 [e]	**9**	−	−	−
DMA/LiCl	1 / 3 / 0.1	2.20 [e]	**10**	−	−	−
DMA/LiCl	1 / 8 / 0.1	2.90 [e]	**11**	−	−	+

[a]Anhydroglucose unit/1,1,1,3,3,3-hexamethyldisilazane/Trimethylsilyl chloride.
[b]Average degree of substitution.
[c]determined by ^{1}H NMR spectroscopy after peracetylation.
[d]No reaction.
[e]determined gravimetrically.
[f]+ soluble, - insoluble.

ester), 1243 ν(SiC), 1035 δ(Si-O), 878, 839, 752 cm^{-1} ν(Si-C). ^{1}H NMR ($CDCl_3$): δ = 5.15 (H-3), 4.80 (H2), 4.42 (H-1,6), 4.08 (H-6'), 3.68 (H-4), 3.51 (H-5), 2.04 (CH_3-acetyl), 0.0 ppm (CH_3trimethylsilyl).

Nanoparticle Preparation

Preparation of the nanoparticles from TMSC synthesized in ILs was carried out by a dialysis process. 20 mg of TMSC was dissolved in 20 mL of purified DMSO, DMA, or THF and was dialyzed against distilled water (Spectra/Por1 membrane, molecular weight cut-off 3500 g/mol) for 4 days. The dialysate was replaced with fresh deionized water five times in a period of 3 days.

Preparation of the nanoparticles from TMSC synthesized in DMA/LiCl was carried out by a dialysis process. 30 mg of TMSC was dissolved in 20 mL of purified DMA and was dialyzed against deionized water (Spectra/Por1 membrane, molecular weight cut-off 3500 $g \cdot mol^{-1}$) for 4 days. The dialysate was replaced with fresh deionized water two times per day.

Results and Discussion

Synthesis

Silylation of cellulose with HMDS was studied applying the ILs, BMIMCl, and EMIMAc, as reaction media as well as DMA/LiCl. The values in Table 1 show that synthesis of TMSC was possible in the ILs studied although the HMDS was not fully soluble in these media, whereas it was well soluble in DMA/LiCl. Trimethylsilyl chloride (TMSCl) was used as catalyst during the reactions in DMA/LiCl. In ILs the TMSC precipitated as white solid, in DMA/LiCl the clear solution became cloudy during the reaction. The conversion proceeded within 1 h at 80 °C in all solvents.

EMIMAc was the most efficient solvent. Even a high excess of HMDS in BMIMCl did not lead to DS values similar to TMSC synthesized in EMIMAc. From this follows that hydroxyl groups of cellulose dissolved in BMIMCl have a significantly smaller activity and availability for the reagent. One reason can be the much higher viscosity of BMIMCl cellulose solutions. Moreover, the pronounced influence of the solvents in silylation reactions of cellulose

with HMDS was found by Nagy et al.[24] Obviously, the EMIM cation has a higher ability of polarization, which makes the transition complex between solvent and reagent more reactive compared to the BMIM cation.

In EMIMAc, an AGU/HMDS ratio of 1/3 gave a DS value as high as 2.67 after 1 hour of reaction (Table 1, sample **1**). Interestingly, the increase in DS occurred rapidly after an initial induction period of 15 minutes, after which the cellulose was still unaltered (DS of 0). The rapid increase in DS, during the next 5 minutes of reaction, manifested itself by the precipitation of a white solid, which was identified as TMSC with a DS of 2.41, at a reaction time of 20 minutes. Prolongation of the reaction time did not lead to a significant increase of the DS value. Figure 1 illustrates that comparable threshold type reactivity is observed if the molar ratio of AGU to HMDS is increased from 1/1 to 1/3. In case of silylation in DMA/LiCl this behavior was not found. Whereas ILs were useful to synthesize highly substituted cellulose derivatives, the DMA/LiCl system was preferred to adjust the DS values below 2.

TMSC with a DS > 2 precipitated during the reaction in ILs and the DS hardly increased afterwards due to heterogeneity. To avoid this effect, the addition of a cosolvent was investigated. Cosolvents, which were able to dissolve the TMSC, were chloroform [25] or toluene.[16e] In this work chloroform was added to the reaction solution. This resulted in an increase of the DS for the reaction of HMDS with cellulose dissolved in BMIMCl with decreasing molar ratio AGU/HMDS. The same reaction conditions as applied for sample **4** (Table 1, no reaction) but using chloroform yielded TMSC with a DS of 1.94. On the contrary, the DS values decreased for the silylation in the system EMIMAc/cellulose, as shown in Table 2. Up to now, there is no explanation for the decrease in DS with increasing molar ratio AGU/HMDS in case of conversion in BMIMCl/$CHCl_3$. The solubility of TMSC in several solvents (Table 1, Table 2) was in good agreement with those of the polymers synthesized in liquid ammonia.[16f]

Homogeneous conversions in DMA/LiCl are not applicable in large scale because regeneration of the reaction media

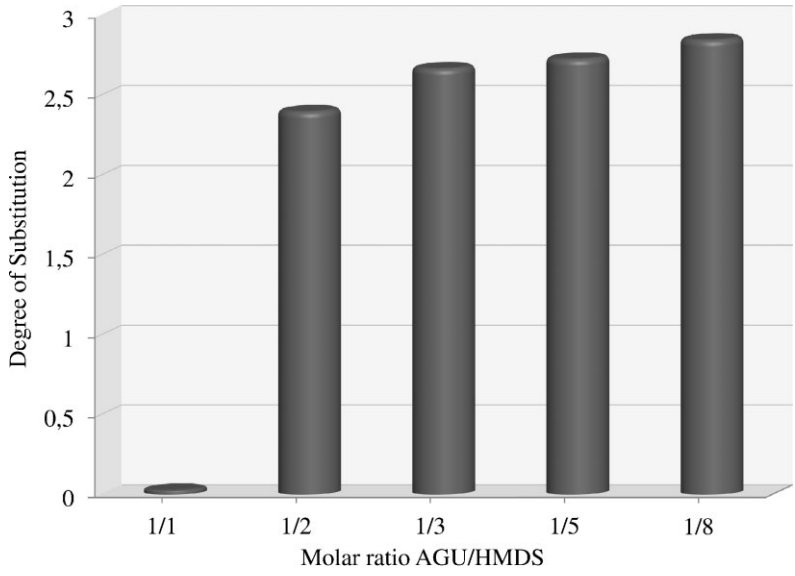

Figure 1.
Degree of substitution of trimethylsilyl cellulose prepared in 1-ethyl-3-methylimidazolium acetate for different molar ratios of anhydroglucose unit (AGU) to 1,1,1,3,3,3-hexamethyldisilazane (HMDS, 1 h, 80 °C).

Table 2.
Influence of chloroform on the efficiency of trimethylsilylation of cellulose with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in ionic liquids (1 h, 80 °C).

Reaction Conditions		Product			
	Molar Ratio[a]			Solubility[c]	
Solvent + 3 mL $CHCl_3$	AGU/HMDS	DS[b]	No.	DMA	THF
EMIMAc	1 / 3	2.19	**12**	−	+
EMIMAc	1 / 5	2.28	**13**	−	+
EMIMAc	1 / 8	2.89	**14**	−	+
BMIMCl	1 / 3	1.94	**15**	+	−
BMIMCl	1 / 5	1.71	**16**	−	+
BMIMCl	1 / 8	0.43	**17**	+	−

[a]Anhydroglucose unit/1,1,1,3,3,3-hexamethyldisilazane.
[b]Average degree of substitution.
[c]+ soluble, - insoluble.

is difficult and time-consuming. In case of ILs recycling could be easily achieved. The reaction mixture of EMIMAc, for example, was treated with ethanol for the complete precipitation of TMSC. After filtration, ethanol was removed from the IL by evaporation. The purity of the recycled EMIMAc was determined by NMR spectroscopy.

Structure of TMSC

The TMSC samples were analyzed by ^{1}H-, ^{13}C-, and FTIR spectroscopy. Figure 2 shows the ^{13}C NMR spectrum of TMSC sample **17**. Only signals for the substituent (0.0 - 2.0 ppm) and the AGU (60.8 - 103.0 ppm) were found. Basically, the same chemical shifts were obtained for all TMSC samples synthesized. No side reactions were observed, which could not have been assumed for EMIMAc because it may not exclusively act as a solvent during the modification of cellulose but also as an acetylating reagent as shown for various derivatization reactions.[26] Furthermore, imidazolium-based ILs can be deprotonated at position 2. The deprotonated imidazolium cation may interact with the carbonyl moiety of the reducing end group.[27] None of that was observed here. The spectrum of sample **17** reveals partial functionalization of the primary OH groups as concluded from the signals at 60.8 ppm (C-6) and 62.0 ppm (C-6s). The two peaks at 102.2 ppm and 103.0 ppm correspond to C-1' and C-1 adjacent to position 2 bearing a trimethylsilyl group and a hydroxyl group at position 2, respectively. Thus, a partial silylation at position 2 occurred.

The DS of the TMSC was calculated from the content of silicon measured gravimetrically as silicon dioxide after decomposition of the polymers with con-

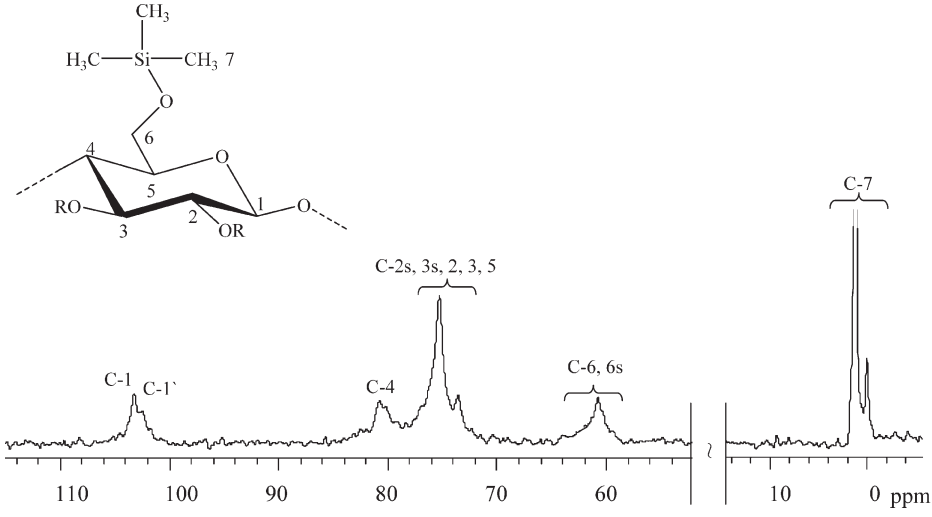

Figure 2.
^{13}C NMR spectrum of trimethylsilyl cellulose (sample **17**, degree of substitution, DS = 0.43) in DMSO-*d6*, R means trimethylsilyl group or H according to DS.

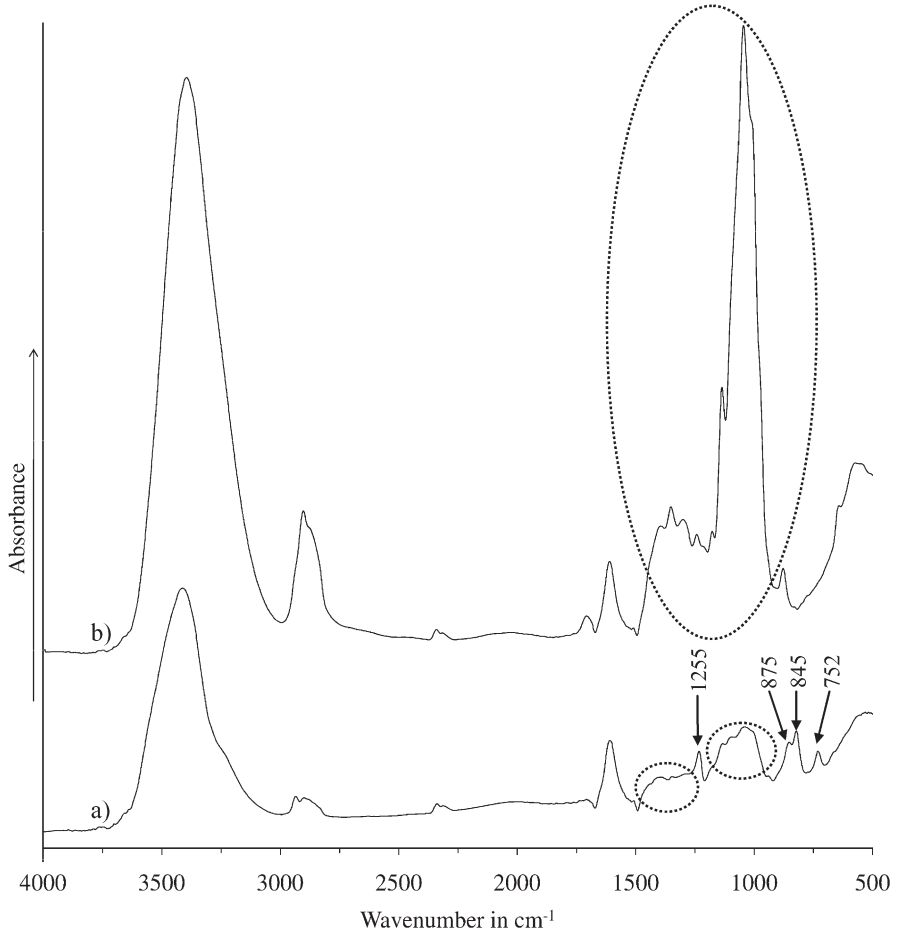

Figure 3.
IR spectra of (a) trimethylsilyl cellulose (sample **8**, degree of substitution, DS = 1.35) and (b) pure cellulose particles formed via dialysis of trimethylsilyl cellulose (TMSC), spectra are not normalized.

centrated sulfuric acid according to McHard.[23] Alternatively, the DS values were determined by ^{1}H NMR spectroscopy after peracetylation of the trimethylsilylated polymers. The complete acetylation occurred under mild conditions without loss of trimethylsilyl groups. In addition to the total DS, the partial DS was calculated by integration of the individual peak areas of the ^{1}H NMR spectrum of the repeating unit and the methyl group of the acetyl moiety.[28] A more pronounced substitution of the primary OH group was found for TMSC synthesized in ILs. For instance, sample **1** with total DS 2.67 exhibited $DS_{O\text{-}6}$ 1.00 and $DS_{O\text{-}2,3}$ 1.67.

The decrease in molar mass of the polymers was evaluated by GPC experiments. Just a small decrease of the degree of polymerization was observed even though high DS values showed a bimodal mass distribution due to the aggregation of the hydrophobic trimethylsilylated regions of the cellulose derivatives.[16f]

Figure 3 shows the IR spectra of sample **8** (a) and pure cellulose particles (b). As expected, it reveals the valence vibrations of the free OH groups at 3434 cm^{-1}. The band is much smaller compared to the pure cellulose which leads to the conclusion that the degree of association between the OH groups in TMSC is not as high as in pure

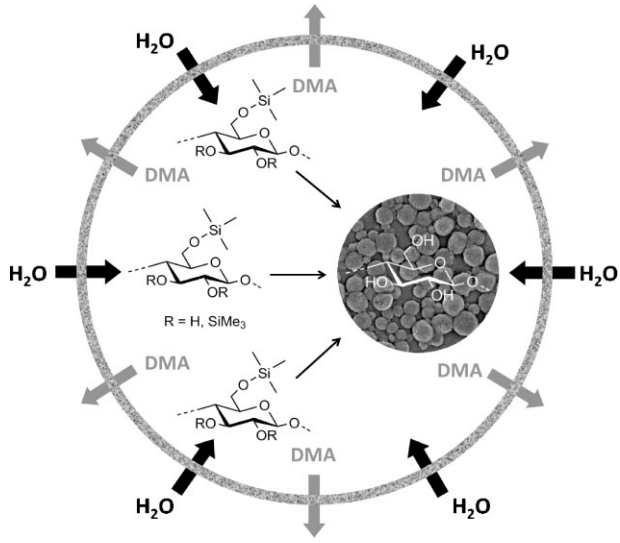

Figure 4.
Dialysing of trimethylsilyl cellulose (TMSC) solution (1.5 mg TMSC/1 mL dimethyl acetamide) for 4 days.

cellulose. Also the in plane OH deformation vibrations (1250 – 1430 cm^{-1}) are much smaller in the TMSC spectrum. Therefore the symmetrically Si-C deformation vibrations at 1255 cm^{-1} appears as sharp signal in this area. Additional Si-C vibrations were found from 752 – 875 cm^{-1}. Accordingly, the decreased intensity of C-O valence vibrations (1000 – 1200 cm^{-1}) of primary and secondary alcohols can be explained as above.

Preparation of Cellulose Particles from Trimethylsilyl Cellulose

Because of their nontoxic and biocompatible properties, cellulose particles are favored over synthetic polymers in many applications, as nanopattern in nanoreactions, for diverse immobilization methods and as separation materials. TMSC was considered as starting material because of its solubility in different organic solvents and because of the strong tendency of TMSC towards the formation of supramolecular structures. The formation of nanoparticles during the dialysis process is based on the slow exchange of an organic solvent against a nonsolvent (Figure 4). Dialysis of TMSC dissolved in THF or DMA against water was performed for 4 days; an aqueous suspension was formed.

The particles were analyzed by FTIR spectroscopy after lyophilization (Figure 3). Surprisingly the particles were pure cellulose. The TMSC were completely hydrolyzed during the solvent exchange. No additional hydrolysis of the trimethylsilyl groups is necessary which makes the dialysis an efficient and easy way to get pure cellulose nanoparticles. The method worked for TMSC synthesized in both solvent systems, ILs and DMA/LiCl. The starting TMSC had different DS values from 1.94 (sample **15**, prepared in IL) to 1.35 (sample **8**, prepared in DMA/LiCl). TMSC with DS values higher or lower than that did not create particles with high quality. Solvents like DMSO, DMF, THF and DMA were used to dissolve TMSC for the exchange. DMA gave the best results with respect to particle size and shape. Figure 5 presents scanning electron microscope images of spherical cellulose particles with particle size about 200 nm formed from TMSC with a DS of 1.35 (sample **8**). It is obvious that the particles are well separated and exhibits a desired shape.

AFM images (Figure 6) of particles from sample **8** show cellulose spheres with a size range of 190 to 250 nm but also particles of about 1000 nm. It can be seen that the

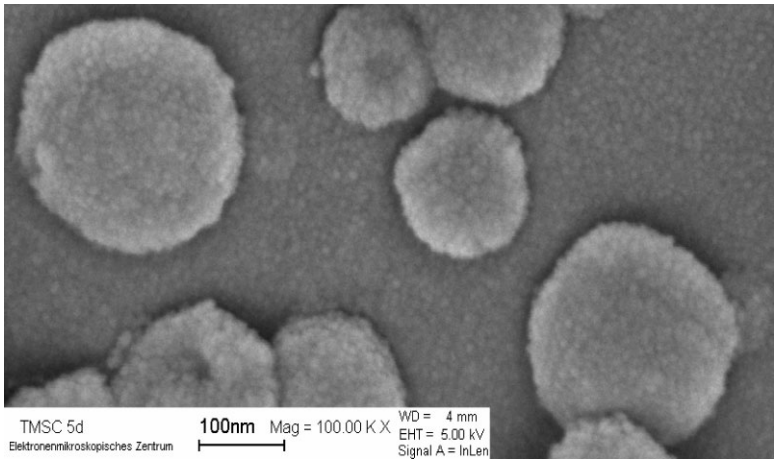

Figure 5.
Scanning electron microscope images of particles formed via dialysis of trimethylsilyl cellulose with a degree of substitution (DS) of 1.35 (sample **8**).

bigger ones are aggregates of small spheres. It is assumed that the aggregation is caused by highly substituted TMSC via interaction of hydrophobic regions before dialysis. Closely interacting chains are able to form bundle like structures and bundle formation increases with the DS which was showed by static and dynamic light scattering.[29] Table 3 summarizes the results of hydrodynamic diameter measurements of particles using a Zetasizer.

Another important point for successful particle preparation is the concentration of the TMSC solution. While 1.5 mg TMSC per mL solvent were used for the sample with a DS of 1.35, an amount of 1 mg TMSC per mL solvent worked for the higher substituted samples. Viscosity measurements of the nanoparticle suspensions revealed viscosity in the range of water, for example, in sample **15**, viscosity of 0.948 mPas at 25 °C as expected. Therefore use in the biomedical field, e.g., as drug carrier or contrasting agent is reasonable because parenteral application is possible.

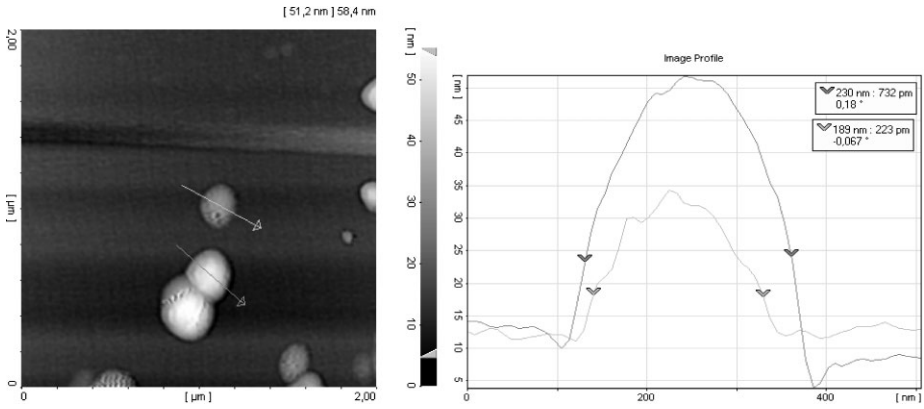

Figure 6.
Atomic force microscopy image of cellulose particles formed via dialysis of trimethylsilyl cellulose with a degree of substitution (DS) of 1.35 (sample **8**).

Table 3.
Hydrodynamic diameter measurements of cellulose particles determined by dynamic light scattering experiments using a Zetasizer.

Sample		Solvent for Dialysis[a]	Particle	
DS	Prepared in		Size in nm	PDI[b]
1.35	DMA/LiCl	DMA	216	0.27
1.85	BMIMCl	DMA	176	0.11
1.94	BMIMCl	DMA	265	0.28
2.26	BMIMCl	THF	1150	0.76
2.85	EMIMAc	THF	3165	0.46

[a]Dialysis for 4 days.
[b]Polydispersity index.

Conclusion

A simple and efficient synthesis of TMSC in various ILs and DMA/LiCl is discussed that leads to products within a wide range of DS in short reaction times and without additional bases or catalysts in case of ILs. The DS of the TMSC can be determined by ^{1}H NMR spectroscopy after peracetylation as well as gravimetrically and comprise values in the range from 0.43 to 2.89. In DMA/LiCl, the DS of the TMSC can be well controlled via the molar ratio of reagent/AGU. In ILs threshold type reactivity is observed. Control of the DS is possible for the conversion of cellulose dissolved in IL if a cosolvent is applied. This leads to the assumption that the uncommon reactivity in pure ILs is due to diffusion barriers. The ILs applied can be reused after simple purification.

TMSC is a favorable starting material to form pure cellulose nanoparticles by a simple dialysis process. The results show that a certain balance of silyl- and hydroxyl moieties at the cellulose backbone influences the size and shape of the particles. Thus, TMSC with DS values in the range from 1.35 to 1.94 forms nanoparticles. FTIR spectroscopy of freeze dried particles showed that they consist of pure cellulose. The TMSC were completely hydrolyzed during the solvent exchange. No additional hydrolysis is necessary. Consequently, this is an efficient and easy way to get pure cellulose nanoparticles. The aqueous suspension formed is storable for several months and exhibits a viscosity in the range of water making these samples sought after materials for biomedical applications such as drug carrier or contrasting agents. Labeling of cellulose nanoparticles with fluorescein isothiocyanate and their incorporation into living cells is currently under investigation. Preliminary results show a successful cellular uptake.

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