Homogenous Carboxymethylation of Cellulose in the New Alkaline Solvent LiOH/Urea Aqueous Solution

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Summary: In this work, the carboxymethylation of cellulose in a new alkaline cellulose solvent, LiOH/urea aqueous solution, was investigated. Carboxymethyl cellulose (CMC) samples were characterized with FT-IR, NMR, HPLC, and viscosity measurements. Water-soluble CMC with $DS = 0.36 \sim 0.65$ was prepared, from both Avicel cellulose and cotton linters in the LiOH/urea system. The total DS of CMC could be controlled by varying the molar ratio of reagents and the reaction temperature. The results from structure analysis by HPLC after complete depolymerization showed that the mole fractions of the different carboxymethylated repeating units as well as those of unmodified glucose follow a simple statistic pattern. A distribution of the carboxymethyl groups of the AGU was determined to be in the order O-6 > O-2 > O-3 position at the level.

Keywords: carboxymethyl cellulose; LiOH/urea; NMR spectroscopy; solubility; synthesis

Introduction

Nowadays, science and technology have moved toward renewable raw materials and more environmentally friendly and sustainable resources and processes.[1] Being the most abundant renewable organic material on earth, cellulose will be the main chemical resource of the future for its degradability and biological compatibility. However, cellulose cannot be melted or dissolved in common solvents, owing to its well-developed inter- and intra- molecular hydrogen bonding network. Being one of the main routes for utilizing cellulose-based materials, chemical modification has been investigated by polymer scientists for a long time. Although commercial cellulose derivatives used are typically manufactured under heterogeneous conditions, homogenous modification of cellulose has been one focus of cellulose research for it may broaden the diversity of products and synthesis pathways.[2] For example, various cellulose derivatives have been successfully synthesized through homogenous methods in such solvents as *N,N*-dimethylacetamide (DMAc)/lithium chloride (LiCl) and N-methylmorpholine-N-oxide (NMMNO).[3–6] Mixtures composed of diethylamine, SO_2, and dipolar aprotic liquids like dimethyl sulfoxide (DMSO) were used successfully for etherification.[7] And recently, DMSO/tetrabutylammonium fluoride trihydrate(TBAF) was successfully used as a new simple cellulose solvent for effective preparation of cellulose derivatives.[2,8,9] Furthermore, ionic liquids (ILs) as the ''green'' reaction media also proved to be very efficient in homogeneous cellulose functionalization.[10–12] As one of the aqueous solvents for cellulose, NaOH/urea aqueous solution is non-polluting and non-toxic, and also a suitable homogenous reaction medium for the etherification of cellulose. Cellulose ethers such as methyl-

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cellulose, hydroxyethyl cellulose and quaternized cellulose as well as carboxymethyl cellulose have been successfully synthesized through this solvent by Zhang's group.[13–16]

It has been reported by Zhang et al. that the LiOH/urea aqueous solution is a powerful solvent for cellulose. Cellulose having M_η of 37.2×10^4 can be dissolved in LiOH/urea aqueous solution precooled to -10 °C in about 2 min. It proved to be more efficient than NaOH/urea, which was also used for the dissolution and derivatization of cellulose as aqueous alkaline solvent.[17] A channel inclusion complex (IC) hosted by urea encaged the cellulose macromolecule in LiOH/urea solution with prior cooling, and could provide a rationale on forming a good dispersion of cellulose, leading to the dissolution of cellulose in the aqueous solution at low temperature.[18] Moreover, cellulose membranes have also been prepared from LiOH/urea aqueous solution.[19]

In the present work, LiOH/urea aqueous solution, as an alkaline cellulose solvent was applied for the carboxymethylation of Avicel and cotton linters. The reaction was possible by a simple addition of sodium monochloroacetate because the solvent provides the necessary basicity to initiate the reaction. Various reaction parameters were studied, such as the molar ratio of reagent, reaction temperature and reaction time. We report the effects of these reaction conditions on total DS, on the pattern of substitution within the AGU and on the formation of different repeating units in the polymer chains.

Experimental Part

Materials

Three kinds of cellulose samples, Avicel® (Fluka, degree of polymerization, DP 330), cotton linters 1 (supplied by Hubei Chemical Fiber Group Ltd., Xiangfan, China, DP 500) and cotton linters 2 (Fluka, DP 2000), were used. The DP of cellulose samples were determined by viscometry in Cuen at 25 °C. The cellulose samples were dried in a vacuum at 60 °C for 24 h before use. All other reagents were of analytical grade.

Carboxymethylation of Cellulose

Into a 250 mL beaker, an adequate amount of LiOH, urea and distilled water (4.6: 12: 83.4 by weight) were added. The cellulose was added into this solvent with stirring to obtain a slurry mixture. Then the mixture was stored in a refrigerator. After being precooled to -10 °C, the mixture was stirred vigorously at ambient temperature to obtain the transparent cellulose solution.

In a typical preparation, for example (**a3**), 17.25g sodium monochloroacetate were added into 100 g of cellulose solution (4 wt%) under vigorous stirring. The temperature was raised to 55 °C. After 5 h the mixture was cooled to room temperature and put into 300 mL 80% (v/v) methanol and neutralized with dilute acetic acid. After filtration the product was washed three times with 80% (v/v) ethanol and with ethanol and dried in a vacuum at 60 °C. Degree of substitution, (DS) 0.25 (revealed by HPLC analysis [19,20]) mole fractions of the different repeating units, see Table 2); Yield of sample **a3**: mass = 4.52g; Calculated yield = 90.6% (according to cellulose, and DS of CMC is 0.50), IR (KBr) 1607, 1426 cm^{-1} (C=O, carboxylate group); ^{13}C NMR spectroscopy (D_2O): 177.0–179.3 ppm (C=O), 59.3–103.7 ppm (cellulose backbone); ^{1}H NMR spectroscopic analysis after hydrolysis led to a partial DS at O-6 of 0.13, O-2 of 0.10, and O-3 of 0.04 resulting in a total DS of 0.50. Elemental analysis: C) 37.90%, H) 5.89%, N) 0.11%.

Measurements

The HPLC analysis of the CMC samples was carried out as described by Heinze et al.[20,21] In brief, the samples were hydrolysed with perchloric acid. 0.1 g of CMC was dispersed in 2 cm^3 $HClO_4$ (70%) and after 10 min at room temperature diluted with 18 cm^3 distilled water. This mixture was kept at 100 °C for 16 h. The solution obtained was carefully neutralised with 2 M KOH and kept at 4 °C for 1 h to guarantee a complete precipitation of the $KClO_4$: The salt was filtered off and washed three times with distilled water. The solution obtained was reduced to approximately 3 cm^3 and diluted with distilled water to give exactly 5 cm^3 sample. Chromatographic experiments were carried out at 65 °C with 0.05M H_2SO_4 as eluent with a flow rate of 0.5 cm^3/min. The column used was a Bio-Rad Aminex HPX-87 H. The mol fractions of glucose; 2-, 3-, and 6-mono-; 2, 3-, 2, 6-, and 3, 6-di-; and 2, 3, 6-tri-O-carboxymethylated glucoses (CMG) were determined from the HPLC.

FTIR spectra were recorded on a Bio-Rad FTS 25 PC using the KBr pellet technique. Standard ^{13}C-NMR spectra with proton-decoupling were recorded in D_2O (4% polymer) on a Bruker 400 AMX NMR spectrometer. The scan number was between 6000 and 10000. ^{1}H NMR analyses were performed as described by Heinze and Pfeiffer.[22] For this purpose, the CMC samples were hydrolyzed in a mixture of 25% (v/v) D_2SO_4/D_2O (50 mg/mL) 5 h at 90 °C. The spectra were obtained on a Bruker AMX 400 spectrometer operating at 250.13 MHz, the accumulation number was 16. A CHNS 932 Analyzer (Leco) was used for elemental analysis.

Intrinsic viscosities ([η]) of CMC were determined in 6 wt% NaOH aqueous solution at 20 °C using an Ubbelohde viscometer proposed by Crössmann et al.[23] The original concentration of CMC in water was 0.2 g/L. Then the degree of polymerization (DP) of CMC can be obtained by the following equation [23]:

$$\mathrm{DP} = [\eta] / 0.0066 \qquad (1)$$

Results and Discussion

Three kinds of cellulose including cotton linters with high DP of 2000 were dissolved very well in the LiOH/urea aqueous solution. It was further demonstrated that LiOH/urea aqueous solution was more efficient than NaOH/urea system at the same condition.[17] The carboxymethylation of cellulose in LiOH/urea aqueous solution was simply possible by adding sodium monochloroacetate as etherifying agent to the solution because of basicity of the solvent, which is sufficient to initiate the etherification reaction (shown in Equation 1). Under the conditions for the reaction (Table 1), the solution was kept transparent and remained completely homogenous as the reaction proceeded. This process is similar to the homogeneous carboxymethylation of cellulose in NaOH/urea aqueous solution.[16]

Table 1 displays the conditions of homogeneous carboxymethylation of cellu-

Table 1.
Conditions and results of carboxymethylation of cellulose dissolved in LiOH/urea aqueous solution.

Materials	Molar ratio[a]	Temperature (°C)	Time (h)	Carboxylmethyl cellulose		
				Samples	DS_{HPLC}[b]	Solubility in water[c]
Avicel	1/7.5/7.8/1	55	5	**a1**	0.10	−
Avicel	1/7.5/7.8/3	55	5	**a2**	0.26	o
Avicel	1/7.5/7.8/6	55	5	**a3**	0.50	+
Avicel	1/7.5/7.8/9	55	5	**a4**	0.65	+
Avicel	1/7.5/7.8/6	55	3	**a5**	0.42	+
Avicel	1/7.5/7.8/6	55	7	**a6**	0.60	+
Avicel	1/7.5/7.8/6	55	17	**a7**	0.61	+
Cotton linters 1	1/11.5/12/6	55	5	**b1**	0.36	+
Cotton linters 1	1/11.5/12/6	55	17	**b2**	0.39	+
Cotton linters 2	1/15/15.6/6	55	5	**c1**	0.24	o
Cotton linters 2	1/15/15.6/6	55	17	**c2**	0.23	o

[a] Anhydroglucose unit: LiOH: urea: $ClCH_2COONa$.
[b] Degree of substitution (DS) determined by HPLC after hydrolytic chain degradation.
[c] + soluble, − insoluble, o swelling.

Table 2.
Intrinsic viscosity ([η]) and degree of polymerization (DP) of some carboxymethyl cellulose (CMC).

Sample	[η] ml.g^{-1}	DP
a2	85.8	130
a3	94.1	143
a4	125.5	190
a7	108.5	164
b1	206.0	312

lose dissolved in LiOH/urea aqueous solution and DS values (obtained by HPLC of the depolymerized samples) of the carboxymethyl cellulose samples (CMCs). In any case, the DS of the CMC samples obtained applying this procedure depends on the amount of reagent used. Applying a molar ratio of anhydroglucose unit (AGU): $ClCH_2COONa$ of 1:1, a rather low DS of about 0.10 (**a1**) is determined, which increases with increasing molar ratio up to 0.65 (**a4**). By changing the mole ratio of AGU to sodium monochloroacetate up to 1:6 and 1:9, the CMC (**a3** and **a4**) samples display good solubility in water. Therefore, water-soluble carboxymethyl celluloses (CMCs) were prepared from both Avicel cellulose and cotton linters under completely homogeneous conditions (Table 1).

In addition, it was found that changing the reaction time exhibited a significant influence on the total DS. For example, a DS of 0.50 (**a3**) can be obtained for 5h at 55 °C (Table 1). With shorter time such as 3h CMC with only a DS of 0.42 (**a5**) were produced. And reaction for 7h yields water-soluble CMC (**a6**) with a DS of 0.60. However, with longer time more then 7h, reaction yields CMC with a comparable DS of 0.61 (**a7**). Furthermore, the comparison of the carboxymethylation reaction of Avicel cellulose and the other two kinds of cotton linters dissolved in LiOH/urea at different conditions show only slight differences of the reactivity between these cellulose materials (Table 1). However, the CMCs prepared from cotton linters with high DP (DP = 2000) can only be swelling in water, with a DS of about 0.23 even after a long reaction time. Elemental analysis results show that there are traces of nitrogen (0.11 – 0.13 wt.%) in the products even after carefully purifying. The same results were also found for the carboxymethylation of cellulose in NaOH/urea aqueous solution.[16]

The intrinsic viscosity ([η]) of some of the CMC samples at 25 °C and their DP values are listed in Table 2. The solution of CMC displays high viscosity in aqueous solutions. The DP values of the CMC are lower then that of the original cellulose, revealing degradation of the polymer during reaction at high temperature in this alkaline aqueous solution.

The molecular structure of the CMC was analyzed by means of FTIR spectra and ^{13}C NMR spectroscopy of the intact polymer. It can be observed that in the FTIR spectrum (not shown) of CMC as compared to the original cellulose, additional strong absorption bands appear at 1607 and 1426 cm^{-1}, which confirm the presence of COO^- groups. No evidence for a side reaction is found. A representative ^{13}C NMR spectrum of CMC sample (**a3,** DS = 0.50) in D_2O at 25 °C is shown in Figure 1. The peak at the lower field (102.3 ppm) corresponded to C-1 and C-1' (the peak for C-1 was influenced by the reaction at O-2); the peak at 59.9 ppm was assigned to the pendant methylene carbon C6. The typical signal of the carboxymethyl groups appeared at around 177–179 ppm.[16] The other carbon atoms present in the basic polymer backbone were determined between 70 and 85 ppm. Therefore, the results of NMR further proved the successful synthesis of carboxymethyl celluloses in LiOH/urea aqueous solutions without side reactions at the polymer backbone.

The DS values were determined by HPLC analysis after complete acidic depolymerization. Moreover, this analytical tool reveals the mol fraction of the different repeating units, i.e. the substituted units (2-, 3-, and 6-mono-; 2,3-, 2,6-, and 3,6-di- and 2,3,6-tri-O-carboxymethylated glucoses) and unmodified glucose. The mol fractions analyzed by HPLC are compared with a statistic model (Figure 2), which simulates

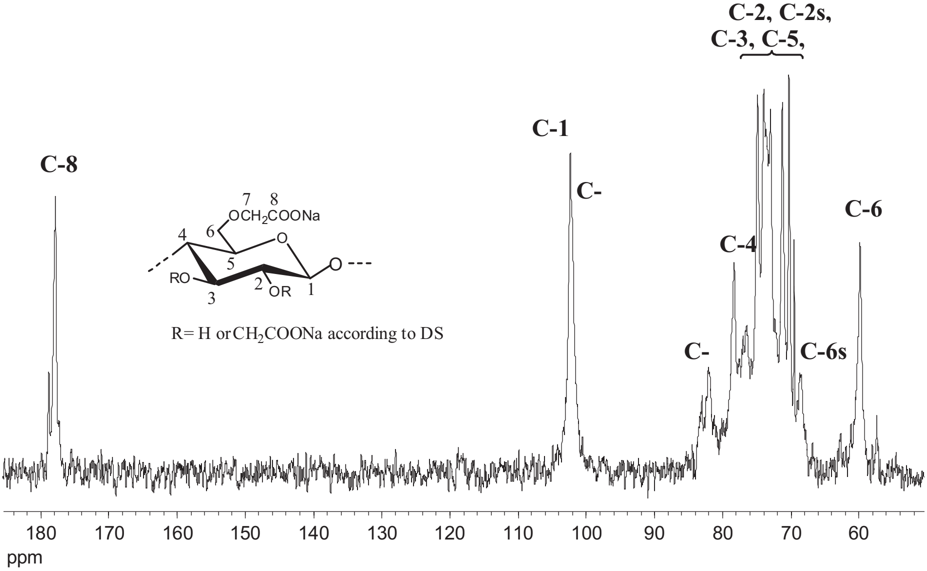


Figure 1.
^{13}C NMR spectrum of carboxymethyl cellulose (**a3**) recorded in D_2O. The index s refers to substituted hydroxyl group and C-1' means influenced by carboxymethylation at O-2.

the amount of the different repeating units. The model assumes that no preference for any OH groups (position 2, 3, and 6) exists and that the relative reactivity of the three OH groups in the AGU are constant throughout the reaction and independent of the DS of the cellulose chain or of the state of substitution at another position within the same anhydroglucose unit.[24] The good agreement between the mol

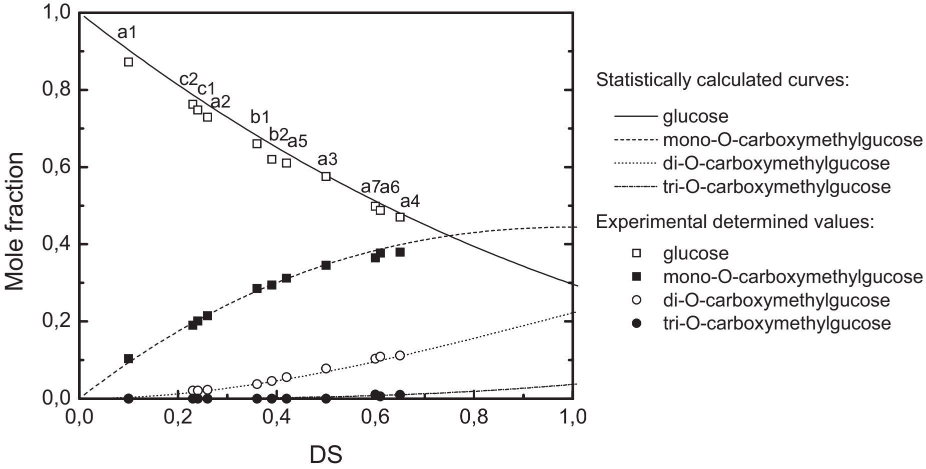


Figure 2.
Mol fraction of glucose (calculated: –; found: □); 2-, 3-, 6-mono-O-carboxymethyl glucose (calculated: - - -; found: ■); 2,3-, 2,6-, 3,6-di-O-carboxymethyl glucose (calculated: ···; found: ○); and 2,3,6-tri-O-carboxymethyl glucose (calculated: –·–·–; found: ●) of hydrolytically depolymerized CMC samples synthesized in LiOH/urea aqueous soultion, plotted as a function of DS. The curves are calculated (see text).

fractions analyzed and the statistics indicates that the LiOH activates the polymer chain evenly. Obviously there is no reactivity variation between regions of the polymer dissolved in LiOH/urea aqueous solution. It is similar to the reaction of the homogeneously carboxymethylation of cellulose in NaOH/urea,[16] as well as a totally homogeneous reaction (cellulose dissolved in Ni[tris(2-aminoethyl)amine]$(OH)_2$) or heterogeneous reaction in a highly activated state (alkali cellulose suspended in organic liquid or a conversion in DMAc/LiCl with NaOH in the presence of water).[25] This result further proved that both activation of cellulose with aqueous NaOH and the complete dissolution of the polysaccharide lead to a similar accessibility along the polymer chain.[22]

The partial degrees of substitution on the three reactive sites of the AGU can be determined by ^{1}H NMR spectroscopy after acidic depolymerization. A typical ^{1}H NMR spectrum (**a4**) is shown in Figure 3. Due to the cleavage of the glycosidic linkage, the α and β anomers of the glucose and modified glucose units are generated.

Table 3.
Partial degree of substitution (DS) determined by ^{1}H NMR analysis after depolymerization.

Sample[a]	Partial degree of substitution (x_i) at position			Total DS_{NMR}[b]	DS_{HPLC}[c]
	2	3	6		
a2	0.10	0.05	0.19	0.34	0.26
a3	0.20	0.09	0.27	0.56	0.50
a4	0.26	0.14	0.36	0.76	0.65
a7	0.23	0.10	0.32	0.65	0.61
b1	0.15	0.06	0.23	0.44	0.36

[a] Reaction conditions see Table 1.
[b] Total degree of substitution (DS_{NMR}) = Σ of x_i (i = 2, 3, and 6).
[c] Degree of substitution (DS) determined by HPLC.

The two sets of doublets in the spectral region between 4.6 and 5.6 ppm are assigned to the proton at C-1 of the α-anomer (at the lower field) and to the proton at C-1 of the β-anomer (at the higher field) coupled with the single proton at C-2. Protons from the carboxymethyl group are observed in a spectral region between 4.2 and 4.6. The determination of the partial percentage of substitution was carried out according to ref. [21] Typical results are listed in Table 3. A distribution

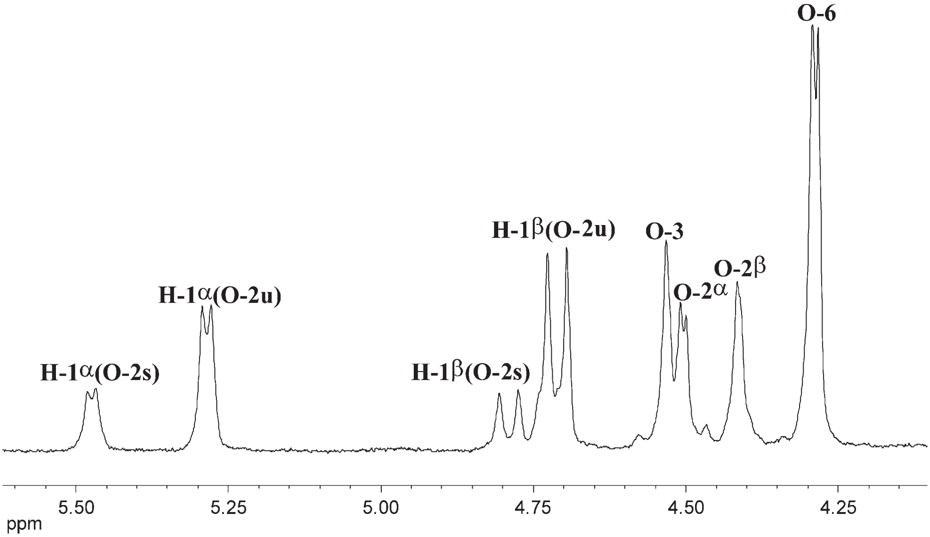
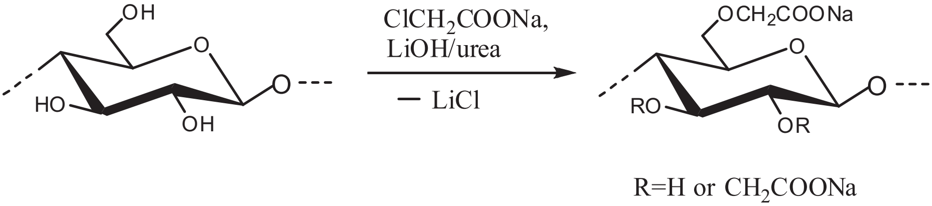


Figure 3.
^{1}H NMR spectrum of carboxymethyl cellulose (**a4**) depolymerized in D_2SO_4/D_2O. The index s and u of the signals refers to substituted and unsubstituted hydroxyl group.



Scheme 1.
Reaction scheme of cellulose carboxymethylation in LiOH/urea aqueous solution.

of substituents at the level of the AGU in the order O-6 > O-2 > O-3 was found, which is similar to CMC prepared from the homogeneously carboxymethylation of cellulose in NaOH/urea.[16] As the same reason, this reactivity order is a consequence of the higher steric accessibility of the primary hydroxyl group at position 6, while the secondary OH groups show a lower reactivity due to steric reasons.[16,26] Nevertheless, it is in contrast to the distribution of substituents found for CMC prepared in slurry, which is in the order O-2 > O-6 > O-3.

Conclusion

The cellulose solvent LiOH/urea aqueous solution is a suitable reaction medium for totally homogeneous etherification process for cellulose. Water-soluble CMC with DS = 0.36∼0.65 was prepared from Avicel cellulose and cotton linters in a one-phase-reaction. As same as that in NaOH/urea aqueous solution, the etherification could be carried out in LiOH/urea aqueous solution without addition of an extra base because of the inherent basicity of this solvent system. The total DS of CMC could be controlled by varying the molar ratio of reagent to AGU and the reaction time. The mole fractions of the different carboxymethylated repeating units as well as those of unmodified glucose follow the simple statistical pattern first proposed by Spurlin. This pattern is comparable to other carboxymethylation reactions under homogeneous conditions such as reaction of cellulose dissolved in NaOH/urea aqueous solution or in Ni[tris(2-aminoethyl)amine]$(OH)_2$. Furthermore, it was found that a distribution of substituents at the level of the AGU in the order O-6 > O-2 > O-3.

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[1] D. Klemm, B. Heublein, H.-P. Fink, A. Bohn, *Angew. Chem. Int. Ed.* **2005**, *44*, 3358.
[2] T. Heinze, R. Dicke, A. Koschella, A. H. Kull, E.-A. Klohr, W. Koch, *Macromol. Chem. Phys.* **2000**, *201*, 627.
[3] T. R. Dawsey, C. L. McCormick, *Polym. Rev.* **1990**, *30*, 405.
[4] B. Tosh, C. N. Saikia, N. N. Dass, *Carbohydr. Res.* **2000**, *327*, 345.
[5] J. Schaller, T. Heinze, *Macromol. Bio.* **2005**, *5*, 58.
[6] S. N. K. Chaudhari, K. C. Gouden, G. Srinivasan, V. S. Ekkundi, *J. Polym. Sci. Polym. Chem.* **1987**, *25*, 337.
[7] A. Isogai, A. Ishizu, J. Nakano, *J. Appl. Polym. Sci.* **1986**, *31*, 341.
[8] B. A. P. Ass, E. Frollini, T. Heinze, *Macromol. Biosci.* **2004**, *4*, 1008.
[9] M. A. Hussain, T. Liebert, T. Heinze, *Macromol. Rapid Commun.* **2004**, *25*, 916.
[10] S. Barthel, T. Heinze, *Green Chem.* **2006**, *8*, 301.
[11] Y. Cao, T. Meng, J. Zhang, J. He, H. Li, Y. Zhang, *Carbohydr. Polym.* **2007**, *69*, 65.
[12] T. Heinze, K. Schwikal, S. Barthel, *Macromol. Biosci.* **2005**, *5*, 520.
[13] H. Ke, J. Zhou, L. Zhang, *Polym. Bull.* **2006**, *56*, 349.
[14] J. Zhou, Y. Qin, S. Liu, L. Zhang, *Macromol. Biosci.* **2006**, *6*, 84.
[15] Y. Song, Y. Sun, X. Zhang, J. Zhou, L. Zhang, *Biomacromolecules* **2008**, *9*, 2259.
[16] H. Qi, T. Liebert, F. Meister, T. Heinze, *React. Funct. Polym.* **2009**, *69*, 779.
[17] J. Cai, L. Zhang, *Macromol. Biosci.* **2005**, *5*, 539.

[18] J. Cai, L. Zhang, C. Chang, G. Cheng, X. Chen, B. Chu, *ChemPhysChem*. **2007**, *8*, 1572.

[19] S. Liu, L. Zhang, *Cellulose* **2009**, *16*, 189.

[20] T. Heinze, U. Erler, I. Nehls, D. Klemm, *Angew. Makromol. Chem.* **1994**, *215*, 93.

[21] T. Liebert, Th. Heinze, "*Cellulose derivatives: modification, characterization and nanostructures*", T. Heinze, W. G. Glasser, Eds., ACS Symposium Series 688, **1998**, p. 61.

[22] T. Heinze, K. Pfeiffer, *Angew. Makromol. Chem.* **1999**, *266*, 37.

[23] F. Crössmann, W. Klaus, F. Mergenthaler, S. W. Souci, *Z. Lebensmitt. Unters.* **1964**, *125*, 413.

[24] H. M. Spurlin, *J. Am. Chem. Soc.* **1939**, *61*, 2222.

[25] T. Heinze, T. Liebert, P. Klüfers, F. Meister, *Cellulose* **1999**, *6*, 153.

[26] L. A. Ramos, E. Frollini, Th. Heinze, *Carbohydr. Polym.* **2005**, *60*, 259.