



Hydrogen bond formation in regioselectively functionalized 3-mono-*O*-methyl cellulose

Tetsuo Kondo ^{a,*}, Andreas Koschella ^{b,†}, Brigitte Heublein ^{b,†}, Dieter Klemm ^{c,‡}, Thomas Heinze ^{b,*,†}

^a Bio-Architecture Center (KBAC) and Graduate School of Bioresource and Bioenvironmental Sciences, Kyushu University, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

^b Centre of Excellence for Polysaccharide Research, Friedrich Schiller University of Jena, Humboldtstraße 10, D-07743 Jena, Germany

^c Polymet Jena e.V., Technologie- und Innovationspark, Wildenbruchstraße 15, D-07745 Jena, Germany

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ABSTRACT

The hydrogen bond systems of cellulose and its derivatives are one of the most important factors regarding their physical- and chemical properties such as solubility, crystallinity, gel formation, and resistance to enzymatic degradation. In this paper, it was attempted to clarify the intra- and intermolecular hydrogen bond formation in regioselectively functionalized 3-mono-*O*-methyl cellulose (3MC). First, the 3MC was synthesized and the cast film thereof was characterized in comparison to 2,3-di-*O*-methyl cellulose, 6-mono-*O*-methyl cellulose, and 2,3,6-tri-*O*-methyl cellulose by means of wide angle X-ray diffraction (WAXD) and ¹³C cross polarization/magic angle spinning NMR spectroscopy. Second, the hydrogen bonds in the 3MC film were analyzed by means of FTIR spectroscopy in combination with a curve fitting method. After deconvolution, the resulting two main bands (Fig. 3) indicated that instead of intramolecular hydrogen bonds between position OH-3 and O-5 another intramolecular hydrogen bond between OH-2 and OH-6 may exist. The large deconvoluted band at 3340 cm⁻¹ referred to strong interchain hydrogen bonds involving the hydroxyl groups at C-6. The crystallinity of 54% calculated from the WAXD supports also the dependency of the usually observed crystallization in cellulose of the hydroxyl groups at C-6 to engage in interchain hydrogen bonding.

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1. Introduction

Formation of hydrogen bonds in cellulose and cellulose derivatives is considered as one of the most important factors that influences their physical- and chemical properties. To date we have been extensively attempting the characterization using regioselectively functionalized methyl celluloses^{1–12} like 2,3-di-*O*-methyl cellulose (23MC),¹³ 6-mono-*O*-methyl cellulose (6MC),¹⁴ and 2,3,6-tri-*O*-methyl cellulose (236MC)¹⁵ as model compounds (Fig. 1). In addition, the functionalization pattern of the methyl ether groups had also an influence on the enzymatic hydrolysis of methyl cellulose by cellulase.¹⁶ Through those investigations, the intramolecular hydrogen bonds between the OH groups of C-3 and the adjacent ring oxygen of the anhydroglucose unit (O-5), which may determine the molecular stiffness, have also been formed, as a key factor for properties of cellulosic materials.

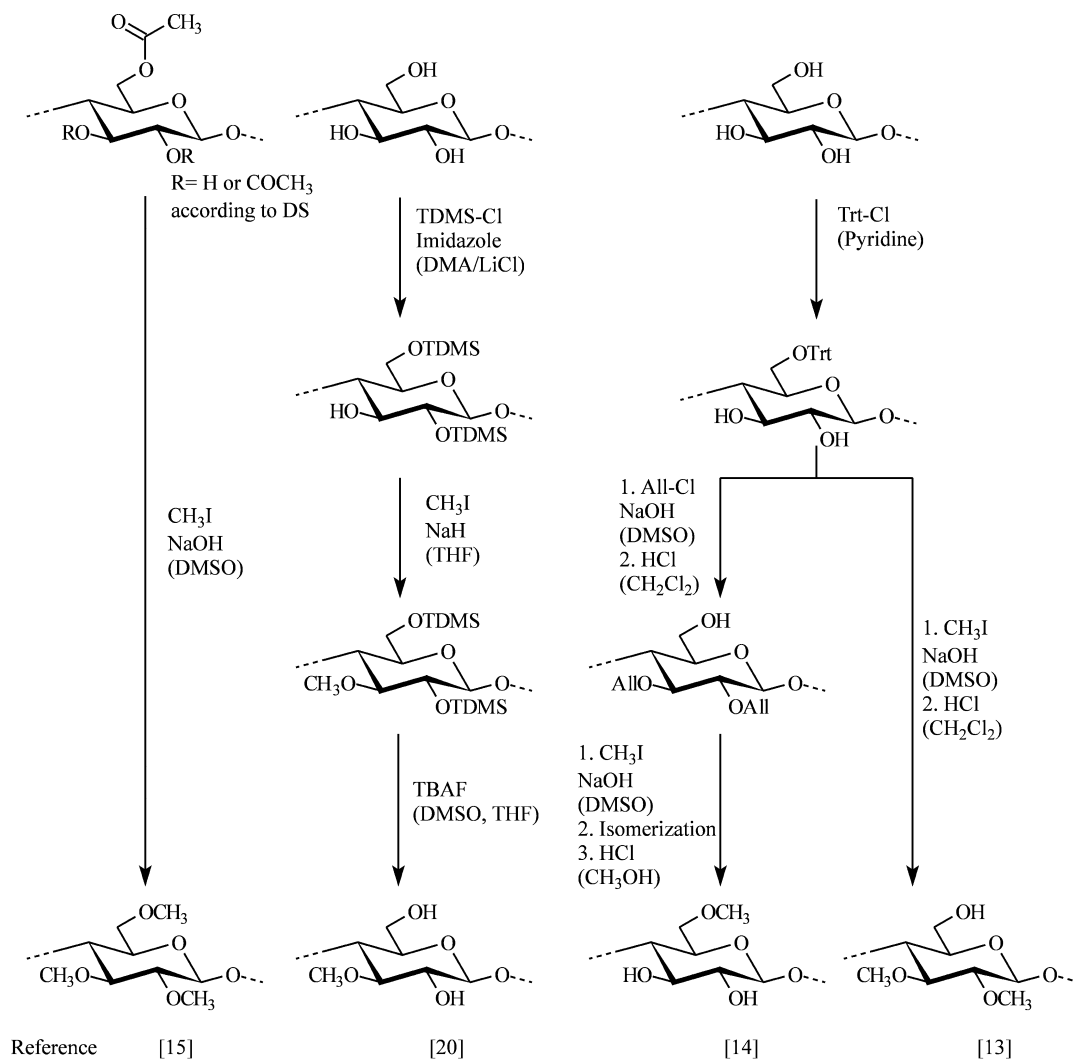
* Corresponding authors. Fax: +49 0 3641 948 272 (T.H.).

E-mail addresses: tekondo@agr.kyushu-u.ac.jp (T. Kondo), thomas.heinze@uni-jena.de (T. Heinze).

[†] Member of the European Polysaccharide Network of Excellence (EPNOE) <http://www.epnoe.eu>

[‡] Fax: +49 3641 548281.

Recently, regioselectively functionalized cellulose derivatives were prepared via cellulose silyl ethers under homogeneous- and heterogeneous reaction conditions.^{17–19} The conversion of cellulose in *N,N*-dimethylacetamide/LiCl with 2,3-dimethyl-2-butyl dimethylchlorosilane (2,3-dimethyl-2-butyl = hexyl, TDMS-Cl) in the presence of imidazole yields structurally uniform 2,6-di-*O*-TDMS cellulose without affecting the OH at C-3 which is the less reactive OH group in the anhydroglucose unit. However, it was shown that even this position can be completely functionalized by conversion with alkyl halides in the presence of sodium hydride. Thus, regioselectively functionalized 3-mono-*O*-alkyl celluloses are accessible after cleavage of the TDMS groups (Fig. 1). This blocking group technique was found to be a universal concept for the preparation of a variety of 3-mono-*O*-functionalized cellulose ethers. The poor solubility of 3-mono-*O*-methyl cellulose (3MC) was explained with the strong intra- and intermolecular hydrogen bonds.²⁰ The solubility of 3-mono-*O*-alkyl celluloses depends on the chain length of the ether substituent. 3-Mono-*O*-allyl cellulose dissolves in, for example, dimethyl sulfoxide.²⁰ 3-Mono-*O*-ethyl cellulose²¹ and 3-mono-*O*-methoxyethyl cellulose²² dissolve also in water. The corresponding 3-mono-*O*-pentyl-, -isopentyl-, and -dodecyl ethers are soluble in less polar solvents like tetrahydrofuran.²³



Allyl (All), degree of substitution (DS), *N,N*-dimethylacetamide (DMA), *N,N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), tetrabutylammonium fluoride trihydrate (TBAF), tetrahydrofuran (THF), hexyldimethylsilyl (TDMS), triphenylmethyl (Trt),

Figure 1. Simplified reaction schemes for the preparation of 2,3,6-tri-*O*-methyl-, 3-mono-*O*-methyl-, 6-mono-*O*-methyl-, and 2,3-di-*O*-methyl cellulose (from left to right).

Therefore, the involvement of 3MC to other regioselectively functionalized methyl celluloses (23MC, 6MC, 236MC) as cellulose model compounds would enable us to further elucidate the character of the intramolecular hydrogen bonds.

2. Results and discussion

In Figure 2, the ^{13}C cross polarization/magic angle spinning (CP/MAS) NMR spectra of 6-mono-*O*-methyl cellulose (6MC), 2,3-di-*O*-methyl cellulose (23MC), 2,3,6-tri-*O*-methyl cellulose (236MC), and amorphous cellulose² as well as of 3-mono-*O*-methyl cellulose (3MC) are shown. The introduction of an alkyl group promotes a strong deshielding of the ^{13}C -nuclei of the functionalized carbinol group, usually by 9 ppm in the solution NMR.^{24,25} In the spectra of cellulose ethers, these characteristics should be reflected in the chemical shifts of the carbon atoms of C-2, C-3, and C-6 bearing alkoxy substituents. Considering the ^{13}C CP/MAS NMR assignments² and the solution-state NMR results of Parfondry and Perlin,²⁶ the chemical shifts in the ^{13}C CP/MAS NMR spectrum of 3MC were assigned.

The signals of the carbon atoms of C-6 bearing OH groups and the signals of the OCH₃ group are overlapped to some extent in the range of 60–70 ppm. If C-3 is methylated, the adjacent carbon atom at C-4, which is assignable in the amorphous cellulose, is supposed to be shifted upfield and then overlapped with the peak of C-5 as shown in the spectra of 23MC and 236MC. Thus, the signal of C-4 in 3MC was detected at 77.84 ppm. Reversibly, the carbon atom of the methylated C-3 is clearly identified in the spectrum and shows a downfield shift to 86.51 ppm due to the strong deshielding. Concerning the chemical shift of C-2 in 3MC, the value may correspond to that of 6MC and amorphous cellulose, which overlapped with the signals of C-4 and C-5 and cannot be clearly identified. The peak of C-1 at 103.54 ppm was easily assignable as those for other derivatives. In a previous report,² the upfield shift was explained by the formation of intramolecular hydrogen bonds between the hydroxyl groups at C-2 and C-6. In this case it is also possible to form a similar type of the intramolecular hydrogen bonds since the slight upfield shift can be seen compared with 236MC. However, it is still hard to recognize the effect. It should be noted that the chemical shift of C-1 of 3MC appeared more

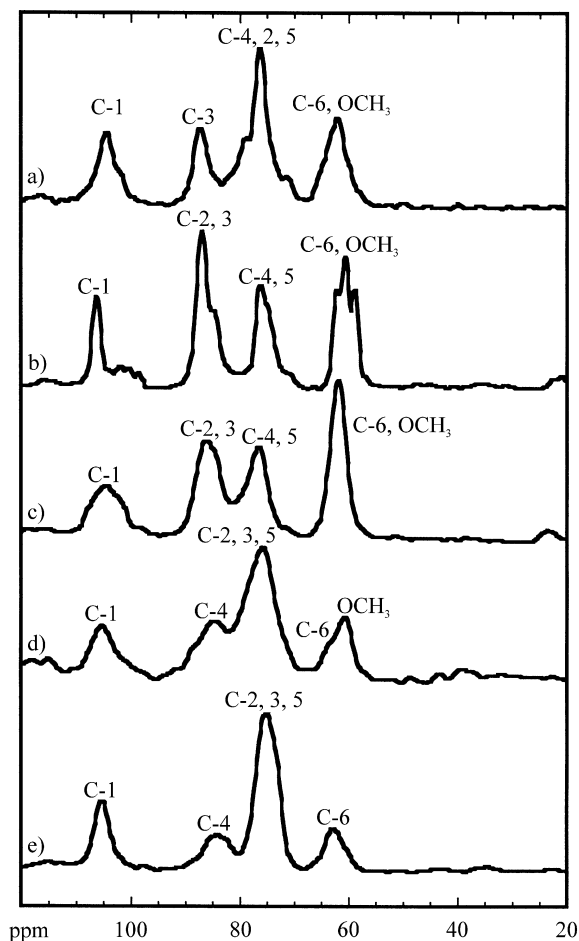


Figure 2. ^{13}C cross polarization/magic angle spinning NMR spectra of 3-mono-*O*-methyl- (a), 2,3,6-tri-*O*-methyl- (b), 2,3-di-*O*-methyl- (c), 6-mono-*O*-methyl- (d), and amorphous cellulose (e).

upfield than 105 ppm, which may be considered due to the intramolecular hydrogen bonds between OH groups at C-2 and C-6 according to the calculation of Kamide et al.^{2,27}

The results of FTIR spectroscopy revealed more clearly the evidence for intramolecular hydrogen bonds. In previous papers, Kondo et al. introduced a curve fitting method to deconvolute IR absorption bands caused by hydroxyl groups in order to characterize hydrogen bond formation in the sample.^{7,10} Therefore, the region of the OH stretching vibration in the range from 3700 to 3050 cm^{-1} was recorded and subjected to the curve fitting. Two main individual bands and their fitting line shape with the original IR absorption band for 3MC were found after deconvolution (Fig. 3).

As the OH group at C-3 is blocked by the methyl ether, the sample cannot have a typical type of intramolecular hydrogen bonds between the OH group at C-3 and the ring oxygen (O-5). However, the deconvoluted band at 3475 cm^{-1} indicates the presence of an intramolecular hydrogen bond. The only possibility for another intramolecular hydrogen bond here is between the hydroxyl groups at C-2 and C-6. A large deconvoluted band at 3340 cm^{-1} indicates that some strong interaction caused by hydrogen bonds may exist.¹⁰ It should be mentioned that even though the hydroxyl group at C-3 was completely methylated, the content of hydroxyl groups, which were not involved in hydrogen bonds, was quite small (at 3583 cm^{-1} due to free OH at C-2),⁷ indicating that almost all hydroxyl groups were included in those interactions. The possible hydrogen bonds in regioselectively functionalized methyl celluloses are shown in Figure 4.

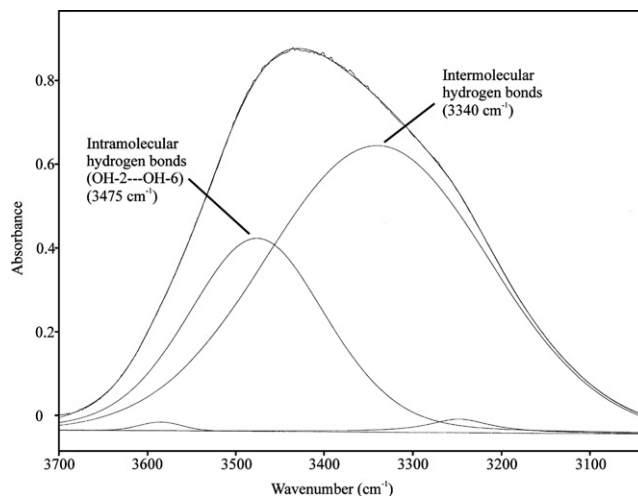


Figure 3. Curve fitting and peak assignments for the OH stretching region in 3-mono-*O*-methyl cellulose.

As crystalline structures sometimes cause strong intermolecular hydrogen bonds, X-ray diffraction measurements were performed to investigate the characteristics of the films. An apparent X-ray crystallinity of 54% was calculated from the diffraction pattern of 3MC (Fig. 5a).

The film samples a, b, and d (Fig. 5) were cast from their solutions in *N,N*-dimethylacetamide, while c was cast from methanol/methylene chloride (1/4, v/v) solution. It was already proposed that hydroxyl groups at C-6 of the anhydroglucose unit in cellulose may strongly contribute to the crystallization.⁶ As shown in Figure 5b and c, this phenomenon was also observed in the case of 23MC, which bears hydroxyl groups at C-6. Thus, as already reported for 6MC and 23MC,¹ the present phenomenon also supports that the

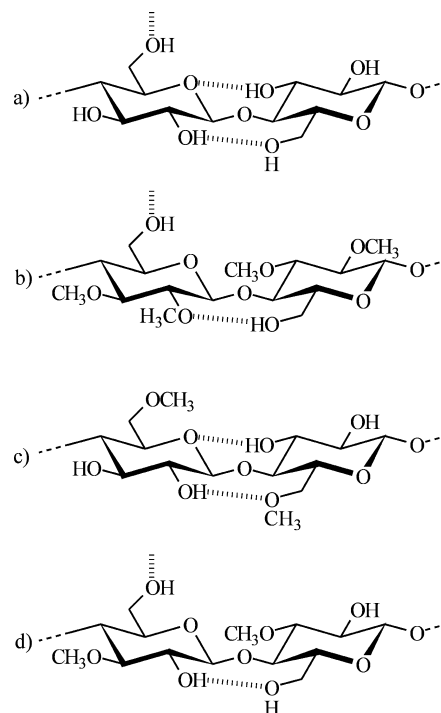


Figure 4. Schematic representation of possible hydrogen bonds in modified cellobiose units of cellulose (a), 2,3-di-*O*-methyl cellulose (b), 6-mono-*O*-methyl cellulose (c), and 3-mono-*O*-methyl cellulose (d).

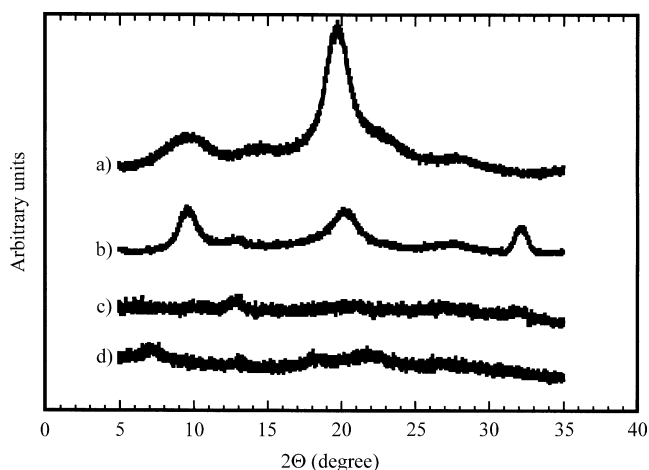


Figure 5. Wide-angle X-ray diffraction patterns for 3-mono-*O*-methyl cellulose (a), crystalline 2,3-di-*O*-methyl cellulose (b), amorphous 2,3-di-*O*-methyl cellulose (c), and 6-mono-*O*-methyl cellulose (d).

usually observed crystallization in cellulose may be dependent on the ability of the hydroxyl groups at C-6 to engage in the formation of intermolecular hydrogen bonds.

To conclude, intramolecular hydrogen bonds in cellulose and cellulose derivatives are known to strongly affect their characteristics. Thus, in this paper it was tried to characterize 3MC, in which the effect of the major intramolecular hydrogen bonds between the hydroxyl groups at C-3 and the ring oxygen of the adjacent anhydroglucose unit is blocked by regioselective methylation of C-3. The hydrogen bond formation was characterized by comparison with other regioselectively functionalized methyl celluloses, for example, 23MC, 6MC, and 236MC. ^{13}C CP/MAS NMR spectra revealed the presence of hydrogen bonds at C-2 in 3MC. Further studies using FTIR spectroscopy in combination with a line fitting method exhibited that instead of intramolecular hydrogen bonds between the hydroxyl group of C-3 and the O-5 of the adjacent anhydroglucose unit another intramolecular hydrogen bond between the hydroxyl groups at C-2 and C-6 may exist in 3MC. The strong interchain bonds due to the absorption at 3340 cm^{-1} were also formed, causing crystallization with relatively high degree of crystallinity. The comparison of the results from wide angle X-ray diffraction for each regioselectively methylated cellulose may also lead to revealing the contribution of the primary hydroxyl group at C-6. In this way, either of two types of intramolecular hydrogen bonds in cellulose tends to be formed as long as hydroxyl groups exist, which may always affect the properties.

3. Experimental

3.1. General methods

Wide angle X-ray diffraction was recorded on a Rigaku Rint-2500F X-ray generator equipped with a pin-hole collimator (1 mm diameter). The nickel filtered $\text{Cu K}\alpha$ radiation was produced at 40 kV and 200 mA. To avoid a uniplanar orientation effect of the cast film samples, the films were cut into small fragments (less than $50\text{ }\mu\text{m}$) and measured by a transmission mode using a scintillation counter with a scanning speed of $0.5^\circ/\text{min}$. The instrumental broadening was corrected by silicon powder as standard material.

The ^{13}C cross polarization/magic angle spinning NMR spectra were recorded on a Chemagnetics CMX 300 spectrometer working at 300.5 MHz for ^1H and 75.57 MHz for ^{13}C with a contact time of 3.0 ms at room temperature. The pulse recycle time was 10 s and

1000 scans were accumulated. Hexamethyl benzene was used as external standard ($\delta = 17.17\text{ ppm}$).

FTIR-spectra were recorded on a Perkin-Elmer Spectrum 2000 FTIR spectrometer between 4000 and 400 cm^{-1} with a resolution of 2 cm^{-1} . A total of 64 scans were averaged. The deconvolution of the IR bands was carried out by means of the GRAMS/32 peak fitting software. The value and the true shape of the peak involved in the hydroxyl absorption bands for the film samples was set to be flexible from two to four and Lorentzian, respectively. The other conditions were mostly flexible and the calculations were repeated until a best-fit was obtained, which exhibited $R^2 > 0.99$.

3.2. Preparation of films from regioselectively functionalized methyl celluloses

The cellulose derivatives 2,3-di-*O*-methyl cellulose (23MC), 6-mono-*O*-methyl cellulose (6MC), and 2,3-6-tri-*O*-methyl cellulose (236MC) were prepared according to previously reported procedures (Fig. 1).^{13–15} 3-Mono-*O*-methyl cellulose (3MC) was prepared according to Ref. 20. The HPLC-grade solvents were used without further purification.

Each polymer in powder form had a uniform structure, in which every structural unit was regioselectively and completely substituted. The average degree of polymerization was in the range from 150 to 200 on the basis of SEC elution curves calibrated with poly(styrene) standards.

The 23MC, 6MC, and 3MC were dissolved in *N,N*-dimethylacetamide (DMA) under stirring at 50°C and centrifuged at 50°C . 236MC was dissolved in methylene chloride. The polymer concentration was 0.8% in any case. One gram of the solutions in DMA was poured into a flat-bottomed tray and kept for 7 d at 50°C under reduced pressure. The methylene chloride solution was evaporated for 1 d at room temperature and subsequently for 7 d at 50°C under vacuum. Predominantly non-crystalline films of 3MC were obtained by using methylene chloride/methanol (4:1, v/v) as solvent. All films were dried for another 3 d at 50°C under high vacuum to remove residual solvents and stored in a desiccator. Pure amorphous cellulose films were prepared according to Ref. 6.

References

- Kondo, T. *J. Polym. Sci., B: Polym. Phys.* **1997**, 35, 717–723.
- Kondo, T. *J. Polym. Sci., B: Polym. Phys.* **1994**, 32, 1229–1236.
- Kondo, T.; Sawatari, C.; Manley, R. St.-J.; Gray, D. G. *Macromolecules* **1994**, 27, 210–215.
- Itagaki, H.; Takahashi, I.; Natsume, M.; Kondo, T. *Polym. Bull.* **1994**, 32, 77–81.
- Kondo, T.; Sawatari, C. *Polymer* **1994**, 35, 4423–4428.
- Kondo, T.; Sawatari, C. *Polymer* **1996**, 37, 393–399.
- Kondo, T. *Cellulose* **1997**, 4, 281–292.
- Kondo, T.; Miyamoto, T. *Polymer* **1998**, 39, 1123–1127.
- Kondo, T.; Sawatari, C. Interchain Hydrogen Bonds in Cellulose-Poly(vinyl alcohol) Characterized by Differential Scanning Calorimetry and Solid-State NMR Analyses Using Cellulose Model Compounds. In: *Cellulose Derivatives: Modification, Characterization, and Nanostructures*, Heinze, Th., Glasser, W., Eds.; American Chemical Society: Washington, DC, ACS Symp. Ser.; 1998; Vol. 688, pp 296–305.
- Shin, J.-H.; Kondo, T. *Polymer* **1998**, 39, 6899–6904.
- Itagaki, H.; Tokai, M.; Kondo, T. *Polymer* **1997**, 38, 4201–4205.
- Kondo, T. Hydrogen Bonds in Cellulose and Cellulose Derivatives. In *Polysaccharides: Structural diversity and functional versatility*; Dumitriu, S., Ed.; Marcel Dekker: New York, 1998; pp 131–172.
- Kondo, T.; Gray, D. G. *Carbohydr. Res.* **1991**, 220, 173–183.
- Kondo, T. *Carbohydr. Res.* **1993**, 238, 231–240.
- Kondo, T.; Gray, D. G. *J. Appl. Polym. Sci.* **1992**, 45, 417–423.
- Kondo, T.; Nojiri, M. *Chem. Lett.* **1994**, 1003–1006.
- Klemm, D.; Stein, A. J. M. S.-Pure. *Appl. Chem.* **1995**, A32, 899–904.
- Klemm, D.; Heinze, Th.; Stein, A.; Liebert, T. *Macromol. Symp.* **1995**, 99, 129–140.
- Koschella, A.; Klemm, D. *Macromol. Symp.* **1997**, 120, 115–125.
- Koschella, A.; Heinze, Th.; Klemm, D. *Macromol. Biosci.* **2001**, 1, 49–54.
- Koschella, A.; Fenn, D.; Heinze, Th. *Polym. Bull.* **2006**, 57, 33–41.
- Heinze, Th.; Koschella, A. *Carbohydr. Res.* **2008**, 343, 668–673.

23. Petzold, K.; Klemm, D.; Heublein, B.; Burchard, W.; Savin, G. *Cellulose* **2004**, *11*, 177–193.
24. Dorman, D. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1970**, *92*, 1355–1361.
25. Perlin, A. S.; Casu, B.; Koch, H. J. *Can. J. Chem.* **1970**, *48*, 2596–2606.
26. Parfondry, A.; Perlin, A. S. *Carbohydr. Res.* **1977**, *57*, 39–49.
27. Kamide, K.; Okajima, K.; Kowsaka, K.; Matsui, T. *Polym. J.* **1985**, *17*, 701–706.