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Synthesis, control of substitution pattern and phase transitions of 2,3-di-*O*-methylcellulose

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Abstract

An improved heterogeneous procedure has been found for the regioselective introduction of trityl and 4-methoxytrityl groups at the primary positions of cellulose. The 6-*O*-tritylcelluloses produced were completely methylated by MeI–NaOH in Me_2SO solution. The trityl groups were then completely removed to afford 2,3-di-*O*-methylcellulose without significant degradation of the polymer. ^1H and ^{13}C NMR spectroscopy and degradation analysis showed less than 5% deviation from the regular substitution pattern. Under optimum reaction conditions, almost perfectly regular cellulose derivatives could be obtained. Small changes in the substitution pattern had a strong effect on the phase transitions of the *O*-methylcelluloses in water. It was shown by DSC for the first time that perfect 2,3-di-*O*-methylcellulose does not undergo phase separation at elevated temperatures.

Keywords: Cellulose; Methylation; Substitution pattern; Degradation analysis; NMR; Phase transition

1. Introduction

Statistical *O*-methylcelluloses of degrees of substitution (DS) from 1.6 to 1.9 are technologically important as they can form highly viscous solutions in water [1]. These aqueous solutions may undergo thermoreversible gelation and phase separation at elevated temperatures, typically around 60 °C [2–4]. These phase transitions are heavily dependent on the substitution pattern [5–7] and the molecular weights [4,8] of the *O*-methylcelluloses. They have been attributed to aggregation caused by hydrophobic interactions and partial crystallisation of 2,3,6-tri-*O*-methyl glucopyranosyl sequences (so-called 'cross-linking loci') within the polymer [2]. The distribution of the methyl substituents along the cellulose chain therefore has a strong influence on its solubility and viscosity in water. Both statistical *O*-methylcelluloses with a homogeneous distribution of substituents and a heterogeneous 'block-like' distribution are known [5,9,10]. As the phase diagrams are quite complex and sensitive to the conditions of the synthesis [1,6,11–13],

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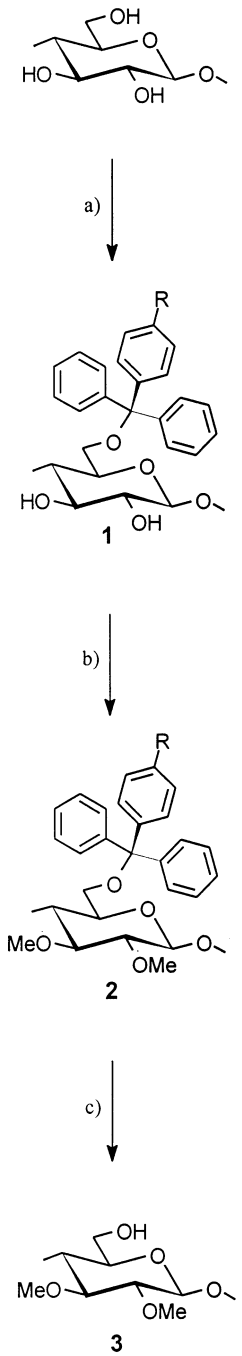
well-defined model compounds have to be generated to achieve a better understanding of the association phenomena.

Except in the synthesis of 2,3,6-tri-*O*-methylcellulose [14,15], regioselective protecting groups have to be used to get a uniform pattern of methylation. Bulky groups such as trityl-, *tert*-butyldimethylsilyl-, thexyldimethylsilyl-(2,3-dimethyl-2-butyl-) are known preferentially to block the readily accessible primary hydroxyl groups OH-6 [10]. Among these groups the trityl moiety appears to provide the greatest regioselectivity. The tritylation of cellulose can be performed either heterogeneously [16,17] or homogeneously in DMAc/LiCl [18]. Complete alkylation of 6-*O*-tritylcellulose and subsequent deprotection affords 2,3-di-*O*-alkylcelluloses [19]. Removal of the trityl groups is known to be sluggish. Klemm, Heinze and co-workers showed that the reactivity of the trityl group can be increased by *p*-methoxy substitution of the phenyl groups. The methoxytrityl chlorides are not only more reactive, but also allow much more rapid deprotection than the unmodified groups [18,20].



Scheme 1. Synthesis of 2,3-di-*O*-methylcellulose via 6-*O*-tritylcellulose (**1a**), R = H, or 6-*O*-(4-O-methoxytrityl)-cellulose (**1b**), R = OMe; (a) trityl chloride or 4-MeO-trityl chloride–Py; (b) MeI–Me_2SO; (c) 5% concd HCl in THF.

The substitution pattern of *O*-methylcelluloses can be monitored by both ^{13}C and ^{1}H NMR spectroscopy [21]. Distribution of the methyl groups between the *O*-2, *O*-3 and *O*-6 positions was already determined from the relative intensities of the signals of C-1, C-4 and C-6. However, the proportionality of their integrals might be questionable because of different relaxation times among the carbon atoms. Small deviations from a regular substitution pattern might also be difficult to detect if they lead only to a broadening of the NMR signal. A more accurate way to determine the substitution pattern of polysaccharides is the detection of monomer or oligomer fragments after degradation by HPLC [18] or by gas–liquid chromatography coupled with mass spectrometry (GLC–MS) [9,22].

In this paper we describe an improved procedure for the synthesis of 2,3-di-*O*-methylcellulose (see Scheme 1) and analysis of its substitution pattern by degradation/GLC–MS. These results are contrasted with those obtained from ^{1}H and ^{13}C NMR spectroscopy. All analytical methods were used to optimise the experimental conditions, leading to an almost perfect 2,3-di-*O*-methylcellulose with highly resolved NMR spectra. The effect of small deviations from the nominal substitution pattern on the phase transitions in water was also measured by differential scanning calorimetry (DSC) and compared with literature data.

2. Results and discussion

*Synthesis of 2,3-di-*O*-methylcellulose* (**3**).—Microcrystalline cellulose with a degree of polymerisation (DP) of 200–220 [23] was used as the starting material since it can readily be activated. Before derivatisation the cellulose has to be mercerised by treatment with 25% sodium hydroxide for 2 days. Lower concentrations or shorter mercerisation times led to incomplete substitution. Tritylation was performed in a suspension of the mercerised cellulose in pyridine under heterogeneous conditions. Both trityl chloride and 4-methoxytrityl chloride reacted selectively with the primary hydroxyl groups at 60 °C. A reaction time of 2 days was required for complete conversion. The DS was determined both gravimetrically [16] and by elemental analysis. The corresponding 6-*O*-tritylcellulose (**1a**) and 6-*O*-(4-methoxytrityl)cellulose (**1b**) were obtained in 80 and 75% yields, respectively.

6-*O*-Tritylcelluloses (**1**) were completely methylated using powdered NaOH and methyl iodide in dimethyl sulfoxide by analogy with the procedures of Ciucanu and Kerek [24] and Gray and Kondo [19]. Iodomethane (MeI) had to be added repeatedly. The completeness of the methylation was monitored by IR [19]. Yields of 6-*O*-trityl-2,3-di-*O*-methylcellulose (**2a**) and 6-*O*-(4-methoxytrityl)-2,3-di-*O*-methylcellulose (**2b**) were 90 and 86%, respectively.

Complete removal of the trityl groups after methylation was more difficult than expected. Several known reaction conditions were tried [17,18,25,26]. Deprotection with concentrated HCl in THF [18] was found to be the most effective method and afforded 2,3-di-*O*-methylcellulose (**3**) in 74% yield. Cleavage of the 4-methoxytrityl group was much faster (5 h) than cleavage of the unmodified trityl group (5 days). Therefore, less degradation occurred during removal of the substituted group. The weight-average DP of **3b′**, $DP_w = 248$, was identical within experimental error to the DP of the starting material. The modified protecting group thus appears considerably better than the trityl group despite its much higher cost.

With slight variations in reaction conditions, five different *O*-methylcelluloses **3** were synthesised having DS values ranging from 1.43 to 2.03 (Table 1). Small differences in substitution patterns were detected by both degradation analysis and NMR spectroscopy.

Determination of the substitution pattern by degradation analysis.—The monomer compositions of the *O*-methylcelluloses **3** were determined by GLC from the fully degraded compounds **3** obtained by total acidic hydrolysis, reduction and acetylation [22,27]. A typical chromatogram is shown in Fig. 1. The total monomer composition of all samples **3** (s_n), and the summarised compositions of un-, mono-, di- and trisubstituted glucose units (c_0, c_1, c_2, and c_3, respectively), as well as the partial DS values at positions *O*-2, *O*-3 and *O*-6 (DS_2, DS_3, and DS_6, respectively) and the total DS were obtained from the peak integrals; they are given in Table 1.

O-Methylcellulose **3a** showed a significant content of monosubstituted glucopyranosyl (Glc*p*) units due to incomplete methylation, mainly at position 3-*O*. This undermethylation was attributed to overly mild conditions, MeI having been added only once. The MeI appears to be consumed by hydrolysis more quickly than it reacts at 3-*O*. Therefore complete methylation requires repeated addition of MeI. The small number ($< 7.2\%$) of monomethylated Glc*p* units in the other compounds **3a′**, **3a″** and **3b′** was attributed to some overtritylation at the secondary positions. It was smaller than the corresponding number found for those *O*-methylcelluloses derived from homogeneously tritylated celluloses [18]. The higher regioselectivity under heterogeneous tritylation conditions might be due to the fact that steric effects are more significant at the surface of mercerised cellulose than in solution.

The substantial content (10.8%) of trimethylated Glc*p* units in **3a″** was attributed to incomplete tritylation. Since the tritylation was in this case performed heterogeneously, conversion of all primary hydroxyl groups demanded complete prior activation of the cellulose.

Heterogeneous derivatisation of cellulose is known to produce copolymers with a hetero-

Table 1
Monomer compositions of *O*-methylcelluloses **3** in the order of increasing total degree of substitution (DS), as determined by methylation analysis, monomer composition (s_n), summarized compositions of un-, mono-, di- and trisubstituted glucose units (c_n) and partial degrees of substitution (DS_n) at positions 2, 3 or 6

Substituent distribution	**3a** [a,c]	**3b** [b,d]	**3b′** [b,e]	**3a′** [a,e]	**3a″** [a,e,f]
s_0 (%)	8.20	5.79	3.09	1.96	3.04
s_2 (%)	31.72	14.17	3.56	1.95	0.82
s_3 (%)	4.58	11.91	3.50	4.84	1.01
s_6 (%)	1.99		0.11		0.31
s_{23} (%)	49.56	66.65	87.68	89.34	83.80
s_{26} (%)	1.00	0.34	0.08	0.56	0.18
s_{36} (%)	0.24	0.27	0.18		0.07
s_{236} (%)	1.07	2.78	1.81	1.35	10.77
c_0 (%)	8.20	5.79	3.09	1.96	3.04
c_1 (%)	38.29	26.08	7.17	6.79	2.14
c_2 (%)	50.80	67.26	87.94	89.90	84.05
c_3 (%)	1.07	2.78	1.81	1.35	10.77
DS_2	0.83	0.84	0.94	0.93	0.96
DS_3	0.56	0.82	0.93	0.96	0.96
DS_6	0.04	0.03	0.02	0.02	0.11
DS	1.43	1.69	1.89	1.91	2.03

[a] Via 6-*O*-tritylcellulose.
[b] Via 6-*O*-(4-methoxytrityl)cellulose.
[c] MeI added once.
[d] MeI added four times.
[e] MeI added five times.
[f] Incomplete mercerisation before tritylation.

geneous distribution of substituents along the polymer chain [9]. Oligomer analysis was carried out to investigate the heterogeneity of methylation in the *O*-methylcelluloses **3**. The samples were fully deuteromethylated using MeI-d_3 and NaOH by analogy with Ciucanu and Kerek [24] prior to a partial depolymerisation. After partial methanolysis the oligomeric mixture was again fully deuteromethylated with MeI-d_3. The resulting product mixture was then analysed by FABMS. For each oligo(*O*-methyl-Glc*p*), the distribution of methyl groups (Fig. 2) could be determined quantitatively from the peak intensities of the fine splitting caused by different deuterium contents [28]. For sample **3a′** the observed numbers of methyl groups were in good agreement with the distributions calculated by Bernoulli statistics from the monomer composition [28]. Thus, the methyl groups of **3a′** were distributed homogeneously along the polymer chain. For the partially overmethylated sample **3a″**, however, there were some measurable deviations from the predicted distributions. There were higher contents of both low-methylated and permethylated oligomers in each oligomeric fraction than expected from theory. This implies that the methyl residues were concentrated in block-like sequences, where 6-*O*-tritylation had not occurred in the first step. The lack of tritylation might have been due to incomplete activation of the cellulose. During mercerisation the mixture must be well stirred, and activated cellulose should never run dry during filtration and storage.

Samples **3b′** and **3a′** displayed an almost perfect substitution pattern. The degrees of methylation at positions 2-*O* and 3-*O* exceeded 93%, while methylation was barely detectable at position 6-*O*. These results show that the regioselectivities of trityl and 4-methoxytrityl groups are equivalent. Thus tritylation and methoxytritylation were both complete at the primary sites.

Determination of the substitution pattern by NMR spectroscopy.—Highly resolved ^{13}C NMR spectra were obtained for the *O*-methylcelluloses **3** in D_2O solution (Fig. 3). The signal of the anomeric carbon C-1 in

particular was very sharp compared with spectra reported previously [21]. Most signals were assigned to regular 2,3-di-*O*-methylcellulose. Assignments were confirmed by heteronuclear COSY NMR spectroscopy of compound **3b′** in Me_2SO-d_6 solution. Only the signals at 81.7 and 61.4 ppm did not belong to 2,3-di-*O*-methylcellulose. They were attributed to undermethylation and overmethylation, respectively. By comparison with earlier work [21,29], the signal at 81.7 ppm was assigned to carbon C-4′ in the vicinity of an unsubstituted C-3 hydroxyl group. Computer calculation by ACD NMR software [30] of the ^{13}C NMR spectrum of a 2,3-di-*O*-methyl-Glc*p* tetramer with one methyl group missing from 3-*O* led to the same assignment. The origin of the small signal at 77 ppm found only in **3a** remains unclear. It might be from C-5′ in the vicinity of an unsubstituted *O*-3.

The integral of the C-4′ signal relative to that of C-1 decreases linearly with the degree of substitution at 3-*O* (as determined by degradation analysis), and this is shown in Fig. 4(a). The slope of the regression line is close to 1, indicating that integration gives reasonable results under the conditions used for this data acquisition. Even small amounts (7%) of undermethylation at *O*-3 are detectable by ^{13}C NMR spectroscopy. In future, therefore, analysis of the signal of C-4′ might be a useful way to quantify undermethylation at 3-*O*.

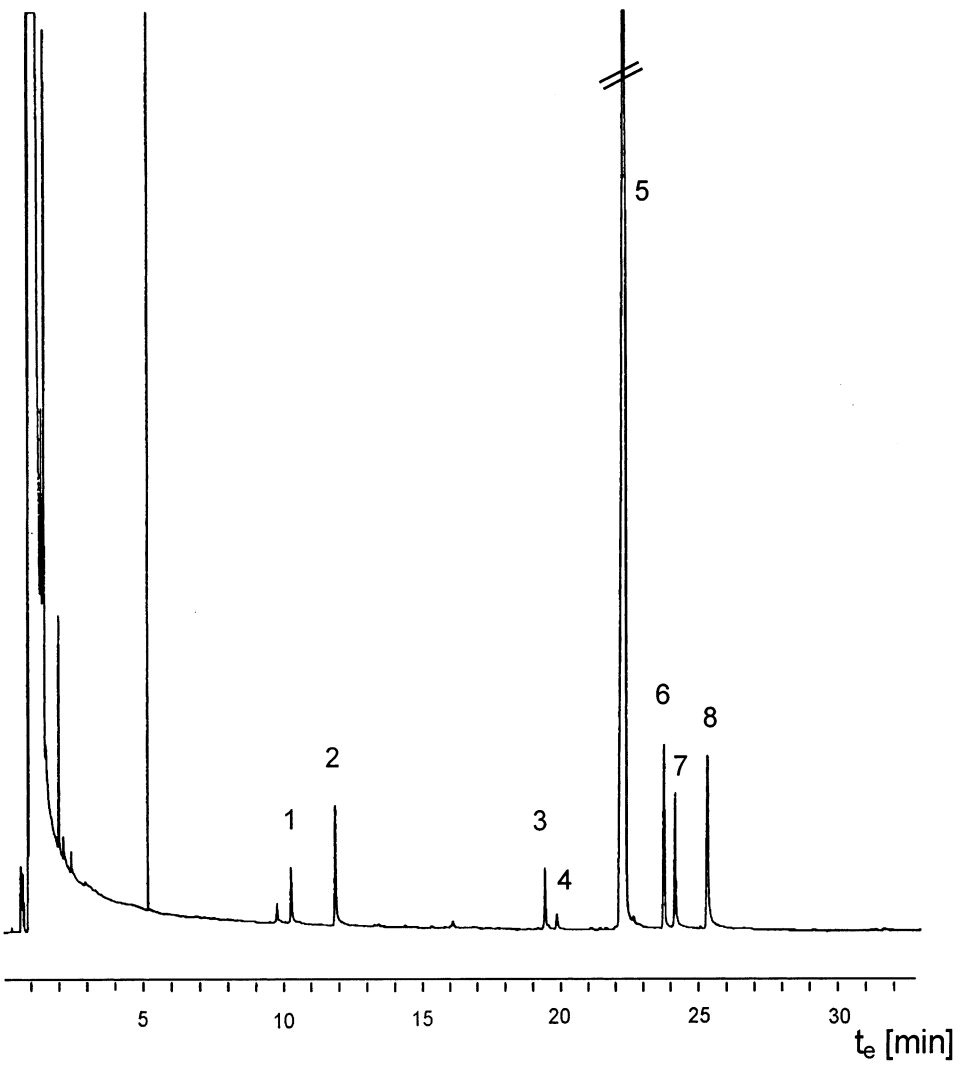


Fig. 1. GLC trace for 2,3-di-*O*-methylcellulose (**3b′**) after hydrolysis. (1) 4-*O*-Acetyl-1,6-anhydro-2,3-di-*O*-methyl-D-Glc*p*; (2) 5-*O*-acetyl-1,6-anhydro-2,3-di-*O*-methyl-D-Glc*f*; (3) 2,3,6-tri-*O*-methylglucose; (4) 2,3,4-tri-*O*-methylglucose; (5) 2,3-di-*O*-methylglucose; (6) 2-*O*-methyl-glucose; (7) 3-*O*-methyl-glucose; (8) glucose.

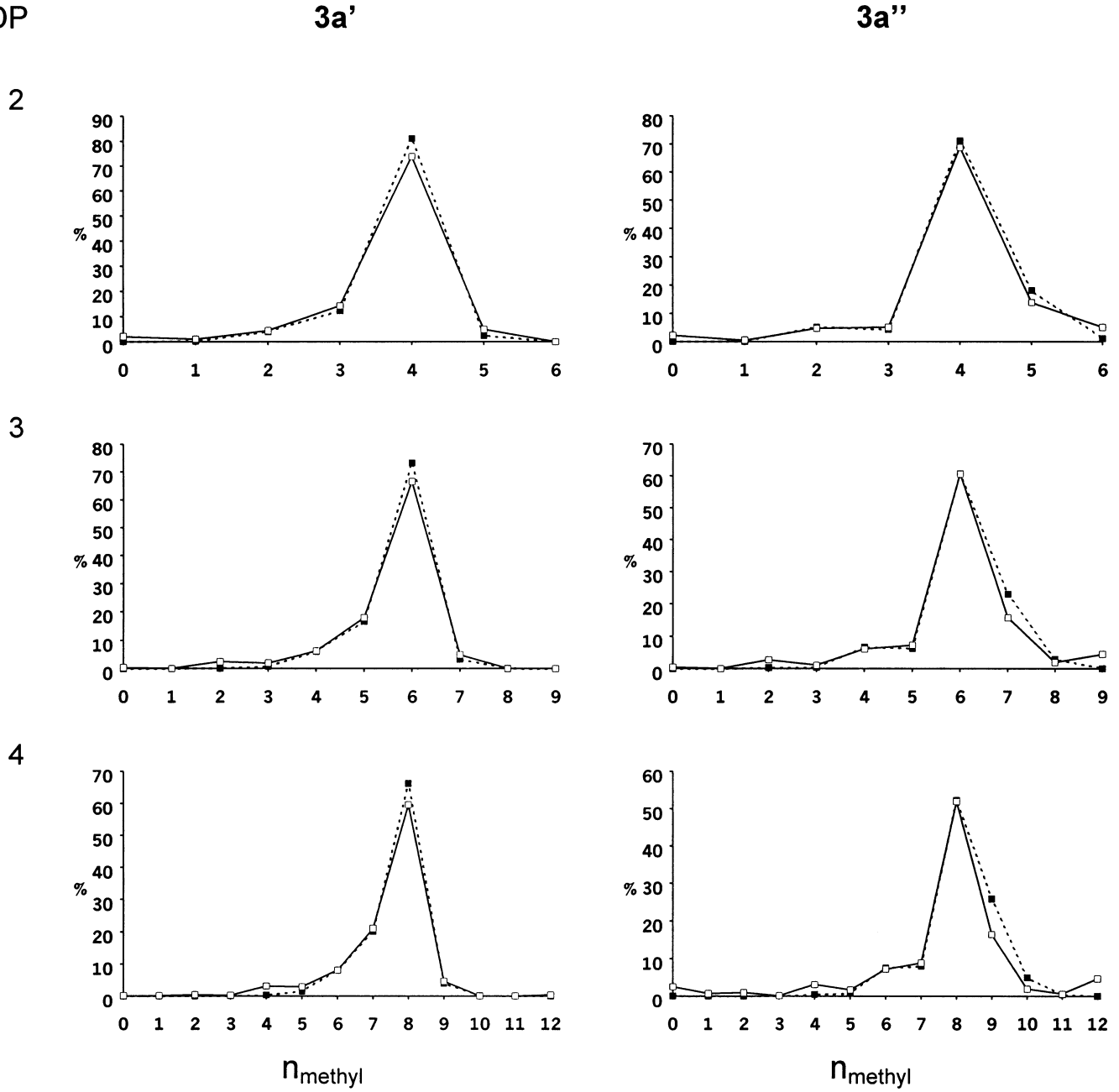


Fig. 2. Distribution of methyl groups in the dimeric (DP = 2), trimeric (DP = 3) and tetrameric (DP = 4) fractions obtained by degradation analysis of *O*-methylcelluloses **3a**′ and **3a**″ in comparison with the pattern calculated for a random substitution of the monomer units in the polymer chain: ■, calculated for a statistical distribution (Bernoulli distribution); □, experimental.

The ^{1}H NMR spectra of the *O*-methylcelluloses **3** dissolved in Me_2SO-d_6 showed a signal at 4.78 ppm, which was also due to undermethylation. This signal was assigned to the secondary hydroxyl groups OH-2 and OH-3. The integral of this signal relative to that of H-2 was plotted as a function of the degree of substitution at positions 2-*O* and 3-*O*, $DS_{2,3}$, as determined by degradation analysis (Fig. 4(b)). Again a straight line was obtained, which could be used for the determination of $DS_{2,3}$ of unknown samples.

The NMR spectra of compounds **3b**′ and **3a**′ were more highly resolved than any precedents in the literature. Practically no signals due to under- or oversubstitution were observed. These cellulose derivatives are therefore suitable starting materials for further synthetic modifications.

Effect of the substitution pattern on the sol–gel phase transition.—According to our degradation and NMR investigations, all the *O*-methylcelluloses **3** except **3a**″ contained methyl substituents only at the secondary sites. Therefore these compounds lend themselves to answering the question of whether only 2,3,6-tri-*O*-methyl-Glc*p* units are responsible as 'cross-linking loci' for the heat-induced gelation and phase transitions of methylcelluloses in water, as stated recently [13].

The phase transitions were studied by both DSC and visual investigation with two different samples. It was started with clear aqueous solutions, which had been annealed for at least 1 h at 5 °C. The concentrations of the *O*-methylcelluloses ranged from 1 to 2.5 wt%. On heating, the undermethylated compound **3b** showed only a weak and broad endothermic signal at around 80 °C (Fig. 5(a)). At this temperature the homogeneous solution first became turbid and then formed a precipitate, which separated from a clear solution. The overmethylated compound **3a**″ showed two distinct endothermic signals at 43 and 62 °C (Fig. 5(b)). First precipitation occurred at 43 °C. Additional precipitation was observed at about 60 °C. These phase transitions exhibited a large hysteresis. On cooling, exothermic

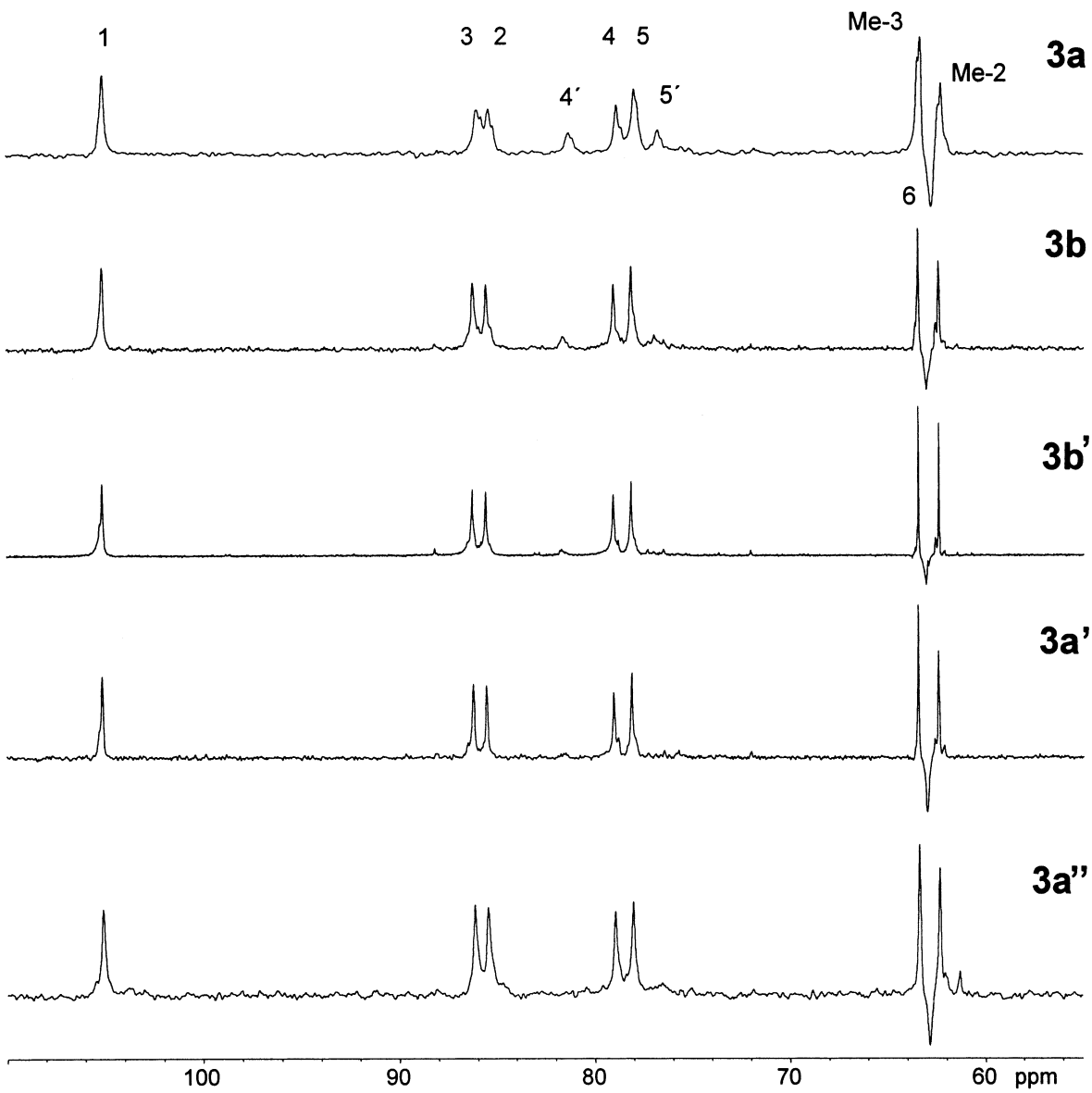


Fig. 3. ^{13}C-DEPT NMR spectra of *O*-methylcelluloses **3** of various degrees of substitution (in D_2O).

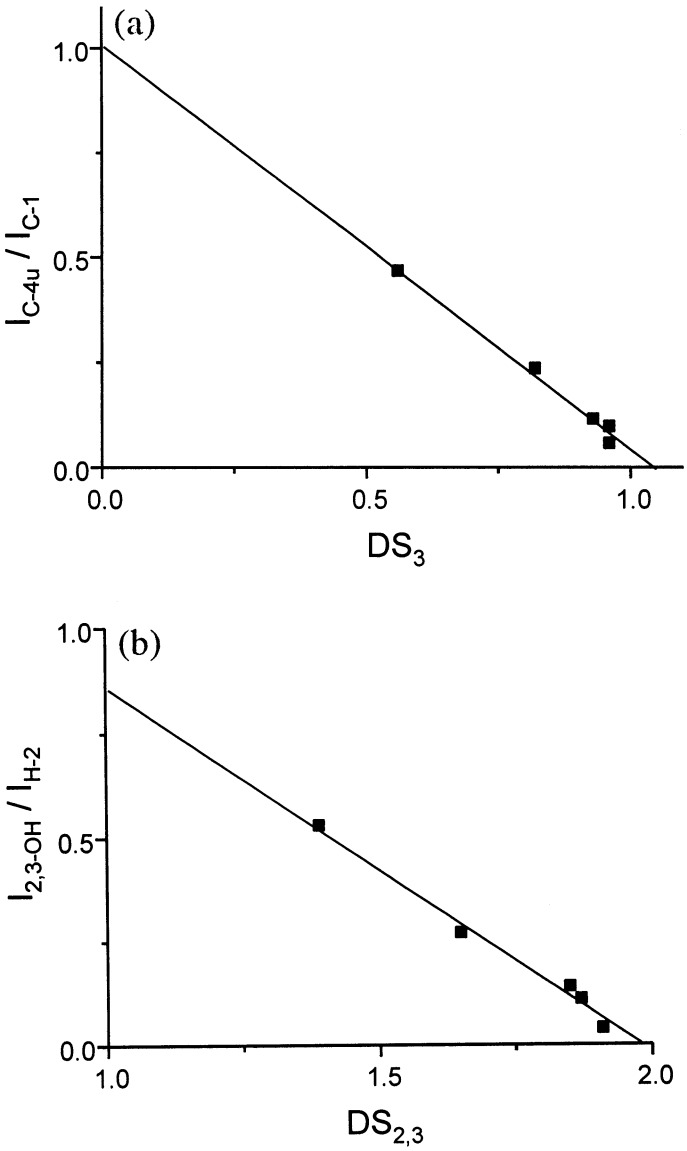


Fig. 4. Detection of the degree of substitution by NMR spectroscopy: (a) the integral ratio of the ^{13}C NMR signals of C-4′ ($\delta = 81.7$ ppm) and C-1 ($\delta = 105.1$ ppm) vs. the degree of substitution at *O*-3, DS_3; (b) the integral ratio of the ^{1}H NMR signals of OH-2,3 ($\delta = 4.78$ ppm) and H-2 ($\delta = 2.77$ ppm) vs. the degree of substitution at *O*-2 and *O*-3, $DS_{2,3}$.

signals were found at very low temperatures (14 °C) where the solution cleared and once again became homogeneous.

The phase transition of the undermethylated sample **3b** (Fig. 5(a)) shows that not only the 2,3,6-tri-*O*-methyl-Glc*p* units can act as 'cross-linking loci' for the aggregation phenomena in water at elevated temperatures, but also monomethylated Glc*p* units. Both hydrogen bonds and hydrophobic interactions between monomethylated Glc*p* units might be responsible for this aggregation. Up until now we have no explanation for the occurrence of two distinct DSC signals for compound **3a**″, which contains significant amounts of 2,3,6-tri-*O*-methyl-Glc*p* units. The phase-transition temperatures are in the range of those of commercial *O*-methylcelluloses [13]. The complete phase diagram of slightly overmethylated 2,3-di-*O*-methylcellulose will be measured in the future.

To our surprise, no DSC signal at all was found across the temperature range 5–90 °C for an aqueous solution of the structurally perfect 2,3-di-*O*-methylcellulose (**3b**′) (Fig. 5(c)). Also, the solution remained clear within this temperature range. There was no experimental evidence for a phase transition below 90 °C. If there is any association, it might be either intramolecular or within submicroscopic aggregates. Further investigations like dynamic light scattering [31] and pyrene fluorescent probe measurements [13] have to be performed to analyse the structure of perfect 2,3-di-*O*-methylcellulose in aqueous solution.

In conclusion, the phase transition of *O*-methylcelluloses might be driven by both intermolecular hydrogen bonds and hydrophobic interactions between Glc*p*, mono-*O*-methyl-Glc*p* units and 2,3,6-tri-*O*-methyl-Glc*p* units. Only 2,3-di-*O*-methyl Glc*p* units seem not to show significant intermolecular interactions. Hence, the solution properties and the phase behaviour of *O*-methylcelluloses are very sensitive to small changes in the substitution pattern.

3. Experimental

Materials.—Commercial microcrystalline cellulose AVICEL-PH101 (Fluka Chemie AG) was used as the starting material. Dimethyl sulfoxide was used as received (Scharlau, 99.6%). THF was dried over KOH and distilled. Pyridine was dried over 3 Å molecular sieves and distilled. Sodium hydroxide, MeI, MeI-d_3, MeOH and acetyl chloride were purchased from E. Merck.

Methods.—IR spectra were recorded by a Bruker type IFS 28 FTIR spectrometer in diffuse reflectance mode by means of the

DRIFT technique. Samples were powdered with KBr. ^{13}C NMR spectra were obtained with a Bruker type AM 400 spectrometer at a frequency of 100.6 MHz, or with a Varian XL 300 spectrometer at a frequency of 75.4 MHz. Dimethyl sulfoxide-d_6, $CDCl_3$, and D_2O were used as solvents. Chemical shifts were referenced to Me_4Si. Elemental analyses were car-

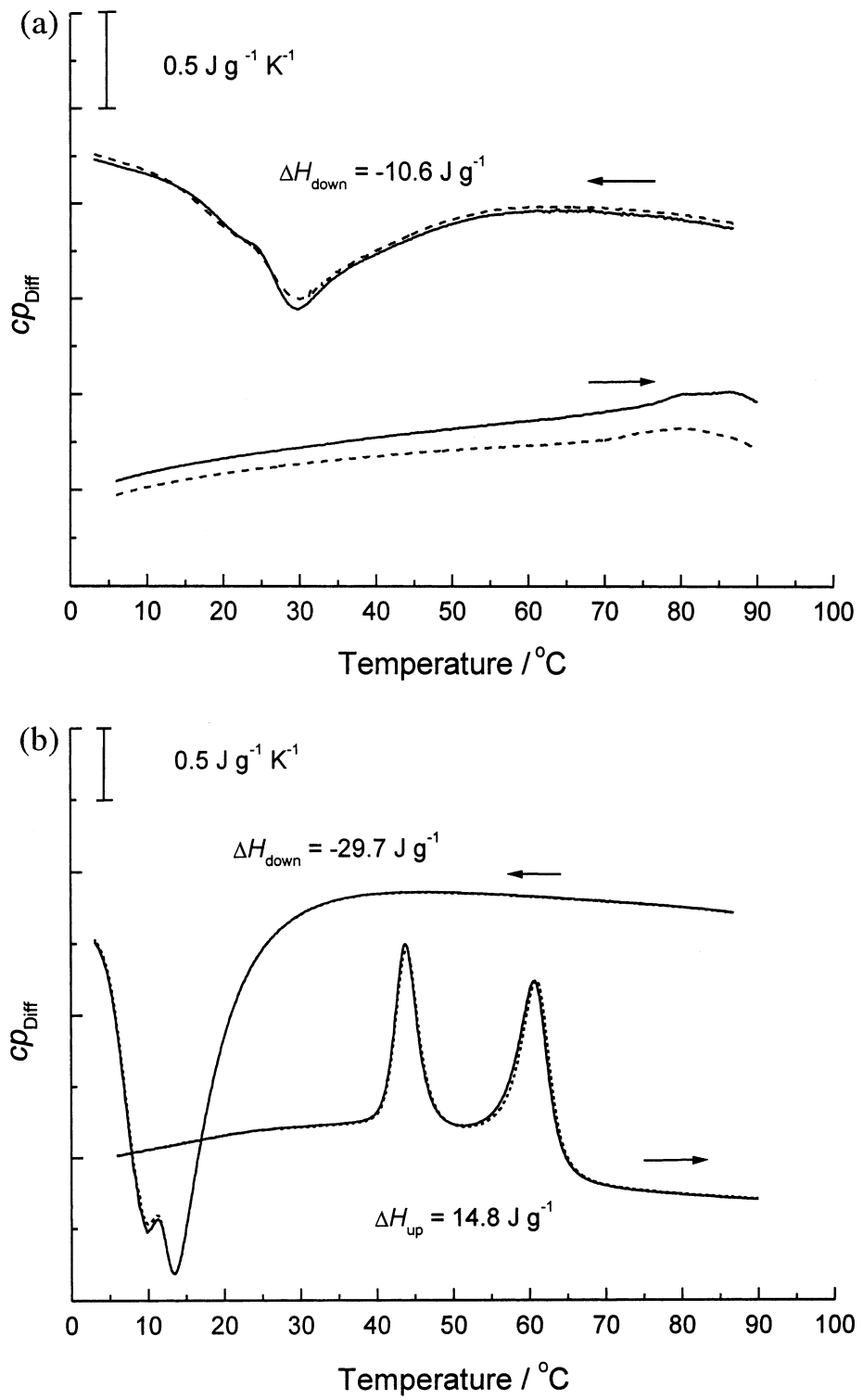


Fig. 5. DSC traces of *O*-methylcelluloses **3** of various degrees of substitution ($c = 25$ mg/mL): differential heat capacities $cp_{Diff.}$ vs. temperature T, — first run, ---- second run: (a) *O*-methylcellulose **3b** (DS = 1.69); (b) *O*-methylcellulose **3a**″ (DS = 2.03); (c) 2,3-di-*O*-methylcellulose (**3b**′) (DS = 1.89).

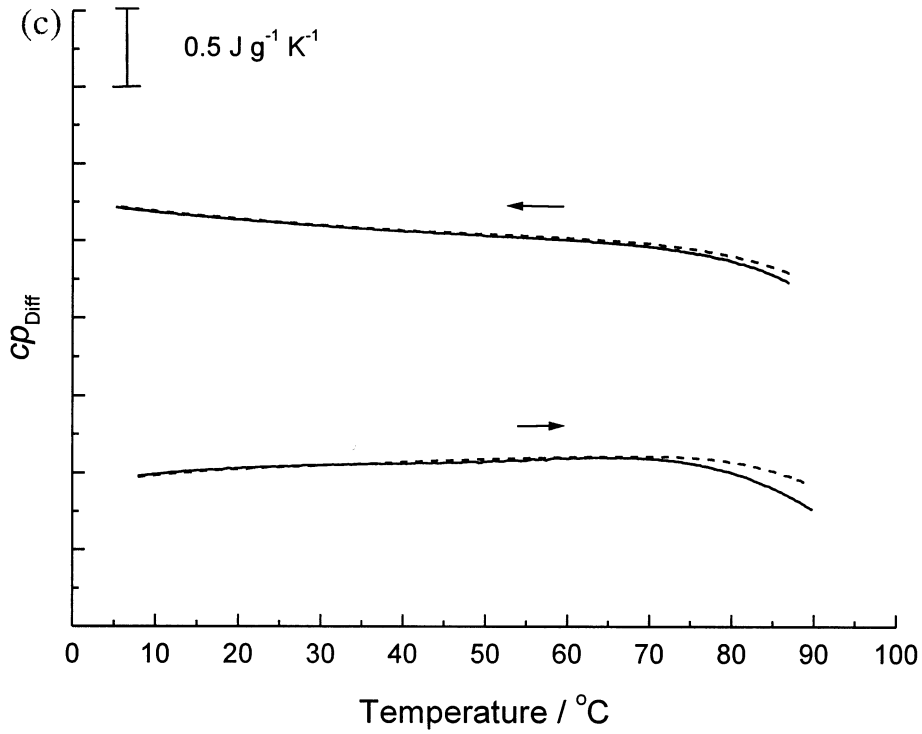


Fig. 5. (*Continued*)

ried out by Analytische Laboratorien in Gummersbach, Germany. FAB mass spectra were measured with a VG/70-250S spectrometer equipped with a Xe source, acceleration voltage 8 kV, positive ion mode, matrix 3-nitrobenzyl alcohol + NaI. The molecular weights of compounds **3b** and **3b′** were determined with a standard Waters–Millipore GPC set-up equipped with a ERC-7512 refractive index detector (Erma Inc.) using SDV columns (Polymer Standards Service, Mainz, Germany) and DMF as eluent. The column was calibrated with narrow-molecular-weight polystyrene standards. For experimental reasons an absolute calibration by light scattering or viscometry was not possible. Therefore the accuracy of the measured molecular weights was only ± 20%. Number-average molecular weights, M_n, and weight-average molecular weights, M_w, were derived. The DSC measurements were performed with a MicroCal VP-DSC scanning calorimeter (MicroCal, Inc., Northampton, MA, USA). The rate of heating and cooling was 0.6 °C/min. The measurements were performed in aqueous solutions at concentrations of 25 mg/mL. Samples were incubated for 1 h at 5 °C, and then measured in a temperature interval from 5 to 90 °C. The reproducibility of the DSC experiments was checked by four consecutive scans of each sample. The accuracy of the phase-transition temperatures was better than ± 2 K. The phase-transition enthalpies were obtained by integration of the peak areas. Specific optical rotation values were determined in aqueous solution ($c = 0.01$ g/mL) with a Perkin–Elmer polarimeter 241.

Monomer analysis.—A sample (2 mg) of a *O*-methylcellulose **3** was fully degraded by treatment with 2 M aq trifluoro acetic acid (1 mL) at 120 °C with stirring for 2 h. The acid was removed in a stream of N_2 at 30 °C and by the subsequent addition of toluene (0.2 mL) dispersed in the same way. The product was reduced using a solution of $NaBD_4$ in water and after removal of borate completely acetylated by Ac_2O–pyridine. The composition of the degradation products was determined by GLC [22,27].

Oligomer analysis.—The *O*-methylcellulose **3** was deuteromethylated twice with powdered NaOH and MeI-d_3 (5 equiv/OH) [9,24]. The product (5 mg) was refluxed in 0.1 M methanolic HCl (1 mL) for 1.5 h. The sample

was then completely dried in a stream of N_2 and deuteromethylated with powdered NaOH and MeI-d_3 (5 equiv/OH). The resulting mixture of oligomeric products was analysed by FABMS [28,32].

Mercerisation of cellulose.—Cellulose (7.5 g, 46.3 mmol) was stirred in 25 wt% aq NaOH (135 mL) at room temperature (rt) for 2 days. After addition of MeOH (180 mL), the suspension was filtered. The residue was washed twice with MeOH and stirred in MeOH (180 mL) for 1 day and then filtered again. The new residue was suspended in pyridine (135 mL) and heated to 60 °C for 4 h. Pyridine was partially (70 mL) distilled off at reduced pressure. Dry pyridine (70 mL) was freshly added and the mixture heated to 60 °C for 1 h.

6-O-*Trityl-cellulose* (**1a**).—A solution of trityl chloride (35.7 g, 116 mmol) in dry pyridine (115 mL) was added by drops to a suspension of mercerised cellulose (7.5 g, 46.3 mmol) in pyridine (135 mL) at rt. The mixture was then refluxed at 95 °C for 95 h, cooled to rt and then poured into MeOH (750 mL). The residue was filtered off and dissolved in Me_2SO, then reprecipitated into MeOH (750 mL), and filtered. The new residue was washed with MeOH and dried at 70 °C under vacuum. Yield 14.9 g (80%), DS 0.97 as determined by elemental analysis. ^{1}H NMR see Table 2, ^{13}C NMR see Table 3; IR (KBr); *v* 3475 (OH), 3057 and 3032 (CH arom.), 1597, 1490 (CC arom.); Anal. Calcd for $C_{25}H_{24}O_5$: C, 74.23; H, 5.98. Found: C, 75.51; H, 5.70.

6-O-*(4-Methoxytrityl)-cellulose* (**1b**).—Compound **1b** was synthesised similarly to **1a** starting from 4-methoxytrityl chloride (35.7 g, 115 mmol) and mercerised cellulose (7.5 g, 46.3 mmol) in abs pyridine (130 mL). The suspension was heated at 95 °C for 69 h. Yield after reprecipitation from Me_2SO–MeOH 15.4 g (76%). DS 1.02 as determined by elemental analysis. ^{1}H NMR see Table 2, ^{13}C NMR see Table 3; IR (KBr); *v* 3479(OH), 3057, 3032 and 2997 (CH arom.), 1607, 1509 (CC arom.), 1251 ($PhOCH_3$), 832 (Ph); Anal. Calcd for $C_{26}H_{26}O_6$: C, 72.07; H, 6.03; O, 22.09. Found: C, 71.93; H, 6.04; O, 21.89.

6-O-*Trityl-2,3-di*-O-*methylcellulose* (**2a**).—Powdered NaOH (20 g, 500 mmol) was dispersed in a soln of 6-*O*-tritylcellulose (**1a**) (8.7 g, 19.7 mmol) in 300 mL Me_2SO (water con-

Table 2
^{1}H NMR data of the cellulose ethers **2** and **3**

No.	Solvent	H-1	H-2	H-3	H-4	H-5	H-6	OMe-2	OMe-3	OH-2,3	OH-6
1a	Me_2SO-d_6	4.68	←		4.0–2.8		→			4.8	
1b	Me_2SO-d_6	4.58	←		4.3–2.7		→			4.80	
2a	$CDCl_3$	4.13	2.86	2.93	4.05	3.05	3.55	3.58, 3.21			
2b	$CDCl_3$	4.00	2.84	2.93	4.14	3.10	3.65	3.56, 3.22			
3b′	Me_2SO-d_6	4.46	2.77	3.20	3.54	3.24	3.72, 3.58	3.45	3.41	4.78 [a]	4.52
3b′	D_2O	4.56	3.17	← 3.77–3.42 →			4.00, 3.77	3.62, 3.61			

[a] Minor signal due to traces of monomethyl-Glc*p* units.

Table 3
^{13}C NMR data of the cellulose ethers **1**, **2**, and **3**

No.	Solvent	C-1	C-2	C-3	C-4	C-5	C-6	OMe-2	OMe-3
1a	Me_2SO-d_6	100.3	←	76.1–73.9		→	61.8		
1b	Me_2SO-d_6	100.1	←	76.2–73.5		→	62.3		
2a	$CDCl_3$	101.0	84.3, 83,6		74.0, 73.8	61.4		60.6, 59.7	
2b	$CDCl_3$	100.9	84.9, 83.8		74.2		61.5	61.0, 60.0	
3b′	Me_2SO-d_6	101.6	83.5	83.9	76.5	75.6	60.7	60.2	59.4
3b′	D_2O	105.1	85.6, 86.3		79.1, 78.1		63.1	63.5, 62.4	

tent 0.1%). After stirring the mixture under N_2 for 24 h at rt, MeI (16.6 mL, 267 mmol) was added by drop to the dispersion. After a further 2 h, MeI (2.8 mL, 44 mmol) was added by drop and the mixture heated to 70 °C for 65 h. After addition of another portion of MeI (2.8 mL, 44 mmol) the mixture was stirred at 70 °C for 18 h. The addition of MeI was further repeated until no hydroxyl groups could be detected by IR at 3475 cm^{-1}. The product was precipitated in MeOH, and filtered off. The residue was then washed with MeOH, water and MeOH again, and dried at 70 °C under vacuum. The product was twice reprecipitated from THF solution, first into water, secondly into MeOH. Yield of **2a** 8.4 g (90%). ^1H and ^{13}C NMR in Tables 2 and 3; Anal. Calcd for $C_{27}H_{28}O_5$: C, 74.97; H, 6.35. Found: C, 74.33; H, 6.37.

6-O-(4-Methoxytrityl)-2,3-di-O-methylcellulose (**2b**).—Compound **2b** was synthesised from **1b** (8.7 g, 19.8 mmol) similarly to **2a**. Yield of **2b** 7.9 g (86%). ^1H and ^{13}C NMR in Tables 2 and 3; IR (KBr); *v* 3057, 3032 and 2997 (CH arom.), 2834 (OCH_3), 1607, 1509 (CC arom.), 1251 ($PhOCH_3$), 832 (Ph); Anal. Calcd for $C_{28}H_{30}O_6$: C, 72.73; H, 6.49; O, 20.78. Found: C, 73.28; H, 6.45; O, 20.23.

2,3-Di-O-methylcellulose (**3b′**).—Compound **2b** (7.2 g, 15.4 mmol) was dissolved in THF (640 mL) and concd HCl (32 mL) were added by drop at rt under N_2. After stirring for 5 h at rt the product was precipitated into acetone and stirred overnight. The product was filtered off, washed twice with acetone, and dried at 50 °C under vacuum. Yield of **3b′** 2.2 g (74%). ^1H and ^{13}C NMR in Tables 2 and 3; IR (KBr); *v* 3423 (OH), 2933 (CH), 2838 (OCH_3), 1074 (C–O–C); molecular weights $M_n = 28{,}430$ g/mol, $M_w = 47{,}080$ g/mol, Anal. Calcd for $C_8H_{14}O_5 \cdot H_2O$: C, 46.15; H, 7.75; O, 46.11. Found: C, 46.36; H, 7.71; O, 45.88; $[\alpha]_D^{20}$ −20.7° (*c* 0.01 g/mL, H_2O).

Compound **3b** was synthesised similarly to **3b′**, yield 58%, $[\alpha]_D^{20}$ −19.5° (*c* 0.01 g/mL, H_2O); molecular weights $M_n = 26{,}840$ g/mol, $M_w = 43{,}390$ g/mol. Samples **3a**, **3a′** and **3a″** were synthesised from 6-*O*-trityl-2,3-di-*O*-methylcelluloses (**2a**) by analogous reaction with 5% concd HCl in THF for 100 h at rt. Yields 45–50%.

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