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SYNTHESIS PATH VERSUS DISTRIBUTION OF FUNCTIONAL GROUPS IN CELLULOSE ETHERS

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Different ways for carboxymethylation of cellulose are discussed exemplary for cellulose ether synthesis in terms of the resulting structural features. The industrially applied slurry process yields polymers with statistic amounts of the four differently substituted repeating units glucose, mono-, di-, and tri-O-carboxymethylglucose. Surprisingly, the newly developed totally homogeneous carboxymethylation in the efficient cellulose solvent Ni[tris(2-aminoethyl)amine]$(OH)_2$ gives exactly the same result. Thus, the polymer is evenly accessible during both reaction paths. In contrast the carboxymethylation starting from homogeneous solutions of cellulose in N,N-dimethyl acetamide /LiCl or solutions of reactive derivatives of cellulose in dimethyl sulfoxide (DMSO) yields polyelectrolytes with a nonstatistic content of the building units. This is achieved via an induced phase separation forming highly reactive microstructures.

INTRODUCTION

A variety of new cellulose solvents was found during the last decade and investigated as reaction medium for polymeranalogeous cellulose derivatization to overcome the disadvantages like irreproducibility and resulting non-uniform structures of totally heterogeneous conversions. Non-aqueous solvent systems like N,N-dimethyl acetamide (DMA)/LiCl [1] and dimethyl sulfoxide (DMSO)/SO_2/diethylamine [2] were believed to be the desired tool for the preparation of cellulose derivatives with defined molecular structures both on the level of the repeating unit

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as well as along the polymer chain. It was shown that these systems are usable for preparing uniform samples of high degree of substitution (DS) and even fully substituted ethers and esters can be obtained. In case of partially functionalized products (DS <3) cellulose esters with an even distribution along the polymer chain may be synthesized [3]. However, for the ether synthesis drastic limitations in synthesizing partially substituted polymers were stated [4]. One alternative approach was the application of soluble protected celluloses which can be obtained by the reaction of cellulose with bulky reagents like triphenylchloromethane. Via these protected celluloses the preparation of 2,3-di-O-carboxymethyl cellulose [5] and 2,3-di-O-methyl cellulose [6] was possible. In this way a defined molecular structure on the level of the repeating unit is accessible. In contrast the synthesis of polymers with a defined distribution of substituents along the polymer chain is still not possible via a polymeranalogeous path. Consequently, new synthesis concepts as well as appropriate analytical tools need to be established for this purpose.

This paper combines a summary of our results concerning new approaches to control the content and the distribution of the differently modified repeating units of cellulose ethers exemplified for carboxymethyl cellulose (CMC). Moreover, adapted analytical techniques for the determination of structural features for such cellulose ethers are presented.

EXPERIMENTAL

Materials

Starting celluloses used were Avicel (degree of polymerization, DP=280), spruce sulfite pulp (DP=680) and cotton linters (DP=1350). N,N-dimethyl acetamide (DMA), NaOH, sodium monochloroacetate and LiCl were purchased from FLUKA. DMA was dried over CaH_2 and distilled under reduced pressure. All other chemicals were used after drying at 105°C for 5 h in vacuum. Solutions of cellulose in DMA/LiCl (1.7 % w/v) were prepared according to Ref. [1].

The synthesis of the intermediates is described: cellulose trifluoroacetate (DS=1.5) [7,8], cellulose formate (DS=2.2) [9] and trimethylsilyl cellulose (DS=1.1) [10].

Heterogeneous Carboxymethylation (Slurry process), 1

2.66 ml of 5 % (w/v) NaOH is added dropwise to a suspension of 1 g cellulose in 30 ml isopropanol over a period of 10 min at room temperature. After 1 hour of vigorous stirring 1.2 g of sodium monochloroacetate was added. The reaction mixture was kept for 5 h at 55°C. Isolation was carried out by filtration, suspension of the polymer in 60 ml aqueous methanol, neutralization with dilute acetic acid and washing with 80 % aqueous ethanol (three times) and ethanol. After drying at 60°C under reduced pressure for 5 h a white product was obtained.

DS_{CMC}(HPLC)=0.59; IR (KBr) 1630 cm^{-1}, 1410 cm^{-1} ($\nu_{C=O}$, carboxylate group)

Carboxymethylation via induced phase separation, 2

a) Starting from cellulose/DMA/LiCl (2a): To a solution containing 1g cellulose a suspension of 2.47 g pulverized NaOH in 20 ml DMA and a suspension of 3.59 g sodium monochloroacetate in 20 ml DMA were added under vigorous stirring. The temperature was raised to 70°C. After 48 h the mixture was cooled to room temperature and was precipitated into 300 ml methanol. The precipitates were filtered off, dissolved in 75 ml distilled water, neutralized with acetic acid and reprecipitated into 300 ml ethanol. After filtration the products were washed with ethanol and dried in vacuum at 50°C.

DS_{CMC}(HPLC)=2.07; IR (KBr) 1620 cm^{-1}, 1410 cm^{-1} ($\nu_{C=O}$, carboxylate group)

b) Starting from cellulose intermediates in DMSO (2b-2e): For a typical preparation, 1g of the intermediate was dissolved in 17.5 ml DMSO under nitrogen. A suspension of dried pulverized NaOH (4-40 mol per mol AGU, see table 2) in DMSO (2.75 ml per g NaOH) was added to the solution within 10 minutes, followed by sodium monochloroacetate (2-20 mol per mol AGU, see Table 2) under vigorous stirring. The temperature was raised to 70 °C. After various reaction times (Table 2) the reaction mixture was cooled to room temperature and precipitated into 300 ml methanol. The precipitate was filtered off, dissolved or suspended (in dependence on the DS_{CMC}) in water, neutralized with acetic acid, and reprecipitated into 100 ml of 80 % (v/v) aqueous ethanol.

DS_{CMC} (HPLC) are given in Table 2; IR (KBr): 1620 cm^{-1}, 1410 cm^{-1} ($\nu_{C=O}$, carboxylate group).

Homogeneous Carboxymethylation, 3

1 g cellulose was dissolved at room temperature in 10 ml $Ni(tren)(OH)_2$. 9.87 g NaOH in 32 ml water and 14.32 g sodium monochloroacetate in 40 ml water were added in 4 steps in equal portions over a period of 2 h. After the first addition the temperature was raised to 70°C. This temperature was kept constant during the addition of the reagents and for 2 h, additionally. The obtained polymer was isolated by precipitation in 300 ml methanol, dissolution in water, neutralization with dilute acetic acid and precipitation in ethanol. For removal of the inorganic impurities the samples were suspended in 80 % aqueous ethanol (three times), in ethanol and dialyzed for 5 days against distilled water.

DS_{CMC}(HPLC)=0.71; IR (KBr) 1630 cm^{-1}, 1410 cm^{-1} ($\nu_{C=O}$, carboxylate group)

Measurements

For HPLC analysis according to Ref. [12] the CMCs were hydrolyzed with $HClO_4$ [13]. For this purpose the samples (0.1 g) were dispersed in 2 ml $HClO_4$ (70%) and after 10 min at room temperature dilute with 18 ml distilled water. This mixture was kept at 100°C for 16 h. The solution obtained was carefully neutralized 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 ml and dilute with distilled water to give exactly 5 ml sample. The HPLC-analysis was carried out using a Bio-Rad Aminex HPX-87A (H^+ form) column, 0.001 N H_2SO_4 as eluent, flow rate 0.5 ml/min. ^{1}H-NMR analysis was carried out according to ref. [14]. For FTIR measurements a Bio Rad FTS 175 in combination with an UMA 500 microscope (reflexion mode) was applied.

RESULTS AND DISCUSSION

Analytical tools for the characterization of CMC

An essential step in the evaluation and development of synthesis paths is the establishment of analytical tools for the determination of structural features of the cellulose product in question. The distribution of substituents on the level of the anhydroglucose unit (AGU) is usually characterized by NMR spectroscopy. ^{1}H-NMR can be applied on degraded polymers. With this method it is possible to calculate the partial degrees of substitution (DS) at the three reactive sites [14]. ^{13}C-NMR is carried out for qualitative analysis of the intact polymer [15]. On the other hand, ^{13}C-NMR was used for the determination of the mole fractions of the four basic units (glucose, mono-O-carboxymethyl glucose, di-O-carboxymethyl glucose, 2,3,6 tri-O-carboxymethyl glucose) that built up the polymer chain in case of partially derivatized polymers [16].

A more efficient method was established to obtain information about the distribution of substituents along the polymer chain using HPLC after chain degradation [12]. After treatment of the polymer with perchloric acid and neutralization with KOH the obtained mixture of glucose and carboxymethylated glucoses is separated on a Bio-Rad Aminex (H^+form) column. From these chromatograms the mole fractions of the building units as well as the total degree of substitution is accessible.

Heterogeneous Carboxymethylation

The industrially applied heterogeneous carboxymethylation of cellulose in water / isopropanol is today still combined with a number of irreproducible effects. It was believed that this is due to the heterogeneous reaction conditions and consequently due to structural heterogeneity. Thus, the determination of structural features is a major concern.

If the above discussed methods are applied to commercial CMC samples (e.g. DS_{HPLC}=1.24; **1a**) two basic structural features are revealed. The polymer shows a distribution of substituents on the level of the AGU in the order C-2 > C-6 >> C-3 (DS_{C-2}=0.67, DS_{C-6}=0.36, DS_{C-3}=0.21; DS_{H-NMR}=1.24). Comparison of the HPLC results with statistic calculations, first carried out by [16] and specificly discussed in [12], show no significant deviation (Table 1; Fig. 1). Consequently, the polymers are built up of strictly statistic amounts of glucose, mono-, di-, and tri-O-carboxymethyl glucose. This leads to the assumption that these polymers show no gradient of reactivity along the polymer chain and should be totally accessible during the carboxymethylation reaction.

In a series of experiments the amount of the swelling agent NaOH in the carboxymethylation mixture was diminished successively to partially keep the native superstructure of the polysaccharide. Concentrations of NaOH in the mixture as low as 5 % were applied. Although the DS_{CMC} reachs only a value of 0.59 (with 15 % lye DS=1.24 [17]), surprisingly, the sample obtained (**1b**) again consists of statistic contents of glucose and carboxymethyl glucoses (Table 1; Fig. 1). That means, under the conditions of the Williamson ether synthesis the supramoleculare structure can not be used to control the pattern of functionalization.

Carboxymethylation via induced phase separation

By means of a new synthesis concept developed by us, carboxymethylation was carried out starting from homogeneous solutions of cellulose in DMA/LiCl or from cellulose intermediates

TABLE 1 HPLC-analysis (resulting mole fractions of C_u: unsubstituted glucose; C_m: mono-O-carboxymethyl glucose; C_d:di-O-carboxymethyl glucose; C_t: tri-O-carboxymethyl glucose) of heterogeneously prepared carboxymethyl cellulose samples (synthesized in isopropanol/ aqueous NaOH) after chain degradation

sample	DS_{HPLC}		MOLE	FRACTION		
			C_u	C_m	C_d	C_t
1a*	1.24	determined	0.20	0.43	0.30	0.07
		calculated	0.20	0.43	0.30	0.07
1b**	0.59	determined	0.52	0.38	0.09	0.01
		calculated	0.52	0.38	0.09	0.01

*) prepared with 15 % (w/v) aqueous NaOH

**) prepared with 5 % (w/v) aqueous NaOH

TABLE 2 Conditions and results of carboxymethylation of different cellulose intermediates via "induced phase separation"

CELLULOSE	INTERMEDIATE DS	Ref.	sample code	reaction time in h	ratio of reagent*	maximum DS_{CMC}
cellulose in DMA/LiCl	-	-	2a	48	1:5:10	2.07
cellulose triflouroacetate	1.5	[7,8]	2b	4	1:10:20	1.86
cellulose formate	2.2	[8,9]	2c	2	1:20:40	2.21
cellulose acetate	0.8	-	2d	4	1:10:20	0.45
trimethylsilyl cellulose	1.1	[10]	2e	0.5	1:10:20	2.04

*) molar ratios: AGU/sodium monochloroacetate/NaOH

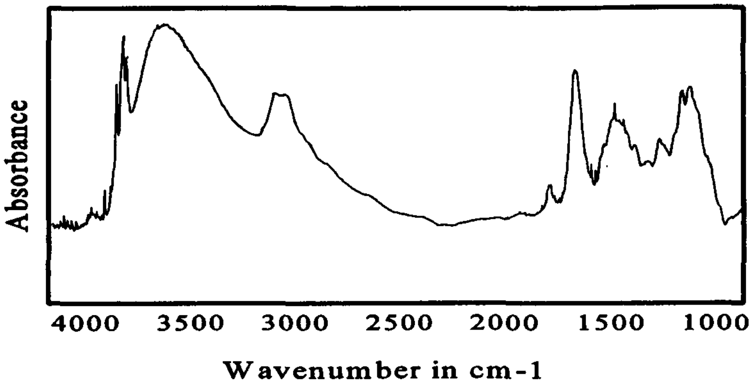

Figure 1 FTIR-spectum of the interface NaOH-regenerated cellulose (from CTFA in DMSO) observed with a FTIR microscope

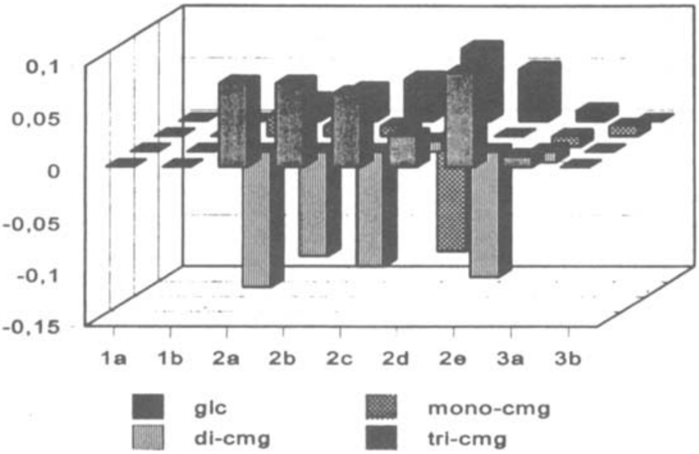

Figure 2 Results of the comparison of HPLC analyses and statistic calculations as absolute deviation for CMC samples prepared by heterogeneous carboxymethylation (sample **1a** and **1b**), carboxymethylation via "induced phase separation" (samples **2a**-**2e**), and homogeneous carboxymethylation (samples **3a** and **3b**)

in dipolar aprotic solvents like dimethyl sulfoxide (DMSO). By adding solid NaOH particles to the various solutions a phase separation is induced forming a reactive microstructure. The different intermediates, which may be applied, showed both a different hydrolytic stability and hydrophilicity (Table 2). In any case it was observed by means of polarizing light microscopy and by deconvoluted FTIR spectroscopy that the treatment of the solutions with the suspended solid NaOH yields a gel-like system of regenerated cellulose [9]. As result the subsequent etherification gives products of changed functionalization pattern within both the level of the AGU (distribution in the order C-6>C-3>C-2, e.g. in case of **2b**: DS_{C-6}=0.81, DS_{C-2}=0.25, DS_{C-3} =0.6; DS_{1H-NMR}=1.66) and along the polymer chain. As can be seen by comparison of the HPLC results with statistic calculations (Table 3; Fig. 1) higher amounts of unfunctionalized and of fully 2,3,6-O-carboxymethylated building units were formed. This nonstatistic distribution disappears if water is present during the reaction. In case of the comparatively hydrophilic cellulose acetate (DS 0.8) even 1% (w/w) in the medium is sufficient.

On the other hand, this synthesis path yields polymers with DS-values as high as 2.2 in a one-step-synthesis. FTIR-microscopy was used to gain information about the reasons for this high reactivity. In a typical spectrum of the interface polymer-NaOH particle (Fig. 2) sharp OH-valence vibrations in the region from 3580 to 3680 cm^{-1} besides the characteristic broad OH bands of cellulose (indicating hydrogen bond interactions) are observed. In correlation with low molecular weight alcohols e.g. n-butanol which exhibit comparable spectroscopic features during dilution with the aprotic solvent tetrachloromethane [18] it was concluded that this observation is due to a partial collapse of the hydrogen bond system. Thus, the increased reactivity might be attributed to the formation of "naked" OH-groups.

Only alkali hydroxides are capable for the preparation of carboxymethyl cellulose in these solvents. Alternative bases like amines or alcoholates do not yield cellulose ether. Thus, no totally homogeneous carboxymethylation is possible in these dipolar aprotic organic solvents.

TABLE 3 Mole fractions (C_u: unsubstituted glucose; C_m : mono-O-carboxymethyl glucose; C_d:di-O-carboxymethyl glucose; C_t: tri-O-carboxymethyl glucose) of carboxymethyl cellulose samples prepared via "induced phase separation" revealed by means of HPLC analysis after chain degradation

CARBOXYMETHYL CELLULOSE			MOLE FRACTION			
	DS_{HPLC}		C_g	C_m	C_d	C_t
2a	2.07	determined	0.05	0.23	0.31	0.4
		calculated	0.03	0.20	0.44	0.32
2b	1.86	determined	0.08	0.28	0.33	0.31
		calculated	0.05	0.27	0.43	0.23
2c	2.21	determined	0.06	0.16	0.31	0.47
		calculated	0.02	0.15	0.42	0.40
2d	0.45	determined	0.69	0.21	0.07	0.03
		calculated	0.62	0.32	0.06	0.00
2e	1.91	determined	0.14	0.19	0.29	0.38
		calculated	0.05	0.25	0.44	0.26

TABLE 4 Results of HPLC analysis (after chain degradation) of carboxymethyl cellulose samples prepared homogeneously in the solvent Ni(tren)(OH)$_2$

CARBOXYMETHYL CELLULOSE			MOLE FRACTION			
	DS_{HPLC}		C_g	C_m	C_d	C_t
3a	0.54	determined	0.57	0.33	0.07	0.02
		calculated	0.55	0.35	0.08	0.01
3b	0.71	determined	0.44	0.44	0.13	0.01
		calculated	0.44	0.41	0.13	0.01

Homogeneous Carboxymethylation

It was found that the highly efficient aqueous cellulose solvent Ni(tren)$(OH)_2$ [11]; [tren=tris(2-aminoethyl)amine] is useful for homogeneous etherifications of the polymer. In a first series of carboxymethylation reactions, solutions of cellulose (10 % w/v) were converted with sodium monochloroacetate without an additional base. The maximum DS reached was 0.22. The basicity of the solvent system is not sufficient for the preparation of soluble CMCs. The addition of aqueous NaOH was necessary. It was possible to add both aqueous solutions of the base as well as the reagent without regeneration of the cellulose. This totally homogeneous carboxymethylation yield polymers with DS values of 0.51 (**3a**) by conversion with molar ratios of 1:20:10 (AGU/NaOH/sodium monochloroacetate) and reaction times of 2 hours. Neither the increase of reagents nor longer reaction times do have a drastic influence on the total DS. To diminish hydrolysis of the sodium monochloroacetate during the conversion addition of the reagents was carried out stepwise. In this way a small increase in DS is possible (up to 0.71; **3b**). The CMCs are soluble in water starting from DS 0.4. This is in the same range as observed for commercial CMCs. Attempts were made to increase the reactivity of the system by partial liberation of OH-groups from the coordination of the solvent but e.g. stepwise addition of ethylenediamine results in inhomogeneous reaction mixtures yielding only insoluble polymers. The ^{1}H-NMR analysis of hydrolyzates reveals a distribution of substituents within the AGU in the order C-6>C-2>C-3 (DS_{C-6}=0.19; DS_{C-2}=0.17, DS_{C-3}=0.08; DS_{1H-NMR}=0.44).

Comparison of the mole fractions of the differently substituted repeating units determined by HPLC after chain degradation with the statistic calculations shows that in any case the polymers are build up of statistic amounts of these units (see Table 4; Fig. 1).

CONCLUSIONS

Three basic synthesis pathways are possible for the preparation of water-soluble carboxymethyl celluloses. A remarkable finding was that homogeneously and heterogeneously prepared samples show comparable structural features. Especially the strictly statistic amounts of basic units (glucose and mono-, di-, and tri-O-carboxymethyl glucoses) that build up the polymer chains lead to the assumption that in both cases an even accessibility of the chain is achieved. The only possible way to obtain polymers with non-statistic amounts of building units e.g. a non-statistic distribution of substituents is a reaction via induced phase separation starting from homogeneously dissolved cellulose materials. These polymers exhibit new properties compared with commercial samples. The limiting value for water solubility is increased from 0.4 to 1.5. A strong tendency towards aggregation can be concluded from GPC measurements, decreased viscosity for samples with comparable DP-values and an increased tolerance of these CMC solutions towards the addition of salts [19]. On the other hand the enzymatic degradation behavior varies if the samples are treated with cellulase mixtures. The drop in viscosity during the degradation of non-statistic CMCs is less drastic. This could be a first hint for the occurrence of polymer fragments with high degrees of substitution. The analysis of these oligomeric fragments is under progress.

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