4.2. Chemical Characteristics of Cellulose Acetate

Thomas Heinze, Tim Liebert*

Center of Excellence for Polysaccharide Research at the Friedrich Schiller University of Jena, Lessingstrasse 8, D-07743 Jena, Germany
Email: thomas.heinze@uni-jena.de

Summary: The chemical structure of cellulose acetates (CA), different synthesis paths, analysis strategies and the correlation of these structural features with properties, especially with the solubility are summarized. Alternative paths, in particular homogeneous procedures, for the synthesis of CA are described focusing on the application of new media and the *in situ* activation of acetic acid. The preparation of selectively substituted CA is reviewed including the defined hydrolysis under acidic or basic conditions. Strategies for the structure analysis by means of ^{1}H- and ^{13}C-NMR spectroscopy and by means of chromatographic methods are discussed. In addition, the preparation and the application of a variety of mixed CA ethers and esters are described.

Keywords: Cellulose acetate, cellulose diacetate, cellulose triacetate, cellulose solvents, *in situ* activation, regioselective synthesis, hydrolysis, solubility, ^{1}H- and ^{13}C-NMR spectroscopy, chromatography, mixed cellulose acetate ethers, mixed cellulose acetate esters.

4.2.1. Introduction

Esterification of cellulose represents one of the most versatile transformations as it provides access to a variety of bio-based materials with valuable properties. A broad spectrum of cellulose esters is known today. However, only the carboxylic acid esters of C_2 to C_4 acids, including mixed products, have gained special technical importance because of their wide range of properties and their relative ease of manufacture.

Although CA has been commercially produced for decades, new synthesis paths for the acetylation still appear. The search for new acetylation procedures was stimulated by the

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development of new solvents for cellulose, which are the essential prerequisites for the homogeneous acetylation, as well as by the application of new reagents. Homogeneous acetylation is believed to enable the cellulose chemist to prepare acetone soluble CA in one step in a reproducible manner. The most fruitful attempts will be reviewed in this chapter. Moreover, synthesis paths for cellulose acetates with defined molecular structures available by regioselective acetylation, tailored de-acetylation and the influence of these structures on properties most important on the solubility will be discussed. Indispensable in this regard is the discussion of modern analytical tools for structure determination.

The evaluation of the huge number of references dealing with the de-acetylation of CA is well beyond the goal of this chapter. Thus, only relevant results describing procedures are included, which yield polymers with a defined solubility. Investigations into the distribution of substituents accessible by, e.g., de-esterification reactions are discussed while selective acetylation or de-acetylation of the polymers by enzymatic treatment is not subject of our work (see Chapter 4.3). Subsequent functionalization yielding polymers with tailored properties is briefly reviewed. In addition, selected subsequent modifications of cellulose acetates are included.

4.2.2. Analytical methodology for structure analysis of cellulose acetate

To establish structure-property relationships of CA and to evaluate synthesis paths and products, a detailed structure analysis is an unambiguous prerequisite. A broad variety of spectroscopic and chromatographic methods were investigated towards their use as analytical tools for the structure elucidation of CA. In this chapter the advantages and disadvantages of the most commonly used techniques ^{1}H- and ^{13}C-NMR spectroscopy as well as the use of GLC, HPLC and MS will be discussed. For most of these methods subsequent functionalization, e.g., deuteroacetylation or methylation of the CA is helpful or even essential. Thus, a number of these subsequent functionalization paths will be presented as well.

4.2.2.1. IR spectroscopy

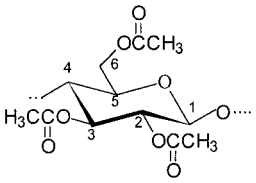
The most convenient method for the elucidation of structural features of CA is IR spectroscopy. In recent years attempts were made to use this method for a quantitative evaluation

of the amount of bound acetic acid and the distribution of the primary and secondary hydroxyl groups in highly substituted CA samples. Thus, IR spectra were recorded in the compensating mode in the 3300 – 3700 cm^{-1} range [1] and the possible types of distribution of the hydroxyl groups were identified. The signals of the carbonyl groups at 1740 – 1750 cm^{-1} can be assigned by applying comparable experiments [2].

4.2.2.2. NMR spectroscopic techniques

The application of NMR spectroscopy was among the first attempts for the structure analysis of CA. The pioneering work of both Goodlett *et al.* in 1971 [3] using ^{1}H-NMR spectroscopy and Kamide and Okajima in 1981 [4] applying ^{13}C-NMR measurements opened major routs for further studies in this field including complete signal assignment, the determination of the functionalization pattern of CA dependent on reaction conditions and the establishment of structure-property relationships. Table 1 shows representative ^{13}C-NMR spectroscopic data of cellulose triacetate (CTA) samples.

Table 1. Chemical shifts of the ^{13}C-NMR signals for cellulose triacetate (assignment according to Ref. [8]).

	δ/ppm[a)]	
	DMSO-d_6 90°C	$CDCl_3$ 25°C
C-1	99.8	100.4
C-2	72.2	71.7
C-3	72.9	72.5
C-4	76.4	76.0[b]
C-5	72.5	72.7
C-6	62.8	61.9

[a)] δ/ppm relative to $CDCl_3$ at 77.0 ppm or DMSO-d_6 at 35.9 ppm.
[b)] The coupled resonance overlaps with the solvent resonance.

The preferred solvent for the investigation of both CTA and partially substituted CA is DMSO-d_6, which dissolves the polymers within a wide range of degree of substitution (DS). The

assignment of the signals was possible based on the chemical shift of model compounds like peracetylated cellobiose, cellotetraose, and cellopentaose as well as cellulose and CTA [5-7].

^{13}C-NMR spectra have been studied not only as proof for the molecular structure but also for determination of both total DS and distribution of acetyl functions within the repeating units concerning position 2, 3, and 6. It was found that chemical shifts due to the ring carbons of the repeating units are sensitive to their distribution [9,10]. The investigation of CA samples with DS of 1.7, 2.4, and 2.9 revealed that one and the same NOE for *C*-1 – *C*-6 appears and thereby a valid basis for the quantitative assessment of partial DS values at position 2, 3, and 6 from the ^{13}C-NMR spectrum was established. The signals at 59.0 ppm (*C*-6 unsubstituted), 62.0 ppm (*C*-6 substituted), 79.6 ppm (*C*-4, no substitution at *C*-3), 75.4 ppm (*C*-4 adjacent to an acetylated *C*-3), 101.9 ppm (*C*-1, no substitution at *C*-2) and 98.9 ppm (*C*-1 adjacent to an acetylated *C*-2) were used for the calculation.

However, the exact distribution of substituents in CA over a wide range of DS is not readily estimated by simple comparison of the relevant peak intensities. A major problem is the overlapping of signals around 70-85 ppm resulting from the unmodified *C*-2 – *C*-5 and the corresponding acetylated position 2 and 3 as well as the influence of an acetylated position 2 on the chemical shift of *C*-4. In addition line broadening of the signals due to the ring carbons is frequently observed in the quantitative mode of ^{13}C-NMR measurements. The fairly long pulse-repetition time applied causes T_2 relaxation of the relevant signals.

Several attempts were made to assign the signals of the C=O of the acetyl moieties. Kamide *et al.* investigated the distribution of substituents via the chemical shift of the C=O of the acetyl groups of CA [11]. A reasonable assignment of the C=O signals was achieved by applying a low-power selective decoupling method to the methyl carbon atoms of the acetyl groups [12]. Acetyl methyl and C=O signals appear as overlapped multi peaks reflecting the detailed substitution pattern with regard to the 8 possible repeating units as well as the hydrogen bond system of CA with DS<3 [13]. The average acetyl group distribution on the glucopyranose units was analyzed via the assignment of the C=O signals and has been correlated with the solubility of CA samples prepared by different methods [11]. Peak assignment of the carbonyl region of CA samples was carried out via C-H COSY spectra of CTA (see Table 2) [14].

An elegant analysis concerning the structure elucidation of cellulose [1-13C] acetates

prepared in different ways with a wide range of DS values was published by Buchanan *et al.* [13]. A total of 16 carbonyl carbon resonances were identified. In the case of *C*-2 and *C*-3 carbonyl carbon resonance, it was possible to assign these resonances to repeating units with a specific pattern of functionalization.

Table 2. Peak assignment of the carbonyl region in the ^{13}C-NMR spectrum of cellulose acetate.

δ/ppm	Carbon at position	Functionalized glucopyranose unit
170.04	6	6-Mono
170.00	6	2,6-Di
169.94	6	2,3,6-Tri
169.89	6	3,6-Di
169.83	6	3,6-Di
169.60	3	3-Mono
169.46	3	3,6-Di
169.41	3	3,6-Di
169.35	3	3,6-Di
169.22	3	2,3-Di
169.11	3 (2)	2,3,6-Tri (2,6-Di)
168.93	2	2-Mono- 2,6-Di
168.79	2	2,3,6-Tri- 2,3-Di
168.71	2	2,3-Di

An alternative route to study the functionalization pattern of CA is the perpropionylation of the remaining hydroxyl groups using the C=O carbons of the ester moieties as sensitive probe [15]. Complete propionylation was achieved by reaction of CA with propionic anhydride using 4-(dimethylamino) pyridine as catalyst. The complete conversion of the hydroxyl groups was confirmed by ^{1}H-NMR- and IR spectroscopic studies (no νOH signal appears). The possibility of ester exchange reactions was excluded because constant total acetyl contents were observed and propionylation of CTA applying standard conditions failed.

The range of C=O carbons in ^{13}C-NMR spectra of CAP are shown in Figure 1. The signals appear clearly resolved corresponding to position 2, 3, and 6 within the repeating unit. The triplet of the acetyl and the triplet of the propionyl moieties are distinctly separated from each other. The expanded spectra of the C=O region of a perpropionylated CA (DS = 1.43) compared to the starting CA reflect quite well the functionalization pattern (Figure 1).

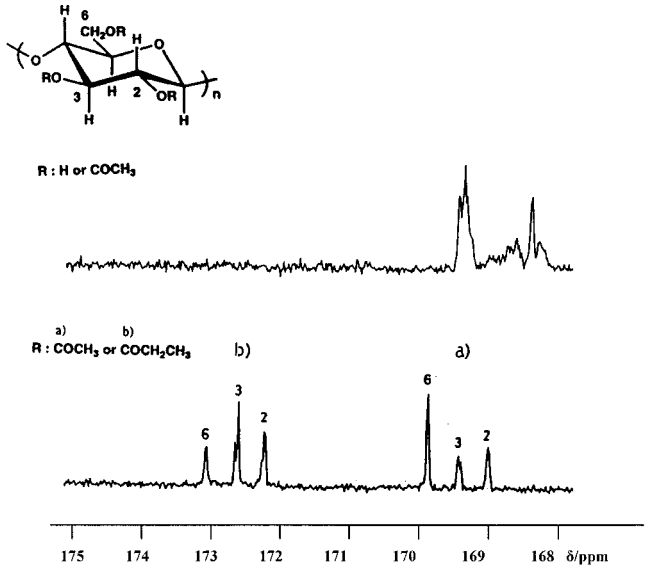


Figure 1. ^{13}C-NMR spectra of the carbonyl region of cellulose acetate (DS 1.43, top) and its propionylated product (bottom; Reproduced with permission from *Carbohydr. Res.* **1995**, *273*, 83. Copyright 1995 Elsevier).

Quantitative mode ^{13}C-NMR measurements of perpropionylated samples give the partial DS at position 2, 3, and 6. Typical ^{13}C-NMR spectra of perpropionylated CA samples with DS_{Ac} ranging from 1.0 to 2.4 are shown in Figure 2.

Attempts were made to exploit ^{1}H-NMR spectroscopy for the structure determination. CTA yields a very well resolved and simple ^{1}H-NMR spectrum (Figure 3, Table 3) while partially substituted CA samples show very complex spectra resulting from the un-, mono-, di- and tri-substituted units with different combinations of the functionalized sites.

Nevertheless, a CA with a DS of 2.46 was studied with phase-sensitive COSY and relayed COSY NMR spectroscopy. Via comparison of these spectra with simulated ones (nine different sub-spectra) and spectra for model compounds, e.g. cellotetrose peracetate, it was possible to find nine different types of spin network. They are four types of 2,3,6-triacetyl glucose residues flanked by different acetyl glucose units, two different types of 2,3-diacetyl glucose residues, a 2,6-diacetyl glucose residue, and a 6-monoacetyl glucose residue [16].

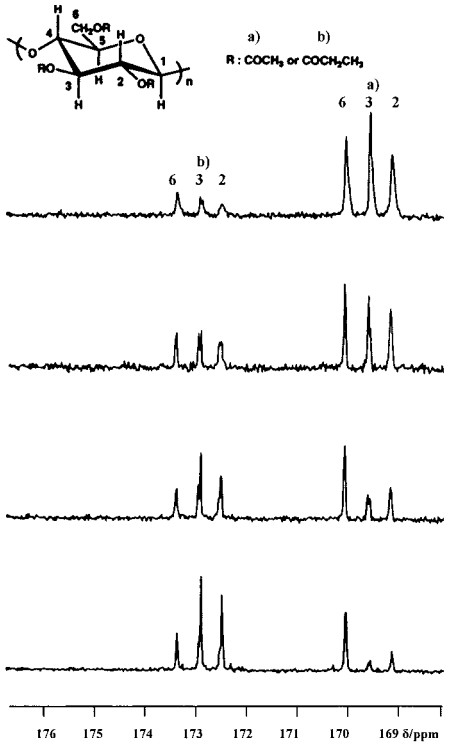


Figure 2. Typical ^{13}C-NMR spectra of perpropionylated CA samples with DS 0.98, 1.43, 1.90, 2.42 (from top to bottom) (Reproduced with permission from *Carbohydr. Res.* **1995**, *273*, 83. Copyright 1995 Elsevier).

It is possible to calculate the partial DS at the free reactive sites from ^{1}H-NMR spectra after peracetylation of the CA derivatives with acetyl-d_3-chloride or acetic anhydride-d_6. Perdeuteroacetylation avoids the spectral complication observed in the methyl proton signals as well as in the signal range of the repeating unit where the protons of remaining OH groups of partially substituted CA appear as well. Three signals of the methyl protons appear, which were assigned to the acetyl moieties attached to position 2, 3, and 6 [3,17] (Figure 4).

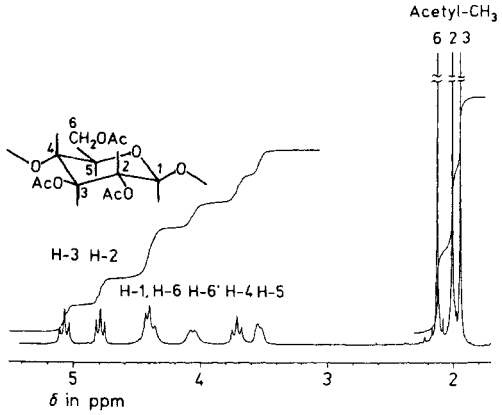


Figure 3. ^{1}H-NMR spectrum of a cellulose triacetate (Reproduced with permission from *Makromol. Chem.* **1991**, *192*, 75. Copyright 1991 Wiley-VCH).

Table 3. Chemical shifts of ^{1}H-NMR signals for cellulose triacetate and cellulose.

Signal	δ/ppm[a] of cellulose triacetate			δ/ppm[a] of cellulose
	DMSO-d_6 25°C	DMSO-d_6 80°C	$CDCl_3$ 25°C	DMSO-d_6 80°C[b]
H-1	4.65	4.65	4.42	4.35
H-2	4.52	4.55	4.79	3.10
H-3	5.06	5.04	5.07	3.38
H-4	3.65	3.68	3.66	3.38
H-5	3.81	3.77	3.47	3.38
H-6_S	4.22	4.26	[c]	3.78
H-6	3.98	4.04	4.06	3.60

[a] In ppm relative to $CDCl_3$ at 7.24 ppm or DMSO-d_6 at 2.49 ppm.
[b] Unsubstituted AGU of cellulose acetate with low DS.
[c] H-6_S (index s means substituted) and H-1 overlap.

The DS is readily calculated from the ratio of the spectral integrals of proton of repeating unit and the methyl protons. The error of calculation increases due to the decrease of absolute signal intensity in case of samples of rather low DS. [17]. Different alternatives for a subsequent derivatization of CA for analytical purposes were developed (see 4.2.7.). Among these subsequent reactions are trifluoroacetylation, nitrobenzoylation, ethylcarbanilation, phenylcarbanilation, trimethylsilylation, and conversion with aceticacidethylester isocyanate (see

Figure 25). Especially the latter one is a very efficient tool, which cannot only be applied for structure elucidation by means of NMR spectroscopy but also for HPLC studies after polymer degradation.

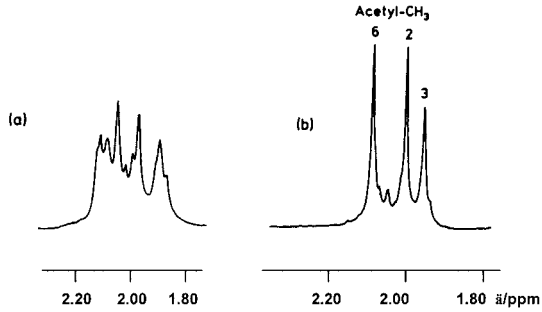


Figure 4. ^{1}H-NMR spectrum of a cellulose acetate before (a) and after (b) deuteroacetylation (Reproduced with permission from *Makromol. Chem.* **1991**, *192*, 75. Copyright 1991 Wiley-VCH).

Table 4. Comparison of the degree of substitution for CA obtained by the silylation method with values given by the suppliers. The DS values were calculated from the integrals of the ring hydrogen and *O*-acetyl resonances (method 1) or from the integrals of the *O*-trimethylsilyl and *O*-acetyl resonances (method 2) in the ^{1}H-NMR spectra of the fully *O*-trimethylsilylated polymers.

Sample[a)]	Degree of substitution		
	Reported	Method 1	Method 2
A	0.80	0.81	0.76
B	2.10	1.97	2.05
C	2.50	2.28	2.50
D	3.00	2.77	3.00
E	2.45	1.86	2.43

[a)] Samples A – D are Eastman products, E is an Aldrich product.

Moreover, trimethylsilylation of CA with a wide range of DS values was carried out with *N,O*-bis(trimethylsilyl)acetamide and 1-methylimidazol in DMF at room temperature. Analysis of the samples by IR showed a complete absence of hydroxyl groups. As evident in Table 4, the DS values obtained by integration of the *O*-acetyl and *O*-trimethylsilyl resonances were in excellent agreement with values provided by the suppliers and *vide infra*, with those found by chemical analysis [18].

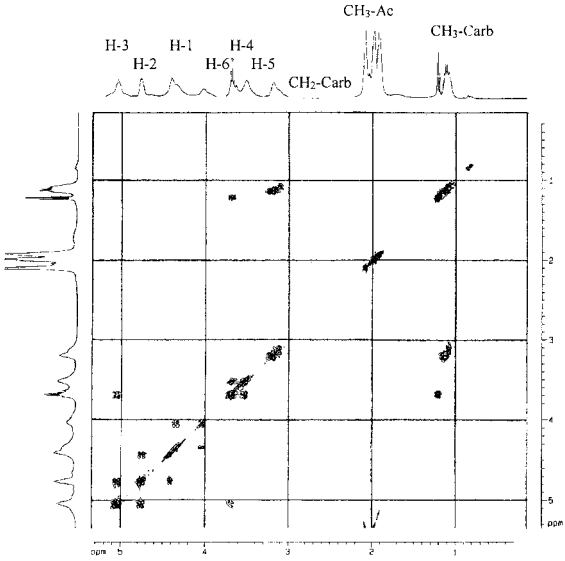


Figure 5. ^{1}H-^{1}H-NMR spectrum of completely modified cellulose acetate ethylcarbamate, DS = 2.46.

A complex problem is the determination of the distribution of the functional groups along the polymer chain and the supramolecular structure of acetylated celluloses. One possible way is the application of NMR spectroscopy on CA samples with ^{13}C-labeled acetyl groups [13]. NOESY and ^{13}C-NMR spectroscopy was applied to study the supramolecular structure and the microscopic conformation of CTA. It was shown that it builds up a 5/4 helix. In addition, formation of domains can be investigated, which may give information on the pattern of substitution [19,20]. Furthermore, NMR spectroscopy after enzymatic treatments of the cellulose esters is capable to give an insight in the composition of the polymer with regard to 8 basic repeating units [21]. The sequence distribution of substituted glucopyranose units along the chain of CA with a DS of 0.64 was reconstructed with this technique [14].

Solid-state NMR spectroscopy was applied in comparison to solution NMR and the presence of ordered and disordered regions was identified [20,22,23]. Recent developments in structure characterization of cellulose esters are solid-state NMR spectroscopy and its combination with other analytical tools like Raman spectroscopy. Lowman nicely reviewed this topic recently [24].

4.2.2.3. Chromatographic techniques

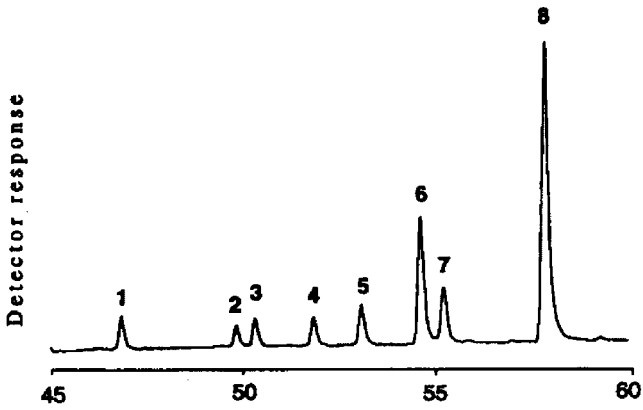
One important alternative to NMR spectroscopy is the determination of the inverse substitution pattern of the hydrolytically unstable cellulose ester by means of chromatographic techniques after subsequent functionalization and de-polymerization. Among the first attempts in this regard was a method developed by Björndal *et al.* [25]. The derivatization of the CA was performed by reaction with methyl vinyl ether in DMF with *p*-toluenesulfonic acid as catalyst. The anhydroalditol acetates were separated by means of gas chromatography after methylation according to Hakomori [26].

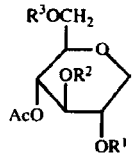
This method was applied to determine both total and partial DS values of acetylation on the three reactive sites. Results were compared with data obtained by ^{13}C- and ^{1}H-NMR spectroscopy. All data is in very good agreement with each other [10] (Table 5).

Table 5. Evaluation of the distribution of ester moieties in different cellulose acetates [10].

Sample Code	Method	DS of *O*-acetyl groups at position			Total-DS
		2	3	6	
CMA	Titration[a)]	-	-	-	1.75
	^{13}C-COM[b)]	0.60	0.55	0.58	1.73
	^{13}C-NME[c)]	0.59	0.56	0.59	1.74
	^{1}H-NMR	0.59	0.56	0.59	1.74
	GC	0.60	0.60	0.59	1.79
CDA	Titration	-	-	-	2.41
	^{13}C-COM	0.84	0.83	0.72	2.39
	^{13}C-NME	0.84	0.84	0.73	2.41
	^{1}H-NMR	0.86	0.82	0.73	2.41
	GC	0.83	0.83	0.71	2.37
CTA	Titration	-	-	-	2.92
	^{13}C-COM	1.00	1.00	0.90	2.90

[a)] Chemical analysis by saponification and titration.
[b)] Proton decoupled mode with NOE.
[c)] Proton decoupled mode without NOE.





	R^1	R^2	R^3
1	Me	Me	Me
2	Me	Et	Me
3	Me	Me	Et
4	Et	Me	Me
5	Me	Et	Et
6	Et	Et	Me
7	Et	Me	Et
8	Et	Et	Et

Figure 6. GLC of anhydroalditol acetates derived from CA with a DS of 2.50 (Reproduced with permission from *Carbohydr. Res.* **1995**, *269*, 167. Copyright 1995 Elsevier).

A comparable method was applied for the determination of the distribution of acetyl groups in CA (DS 2.5) [27,28]. Methylation was carried out with methyl triflate according to Prehm [29]. The acetyl functions were exchanged for higher alkyl groups (ethyl, propyl, pentyl) and the mixed alkyl ethers obtained were degraded by reductive cleavage. The mixture of differently functionalized sugar derivatives was acetylated and analyzed by GLC and GLC-MS. The assignment of the GLC peaks was carried out by comparison with reference compounds and by EI- and CI-mass spectra. The molar ratios of the 8 differently substituted building units could be determined by integration of the GLC peaks (Table 6).

The same method was used for the determination of the pattern of substitution for CAs with DS values in the range 0.8 – 3.0. The results were compared with data obtained from ^{1}H-NMR spectra of trimethylsilylated CA samples (values see Table 4) [18]. The DS values obtained by these two methods were in good agreement.

It should be mentioned that a more convenient technique was studied for CA and halogen-substituted CA using HPLC for the separation step. After methylation the polymers were hydrolyzed by treatment with TFA [30-32].

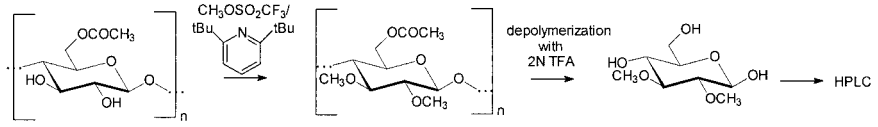


Figure 7. Analytical path for the structure determination of cellulose acetates by HPLC after permethylation and degradation.

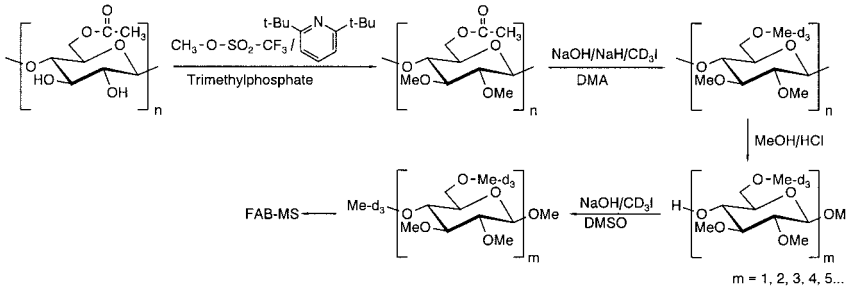


Figure 8. Analytical path for the structure determination of cellulose acetate by FAB-MS after permethylation, perdeuteromethylation, and random cleavage.

CA samples have been investigated to study the functionalization patterns both within the AGU and the polymer chain by permethylation, deacetylative deuteromethylation under alkaline conditions, random cleavage, remethylation with methyl iodide-d_3, and FAB-MS analysis.

Table 6. Mole percent (compound 1-8) of products derived by reductive cleavage of *O*-ethyl-*O*-methyl cellulose (according to ref. [29])

Compound	Sample[a)]		
or parameter	A	B	C
1	49.00	7.46	2.89
2	11.04	4.14	3.79
3	8.86	9.20	3.27
4	12.36	9.16	6.01
5	1.84	5.83	5.78
6	12.34	19.33	24.41
7	2.14	13.68	9.21
8	2.42	31.20	44.64
DS_2	0.293	0.734	0.843
DS_3	0.276	0.605	0.786
DS_6	0.153	0.599	0.629
Σ (DS)	0.72	1.94	2.26

[a)] For values given by the supplier and comparison with NMR data see Table 4.

Comparison of the experimental data with those calculated for a random distribution of acetate groups [33] gave information about the distribution along the chain. A problem of this path may be both undermethylation and migration or cleavage of the primary functional groups during the methylation yielding incorrect results.

4.2.3. Paths for the homogeneous cellulose acetylation

All industrially applied acetylation of cellulose processes start with slurries of activated cellulose in a variety of media. The different processes, activation procedures and the chemistry of the processes are nicely reviewed in Chapter 3.1. by Steinmeier.

The development of a variety of new solvents for cellulose with its extended supramolecular structure was a major stimulation to investigate alternative paths for the acetylation of this polysaccharide. A detailed discussion about cellulose solvents known and the mechanism of dissolution is well beyond the scope of this chapter. Several good, comprehensive

reviews have been published [34-40]. Dissolution of cellulose destroys the highly organized hydrogen-bonding system surrounding the single polyglucan chain. Not only is the physical dissolution of the polysaccharide (non-derivatizing solvents) capable for alternative synthesis paths but also the functionalization after partial derivatization, i.e., after dissolving the polymer in a so-called derivatizing solvent [38-43].

4.2.3.1. Non-derivatizing solvents used as medium for the acetylation of cellulose

Non-derivatizing solvents, which dissolve the polysaccharide only by physical interactions, can be both single and multi-component systems. Although a wide variety of these solvents were developed and investigated in recent years only a few have shown a potential for a controlled and homogeneous functionalization of polysaccharides. Important examples with regard to cellulose acetylation are summarized in Table 7.

Table 7. Solvents and reagents exploited for the homogeneous acetylation of cellulose.

Solvent	Acetylating reagent	DS_{max}	Ref.
N-Ethyl-pyridinium chloride	Ac_2O	Up to 3	[17,44]
N-Methylmorpholine-*N*-oxid	Vinyl acetate	0.3	[45]
DMAc/LiCl	Ac_2O	Up to 3	[46-50]
	Acetyl chloride	Up to 3	[51]
1,3-Dimethyl-2-imidazolidinone/ LiCl	Ac_2O	1.4	[52]
DMSO/SO_2/diethylamine	Ac_2O	-[a)]	[53-56]
DMSO/TBAF	Vinyl acetate	2.7	[57]
	Ac_2O	1.2	[58]

[a)] DS not mentioned.

N-alkyl-pyridinium halides have gained interest as single component solvents for cellulose acetylation. The most powerful solvent in this regard is *N*-ethyl-pyridinium chloride. The advantage of an easy work up procedure after modification of polysaccharides in this solvent is ruled out by the fact that it is solid at room temperature and needs to be applied as melt. Thus, it is often diluted with common organic liquids to give appropriate reaction media. Among the additives for *N*-ethyl-pyridinium chloride (m.p. 118°C) are DMF, DMSO, sulfolane, pyridine and *N*-methyl pyrrolidone leading to a decreased melting point to 75°C [40]. Cellulose with DP values up to 6500 can be dissolved. The homogeneous acetylation of cellulose in the mixture *N*-

ethylpyridinium chloride/pyridine using acetic anhydride was investigated [44]. Although the reaction needs to be carried out at 85°C, the preparation of CTA, which is completed within one hour, proceeds for cellulose with degree of polymerization (DP) values below 1000 without degradation, i.e., strictly polymeranalogous. CA samples with a wide variety of DS values and a defined solubility, e.g. in water, acetone or chloroform, respectively, were prepared in one step (Table 8).

Table 8. Reaction conditions for the preparation of cellulose acetate in *N*-ethyl-pyridinium chloride using pyridine and acetic anhydride as acetylation mixture.

Reaction conditions				Acetyl content	Solubility
Molar ratios per mol AGU		T	t		
Pyridine	Acetic anhydride	[°C]	[min]	[%]	
16.2	5.4	40	60	12.1	H_2O/pyridine (3/1)
16.2	5.4	40	295	27.1	CCl_4/MeOH (4/1)
32.5	32.5	50	120	37.7	CCl_4/MeOH (4/1)
32.0	32.0	85	55	41.3	$CHCl_3$
32.5	32.5	50	285	42.2	Acetone, $CHCl_3$

N-Ethylpyridinium chloride was applied for the synthesis of CA within a wide range of DS values (0.74 -2.65) using acetic anhydride (temperature 85 and 40°C, respectively). Acetylation under these conditions is rather fast (DS 2.65 within 44 min) and can be controlled via the time of treatment. The samples show different solubility and distribution of substituents as revealed by means of ^{1}H-NMR spectroscopy [17] (see Chapter 4.2.2.).

It should be mentioned that the solvent *N*-methylmorpholine-*N*-oxide (NMMNO), the only commercially applied, non-derivatizing cellulose solvent, was used for preliminary acetylation reactions of cellulose [45]. Thus, the dissolved polymer was treated in this medium with vinyl acetate to give a cellulose ester with DS 0.3. The application of an enzyme as acetylation catalyst seems to be necessary (e.g., Proteinase N of *Bacillus subtilis*).

The cellulose solvent DMAc/LiCl shows an enormous potential for cellulose derivatization. Dissolution succeeds without or at least with negligible degradation even in case of high molecular weight polysaccharides, e.g., cotton linters or bacterial cellulose. Although it is the solvent of choice for chemical functionalization of cellulose, a dissolution mechanism has still not been clearly postulated. A number of solvent-polymer structures were proposed [59,60].

Different paths for the homogeneous synthesis of CA in DMAc/LiCl have been investigated. Thus, dissolved cellulose was acetylated using a wide variety of reagents in combination with different bases or catalysts [43,46,51]. Besides acetic anhydride, a number of new acetylating reagents like *in situ* activated acetic acid were investigated for homogeneous acetylation and will be discussed below. In the pioneer work of McCormick the conversion of cellulose dissolved in DMAc/LiCl with acetic anhydride in the presence of sulphuric acid was exploited for the preparation of an acetone-soluble CA with DS of 2.4 [61]. In recent years the system cellulose/DMAc/LiCl was studied intensively to develop methods appropriate for industrial application [46-50].

The dissolution procedure and reaction conditions for the acetylation were modified to create a process that allows excellent control of the DS in the range of 1 to 3 (Figure 9). It was shown that the thermal cellulose activation under reduced pressure is far superior to the costly and time-consuming activation by solvent exchange.

Figure 9. Scheme for the dissolution and acetylation of cellulose in DMAc/LiCl [49].

Reaction at 110°C for 4 hours without an extra base or catalyst gave polymers with almost no degradation of the starting material and a distribution of substituents in the order *C*-6 > *C*-2 > *C*-3 as determined by ^{13}C-NMR spectroscopic experiments. In addition to microcrystalline cellulose, cotton, sisal and bagasse-based cellulose were included into this work to determine the influence of the de-crystallization during the dissolution on the homogeneous acetylation [48]. The results are summarized in Table 9. For the higher molecular weight polymers the order of reactivity is *C*-6 > *C*-3 > *C*-2. However, no simple explanation can be advanced for the difference in reactivity between C_3-OH and C_2-OH. The recovery of the solvent components and the excess of reagent were optimized.

Table 9. Results for the acetylation of different cellulose materials in DMAc/LiCl with acetic anhydride (18 h at 60°C) [46].

Starting materials				Molar ratio	DS
Cellulose from	Molecular weight [g/mol]	α-Content [%]	Index of crystallinity Ic [%]	Anhydride/AGU	
Bagasse	116 000	89	67	1.5	1.0
				3.0	2.1
				4.5	2.9
Cotton	66 000	92	75	1.5	0.9
				3.0	1.9
				4.5	2.8
Sisal	105 000	86	77	1.5	1.0
				3.0	2.0
				4.5	2.8

In addition to DMAc/LiCl, a number of modified compositions of the solvent mixture were investigated. DMAc can be substituted with *N*-methyl-2-pyrrolidone (NMP), *N,N*-dimethylformamide, DMSO, *N*-methylpyridine or hexamethylphosphoric triamide but only NMP, the cyclic analog of DMAc, was found to dissolve the polysaccharides without major degradation. Furthermore, the mixture of 1,3-dimethyl-2-imidazolidinone (DMI) and LiCl represents a suitable cellulose solvent [52]. The advantages of the nowadays commercially available DMI consist in its thermal stability and low toxicity. DMI/LiCl is able to dissolve cellulose samples with DP values as high as 1200 and concentrations of 2-10% (w/w) applying the same procedure as used for DMAc/LiCl, i.e., an activation of the polymer by a heat treatment or a step-wise solvent exchange is absolutely necessary. ^{13}C-NMR spectra of cellulose acquired both in DMI and DMAc in combination with LiCl exhibit the same chemical shifts, i.e., comparable cellulose solvent interactions may be assumed. Consequently, the same functionalization reactions should be possible. CA with DS 1.4 was obtained by conversion of the polymer with acetic anhydride/pyridine in DMI/LiCl. The reactivity of the OH functions is in the order *C*-6 > *C*-2 > *C*-3.

Other non-aqueous, non-derivatizing solvents capable for homogeneous modification are mixtures with the general composition: polar organic liquid/SO_2/primary, secondary or tertiary aliphatic or secondary alicyclic amine. From the wide variety of possible mixtures dimethyl

sulfoxide/SO_2/diethylamine is most versatile. While etherification with a great number of different reagents was very efficient, acetylation reactions succeed just to a limited extent [53-56].

A novel and powerful new solvent for cellulose consists in the mixture DMSO/tetrabutylammonium fluoride trihydrate (TBAF). The advantage of DMSO/TBAF is that cellulose with a DP as high as 650 dissolves without any pretreatment within 15 min. Highly resolved ^{13}C-NMR spectra of cellulose can be obtained showing all the ring carbons at 102.7 (*C*-1), 78.4 (*C*-4), 75.6 (*C*-5), 75.0 (*C*-3), 73.5 (*C*-2) and 59.9 ppm (*C*-6) of the AGU and giving no hints for a derivatization during the dissolution process (Figure 10) [57]. The solutions contain water because TBAF is used as the commercially available trihydrate and the cellulose is air-dried only.

The new solvent was exploited for acetylation reactions [58]. A CA with a DS value of 0.83 was obtained applying a molar ratio acetic anhydride per AGU of 2.3:1.0 for 70 h at 40°C. Experiments were carried out with Sisal cellulose, which represents fast growing lignocellulosic material comparable to sugarcane bagasse and linters [47-49]. The starting material contained about 14% hemicellulose as confirmed by ^{13}C-NMR spectroscopy and HPLC analysis after complete de-polymerization. The conditions suitable for dissolution of cellulose materials (Avicel, wood pulp) in DMSO/TBAF did not yield optically clear solutions in case of Sisal cellulose [58]. A thermal activation of the Sisal cellulose was necessary. Nevertheless, static light scattering experiments of the solution showed a fairly high amount of aggregation. The values of the molecular weight determined were in the range of 20 to 50 x 10^6 g/mol.

Sisal celluloses were esterified homogeneously in DMSO/TBAF using acetic anhydride yielding a product with DS of 0.30. The concentration of TBAF in the solution was varied from 6 to 11% to study this influence on the dissolution and the product features. All mixtures gave clear solutions. The DS values of the CA prepared in these different solvent mixtures decrease with increasing TBAF concentration (Table 10). The amount of water in the medium increases with the salt concentration because the salt applied is a trihydrate. This in turn increases the rate of hydrolysis both of the anhydride and probably of the ester moieties formed as well. Furthermore, the interactions of the water with the cellulosic OH groups may hinder the access of acetic anhydride resulting in a lower DS.

Table 10. Influence of the amount of tetrabutylammonium fluoride trihydrate (TBAF) on the efficiency of the acetylation of Sisal cellulose with acetic anhydride in dimethyl sulfoxide (DMSO)/TBAF.

%TBAF in DMSO	Cellulose acetate	
	DS	Solubility
11	0.30	Insoluble
8	0.96	DMSO, Pyridine
7	1.07	DMSO, Pyridine
6	1.29	DMSO, DMF, Pyridine

Dewatering of DMSO/TBAF is possible by vacuum distillation. The removal of water from a solution of Sisal in DMSO/TBAF is much more inefficient than in case of the pure solvent and of Avicel in DMSO/TBAF leading to the assumption that the water is strongly involved in the solution complex. Reactions in the solvent of reduced water content lead to products with a significantly higher DS under comparable conditions. The DS increases from 0.30 to 1.15. A reaction of cellulose dissolved in anhydrous DMAc/LiCl applying the same molar ratio of acetic anhydride yields a product with a DS of 1.0 [50].

^{1}H-NMR analysis of the perpropionylated product shows a distribution of the acetyl groups at the reactive sites in the order *C*-6 > *C*-2 > *C*-3. In addition to the NMR experiments after perpropionylation, functionalization patterns were studied by HPLC after permethylation. After complete degradation of the polymer, which is coupled with a hydrolysis of the ester functions, the mixture of methyl glucoses obtained was investigated by means of HPLC [30]. A comparison of the results using this analytical path with statistic calculations was performed as applied for the analysis of carboxymethyl cellulose [61-63]. No hints for a non-statistic distribution of substituents along the polymer chain were found, i.e., no significantly increased amounts of glucose or trimethyl glucose were determined.

Molten inorganic salt hydrates with the general formula $LiX*H_2O$ ($X = I^-$, NO_3^-, CH_3COO^-, ClO_4^-) are a rather new class of cellulose solvents used for acetylation. These compounds dissolve cellulose with DP values as high as 1500 [64-67]. Very effective is $LiClO_4*3H_2O$ yielding transparent cellulose solutions within a few minutes. Furthermore, eutectic mixtures of $NaSCN/KSCN*H_2O$ and different amounts of $LiSCN*2H_2O$ were shown to dissolve cellulose. The formation of an additional compound as stated for the interaction between cellulose and perchloric acid was excluded. Furthermore, it is possible to acquire NMR spectra in these systems showing signals for an unmodified cellulose backbone (Figure 10).

Acetylation experiments were performed in $LiClO_4*3H_2O$ at 110°C and in $NaSCN/KSCN/LiSCN*2H_2O$ at 130°C [67]. Among the acetylating reagents were acetic anhydride, ethyleneglycol diacetate, and vinyl acetate. The best results were obtained with the mixture $NaSCN/KSCN/LiSCN*2H_2O$ and acetic anhydride using a remarkable excess of the acetylating reagent in the range of 50 to 100-fold as summarized in Table 11. DS values up to 2.4 were accessible during rather short reaction times (up to 3 hours). ^{1}H-NMR spectra of propionylated samples revealed a preferred functionalization of the primary OH-groups. X-ray experiments show broad signals proving an extended disordered structure. This structural feature should impart a high reactivity towards solid-solid reactions, e.g., blending with other polymers. Furthermore, the CA synthesized in molten salt hydrates show low melting points obviously because of the amorphous morphology.

Recently, it was found that ionic liquids especially salts containing substituted imidazolium ions are capable to dissolve cellulose over a wide range of DP values (even bacterial cellulose) with no covalent interaction (Figure 10) [68,69]. Studies towards their application as reaction medium for the chemical modification of cellulose including acetylation as well as for regeneration of cellulose fibers are under progress [69].

4.2.3.2. Acetylation of cellulose in derivatizing solvents and of cellulose intermediates

Not only is the physical dissolution of the polysaccharide (non-derivatizing solvents) capable for alternative synthesis paths but also the functionalization after partial derivatization, i.e., after dissolving the polymer in a so-called derivatizing solvent. In the latter case cellulose intermediates are formed *in situ* by introducing new functional groups via covalent bonds especially ester moieties of rather low hydrolytic stability.

Furthermore, it is possible to isolate these intermediates or to synthesize similar compounds and to conduct subsequently the homogeneous modification starting from the polymers dissolved in an inert simple organic solvent, which avoids side reactions. A clear line between these cellulose intermediates (or "transient derivatives" as they are frequently called [43]) and true cellulose derivatives cannot be drawn. Important derivatizing solvents and intermediates applied for the acetylation of cellulose are summarized in Table 12.

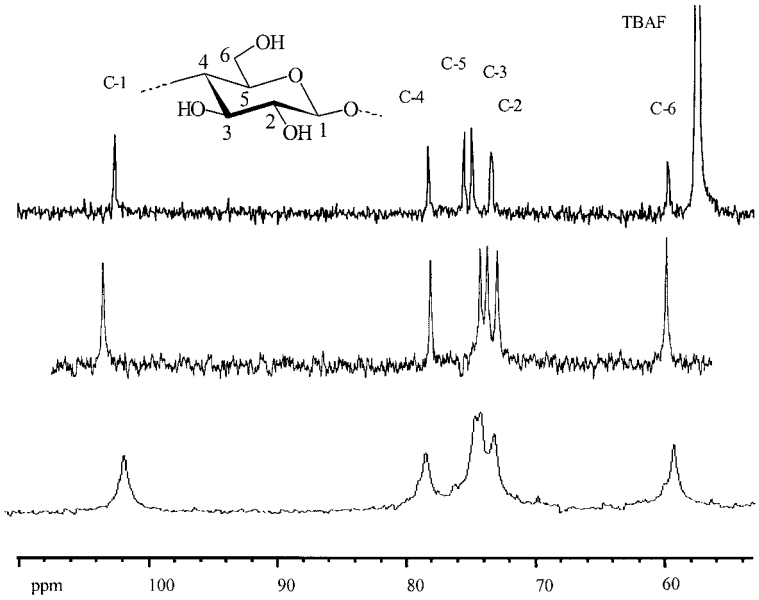


Figure 10. ^{13}C-NMR spectra of cellulose dissolved in the non-derivatizing solvents DMSO/TBAF (upper spectrum), $LiClO_4*3H_2O$ and the ionic liquid 1-butyl-3-methylimidazolium chloride (lower spectrum).

Table 11. Experimental data and analytical results for the acetylation of cellulose in NaSCN/KSCN/LiSCN*$2H_2O$ with acetic anhydride.

Reaction conditions		Partial degree of substitution[a)] at		
Mol anhydride/ AGU	Time [min]	*O*-6	*O*-2 and 3	Σ
100	180	0.91	1.57	2.41
100	60	0.86	1.12	1.98
100	30	0.39	0.85	1.23
75	30	0.51	0.50	1.02
50	15	0.42	0.67	1.09

[a)] Calculated from ^{1}H-NMR spectra after perpropionylation.

Table 12. Derivatizing solvents applied for cellulose acetylation.

Solvent	Intermediate formed	Acetylating reagent	DS_{max}	Ref.
Trifluoroacetic acid	Cellulose trifluoroacetate	Ac_2O	1.4	
		Acetyl chloride	1.7	[70]
N_2O_4/DMF	Cellulose nitrite	Ac_2O	2.0	[71]
Paraformaldehyde/ DMSO	Methylol cellulose	Ac_2O Acetyl chloride Ethylene diactetate	2.0	[72]
Chloral/DMF/pyridine	Cellulose trichloroacetal	Ac_2O	2.5	[73]

The treatment of cellulose with trifluoroacetic acid (TFA) or a mixture of TFA/trifluoroacetic anhydride (TFAA) produces soluble cellulose trifluoroacetates, (CTFA), which can be even isolated and redissolved in common organic solvents [31,74]. Solutions of cellulose in TFA were extensively studied by means of NMR spectroscopy showing that the primary OH groups are almost completely functionalized [75,76]. The dissolution and the reactivity of cellulose in TFA can be varied by the addition of co-solvents [77]. During dissolution of cellulose in mixtures of TFA/CH_2Cl_2 trifluoroacetylation occurs only to a limited extend and the polysaccharide is rather slowly degraded [78]. TFA was investigated towards its application as medium for acetylation reactions on cellulose [70]. The course of reaction was followed by IR spectroscopy leading to the conclusion that partial transesterification occurs using acetic acid anhydrides and acetyl chloride as well as the free acid in combination with TFAA. Isolation in aprotic media yields mixed esters with almost complete functionalization. After reaction for several hours at 50°C, the DS of trifluoroacetyl function is usually at about 1.4 and the DS of the second acyl component ranges from 0.5 to 1.6.

Comparable results were obtained by Salin *et al.* [70]. In this study mixed cellulose esters with DS values in the range from 2.9 to 3.0 were prepared by reacting cellulose in TFA with acetic acid anhydride at 60°C. These esters were studied in terms of their viscosity in solution and T_g. Furthermore, the preparation of mixed esters of cellulose in TFA was investigated using mixtures of acetic anhydride and aliphatic carboxylic acids. It was stated that the method yields polymers with DS higher than 2.8 with DS_{Acetyl} between 1.3 - 1.7. However, the pattern of substitution was not studied.

Besides CTFA, cellulose formate (CF) found some interest as intermediate for the cellulose acetylation [79]. CF samples with complete functionalization of the primary OH-groups (^{13}C-NMR spectrum, Figure 11) are easily formed by dissolving cellulose in formic acid or by conversion with formic acid and partially hydrolyzed $POCl_3$ [80].

Moreover, the cellulose trinitrite formed on dissolving the polymer in the N_2O_4/DMF system (^{13}C-NMR spectrum, Figure 11) could be transesterified with Ac_2O to a CA of DS=2 with the fastest reaction at position 2 [71]. Variation of the solvent components is possible. Instead of DMF, DMSO may be applied and N_2O_4 can be substituted with NOCl, nitrosyl sulfuric acid, nitrosyl hexachloroantimonate or nitrosyl tetrafluoroborate yielding solutions within the same time [81-84].

A rather interesting derivatizing solvent utilized for acetylation is the mixture DMSO/paraformaldehyde (PF). The major advantage of this system is that it dissolves cellulose rapidly and almost without degradation even in case of high molecular weight polymers. Cellulose is dissolved by formation of the hemiacetal, i.e., so-called methylol cellulose is obtained. ^{13}C-NMR spectroscopy revealed that the acetalization occurs preferentially at the 6 position of the AGU [85,86]. This methylol structure remains intact during subsequent functionalization in non-aqueous media resulting in derivatives with a pronounced substitution of the secondary OH groups as can be determined by means of GLC after complete hydrolysis of subsequently etherified cellulose. In contrast, the methylol functions can be easily removed by a treatment with water. Noteworthy is the fact that during the dissolution a growth of oligooxy methylene side chains may occur. In addition to the methylol functions, the free terminal hydroxyl groups of these chains may also be derivatized in a subsequent step. Nevertheless, the solvent DMSO/PF was exploited for the synthesis of esters via homogeneous conversion with a number of carboxylic acid anhydrides in the presence of pyridine at low temperatures [72,87-90].

The DS values reached by acylation are usually in the range from 0.2 to 2.0, except acetylation where DS values of up to 2.5 were realized. By means of ^{1}H- and ^{13}C-NMR spectroscopy it was shown that the hydroxyl groups of the methylol chains are preferentially acylated with the carboxylic acid anhydrides.

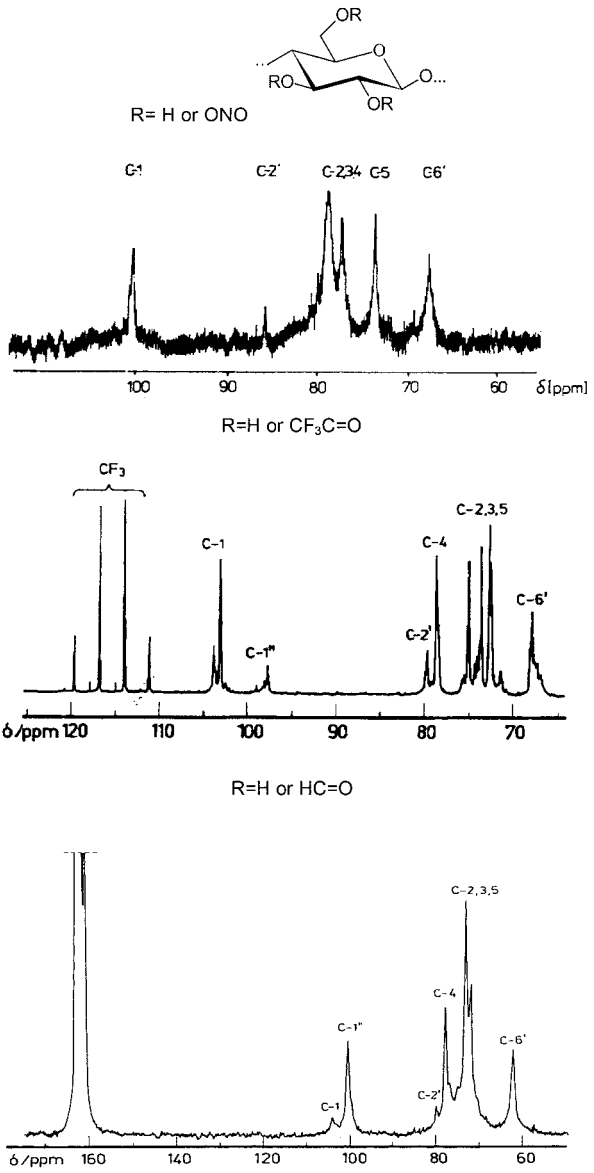


Figure 11. ^{13}C-NMR spectra of cellulose intermediates (cellulose nitrite, cellulose formate, cellulose trifluoroacetate) used for the acetylation of cellulose

Acetylation both with acetyl chloride and with acetic acid succeeded just to a limited extent. Furthermore, CA samples were obtained by transesterification with methylene diacetate and ethylene diacetate in the presence of sodium acetate and potassium acetate at 90°C yielding polymers with high DS values (acetyl content 22%) [72]. An interesting observation was that the DMSO in the solvent system could be substituted with DMF or DMAc.

In the system chloral/DMF/pyridine, cellulose was found to dissolve with complete substitution of the hydroxyl groups by the corresponding half acetyl groups, which could be acetylated to products with DS of 2.5 by Ac_2O or acetyl chloride [73].

4.2.3.3. Reagents for cellulose acetylation

Various new acetylating reagents for cellulose were developed over the last two decades, which were mostly applied under homogeneous reaction conditions.

Acetyl chloride

An important alternative to acetic anhydride [48,49] is acetyl chloride. Especially the homogeneous acetylation in DMAc/LiCl applying acetyl chloride found considerable interest because the process is very efficient. Thus, in the pioneer work of McCormick and Callais acetyl chloride was applied to the homogeneous system cellulose/DMAc/LiCl in combination with pyridine to prepare a CA with DS of 2.4, which is soluble in acetone [61]. A more detailed investigation on the homogeneous acetylation of cellulose in DMAc/LiCl with acetyl chloride/pyridine was done by Ibrahim *et al.* The cellulose studied was dissolving pulp obtained from sugar cane bagasse. After proper dissolution, a DS of 2.65 can be achieved by the use of only 25% excess of acetyl chloride [91].

The acetylation of cellulose dissolved in DMAc/LiCl with acetyl chloride without an additional base and in the presence of different pyridine derivatives was studied [51]. The conversion of cellulose dissolved in DMAc/LiCl with acetyl chloride (experimental details and DS-values see Table 13) shows that the reaction succeeds with almost complete conversion of the reagent, i.e., can be controlled by stoichiometry. ^{1}H-NMR experiments of perpropionylated samples show a preferred functionalization of the primary hydroxyl group.

Table 13. Reaction conditions and results for acetylation of cellulose with acetyl chloride in *N,N*-dimethylacetamide/LiCl.

Molar ratio	Partial DS[a] in position		Σ	Solubility[b]		
Acetyl chloride/AGU	6	2,3		DMSO	Acetone	$CHCl_3$
1.0	0.77	0.44	1.21[c]	+	-	-
3.0	0.90	1.95	2.85	+	-	+
4.5	1.00	1.94	2.94	+	-	-[d]
5.0	1.00	1.94	2.96	+	-	+

[a] Degree of substitution determined via ^{1}H-NMR spectroscopy after perpropionylation.
[b] + Soluble; - insoluble, DMSO, dimethyl sulfoxide.
[c] This stoichiometrically impossible value may result from fractionation during work up.
[d] The insolubility cannot be explained with structural features.

In addition to the NMR spectroscopic experiments, structures were studied by HPLC after permethylation (see Chapter 4.2.2.3.). After complete saponification of the ester functions and degradation of the polymer, the mixture of methyl glucoses obtained can be separated by means of HPLC [30]. DS values calculated from the chromatogram are in good agreement with the DS obtained by ^{1}H-NMR spectroscopy. A comparison of the results obtained using this analytical strategy with statistic calculations was performed as applied for the analysis of carboxymethyl cellulose [62,63]. No significantly increased amounts of glucose or trimethyl glucose were found by means of HPLC. Consequently, CA samples prepared via this path have a statistic and even distribution of substituents along the polymer chain.

Studies on the influence of a base on the course of reaction and on the distribution of substituents lead to the quite unexpected result that the application of pyridine as base yield products of a decreased DS (Table 14). Moreover, ^{1}H-NMR spectroscopy of the products reveals less preferred substitution in position 6. This effect is even more pronounced by an increased concentration of the base. Thus, for a sample with an over-all DS of 2.46 a partial $DS_{O\text{-}6}$ of 0.46 was determined, i.e., all the secondary OH groups are acetylated.

GPC investigations concerning a hydrolytic degradation of the polymer chain during the reaction indicate that little de-polymerization occurs without a base. In case of cellulose powder (Avicel) as starting polymer, de-polymerization is in the range of less than 2% in contrast to experiments with base where about 60% degradation occurs. One possible explanation for the degradation might be the formation of the acidic pyridinium hydrochloride in case of the base-catalyzed reaction. The majority of the HCl formed is liberated from the system if no additional

base is applied. It needs to be mentioned that the influence of the acidic pyridinium hydrochloride yields a product with a different solubility. Thus, the sample prepared with pyridine as base dissolves completely in acetone in contrast to a comparable sample prepared with no base (complete C-6 functionalization) as shown by the results summarized in Table 15 and 16. Permethylation, degradation and HPLC, as described above, did not show any hints for a non-statistic distribution of the substituents along the polymer chain for comparable samples. Consequently, the different solubility is only due to the different distribution of substituents on the level of the AGU. A comparable influence of the functionalization pattern on the level of the AGU on the solubility was determined for samples obtained by hydrolysis of CTA [28].

Table 14. Reaction conditions and results of the acetylation of cellulose with acetyl chloride in the presence of pyridine in *N,N*-dimethylacetamide/LiCl.

Molar ratio		Partial DS[a] in position		Σ	Solubility[b]		
Acetyl chloride/ AGU	Pyridine/ AGU	6	2,3		DMSO	Acetone	$CHCl_3$
1.0	1.2	0.63	0.37	1.00	+	-	-
3.0	3.6	0.94	1.62	2.56	+	-	+
5.0	6.0	0.71	2.0	2.71	+	+	+
5.0	10.0	0.46	2.0	2.46	+	+	+

[a] Degree of substitution determined via ^{1}H-NMR spectroscopy after perpropionylation.
[b] + Soluble; - insoluble, DMSO, dimethyl sulfoxide.

Polymer-bound bases like cross-linked polyvinyl pyridine were applied for the preparation of CA. Table 15 summarizes the reaction conditions and results. Again, a significant decrease of over-all DS values can be recognized in comparison to reactions applying no base. Moreover, high selectivity of the acetylation at position 6 was observed in contrast to acetylation reactions with pyridine as base. A drastic decrease of both the DS values and the yield as well as a different solubility of the product is observed if a large surplus of polymer-bound base is used. Thus, if the molar ratio base/AGU is in the range >10, product isolation is almost impossible. Extraction of the precipitate, which consists mainly of polyvinyl pyridine and CA as can be confirmed by FTIR (signals at 1595 and 2926 cm^{-1} for the polyvinyl pyridine and signals at 1019 and 1740 cm^{-1} for the CA) yields only traces of the product in the range of 1%. The alternative solubility of these CA samples is comparable to derivatives prepared in reactive microstructure, i.e., by conversion of cellulose regenerated from solution on a solid reagent and could be a first indication of a non-

statistic distribution of substituents along the polymer chain.

In contrast, the acetylation of cellulose with soluble, non cross-linked polyvinyl pyridine proceeds without regeneration or precipitation of the polymers, i.e., a completely homogeneous reaction occurred. CA obtained with a DS value of 2.28 is well soluble in acetone and showed no increased values for non- or fully substituted repeating units as confirmed by HPLC analysis after permethylation and depolymerization as described in 4.2.2.3. It may be assumed that during the conversion the cellulose is not permanently fixed to the dissolved polymeric base and an even distribution of substituents resulted from an equilibrium reaction.

Table 15. Conditions and results for the acetylation of cellulose dissolved in *N,N*-dimethylacetamide/LiCl with acetyl chloride in the presence of cross-linked polyvinyl pyridine.

Molar ratio		Partial DS[a] in position		Σ	Solubility[b]		
Acetyl chloride/AGU	Base/ AGU	6	2,3		DMSO	Acetone	$CHCl_3$
1.0	1.2	0.35	0.13	0.48	+	-	-
2.0	2.4	0.82	0.51	1.33	+	-	-
3.0	3.6	0.91	0.65	1.56	+	-	-
5.0	6.0	1.00	1.62	2.62	+	-	-
5.0	10.0	0.97	1.31	2.28[c]	+	+	-

[a] Degree of substitution determined via ^{1}H-NMR spectroscopy after perpropionylation.
[b] + Soluble; - insoluble, DMSO, dimethyl sulfoxide.
[c] Non-cross-linked base was used.

Acetylation via transesterification

An efficient alternative for the preparation of acetylated cellulose is the transesterification using carboxylic acid esters with cellulose. This method is well established and extensively studied in starch chemistry while results for the derivatization of cellulose via this path are rather scarce. First attempts for this reaction were carried out in *N*-methylmorpholine-*N*-oxide applying vinyl acetate. The product obtained possesses a rather low DS of 0.3 only and an enzyme must be applied for the conversion [45].

More efficient is the reaction in the solvent DMSO/TBAF. No enzyme was necessary for the conversion with vinyl acetate as acylating reagent and DS values up to 2.72 were accessible [57,58]. A summary of reaction conditions and results are given in Table 16.

The transesterification with vinyl acetate is more effective than acetylation with acetic anhydride, which is due to the formation of acetaldehyde during this conversion shifting the equilibrium towards the product side. On the other hand, the lower DS in case of the application of acetic anhydride is caused by the comparably fast hydrolysis of the reagent due to the water content of the solvent DMSO/TBAF. Experiments towards the dewatering of the solvent are described in 4.2.3.1.

Table 16. Conditions and results of the acetylation of cellulose (2.9%) dissolved in DMSO/TBAF (16.6%) with vinyl acetate at 40°C for 70h.

Molar ratio[a)]	Catalyst[b)] [mg]	Partial DS at *O*-6[c)]	*O*-2/3	DS[c)]	Solubility
1:2.3	-	0.49	0.55	1.04	DMSO
1:2.3	20	0.52	0.55	1.07	Insoluble
1:1.5	20	0.39	0.24	0.63	Insoluble
1:10.0	20	0.98	1.74	2.72	DMSO

[a)] Molar ratio of vinyl acetate to anhydroglucose unit (mol/mol).
[b)] Mixture of KH_2PO_4 and Na_2HPO_4.
[c)] Degree of substitution calculated from ^{1}H-NMR spectra.

Transesterification for the introduction of acetyl groups into the cellulose backbone is also possible with methylene diacetate and ethylene diacetate. The reaction was carried out homogeneously in DMSO/PF. Cellulose is treated with the reagents in the presence of sodium acetate. In this way CA with an acetyl content of 22% was accessible [72].

In situ activation of acetic acid

In addition to the transesterification, the use of *in situ* activated acetic acid is one of the most promising tools for homogeneous acetylation of cellulose. First attempts of the *in situ* activation of acetic acid for the preparation of CA under heterogeneous conditions were carried out by Shimizu *et al.* [92,93]. Acylation of the polymer was possible by conversion of cellulose suspended in pyridine or DMF using sulfonic acid chlorides as activating agent for the carboxylic acid. Thus, it was demonstrated that CA could be obtained in a wide range of DS values by treatment of the polysaccharide with acetic acid in the presence of Tos-Cl or methanesulfonyl chloride [92]. Highly efficient is the reaction with the alkali or alkaline earth salt of acetic acid in combination with Tos-Cl [93]. The reaction can also be carried out under homogeneous

conditions with cellulose dissolved in DMAc/LiCl. The reactive species involved in this reaction are still a point of discussion.

Both acetic anhydride and the mixed anhydride of toluene sulfonic acid and acetic acid were favoured as reactive species (Figure 12). ^{1}H-NMR experiments on a mixture of acetic acid/tosyl chloride were performed [94]. From the spectra (Figure 13) it can be concluded that a mixture of acetic anhydride (δ = 2.21 ppm) and acetyl chloride (δ = 2.73 ppm) is responsible for the high reactivity of this system.

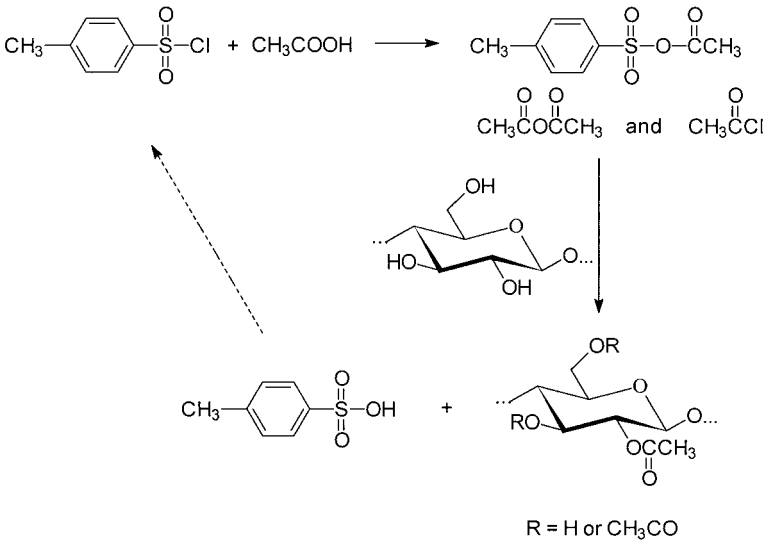


Figure 12. Schematic plot of the reaction via *in situ* activation of carboxylic acids with tosyl chloride.

Esterification of cellulose dissolved in DMAc/LiCl with acetic acid using dimethylaminopyridine (DMAP) and dicyclohexylcarbodiimide (DCC) as dehydrating reagent was reported but there is no information about the structure or the DS of the samples prepared [95].

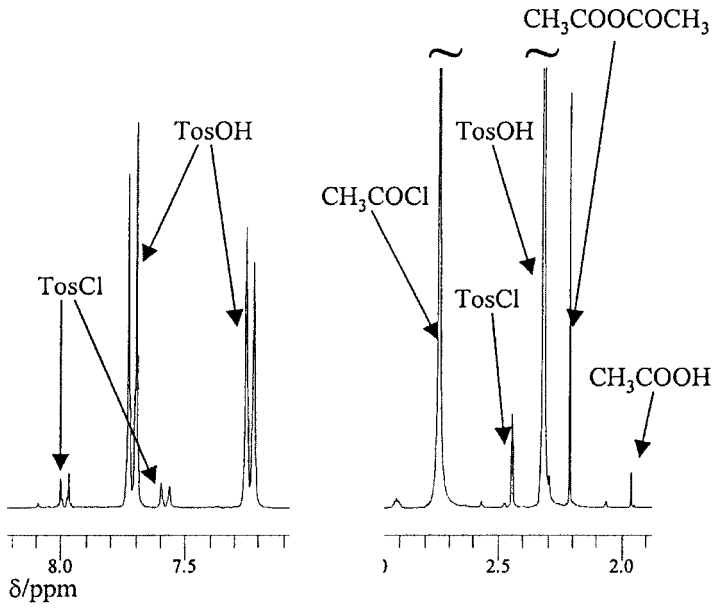


Figure 13. ^{1}H-NMR spectroscopic investigation of the *in situ* activation of acetic acid with tosyl chloride showing the preferred formation of acetic anhydride and acetyl chloride.

Acetylation experiments were carried out using *in situ* activation of acetic acid with *1,1'*-carbonyldiimidazole (CDI, Figure 14). During the conversion the imidazolide of the acid is formed as reactive species [96]. The reaction is rather mild and succeeds with almost no side reactions because only CO_2 and imidazole are formed as by-products. DS values of up to 2.1 were achieved depending on the molar ratio AGU/carboxylic acid/CDI. None of the products obtained dissolve completely in common organic solvents. This finding is comparable to results of the acetylation with vinyl acetate. ^{13}C- and ^{1}H-NMR spectra of perpropionylated samples reveal a highly pronounced acetylation at the position 6.

A rather new method for the esterification of cellulose is the *in situ* activation of the carboxylic acid with iminium chlorides based on the pioneer work of Stadler who investigated the reaction of iminium chlorides with alcohols [97]. Iminium chlorides are simply formed by conversion of DMF with a variety of chlorinating agents including phosphoryl chloride,

phosphorus trichloride or oxalyl chloride. They can be isolated but show a high tendency towards hydrolysis [98]. The reaction is very efficient because only gaseous by-products are formed. The first step of the reaction is carried out at -20°C. Under these conditions the complex is stable and no side reactions like the formation of HCl and the acid chloride were observed. Product purification is rather easy because most of the products are gaseous and during the last step DMF is formed again (Figure 15).

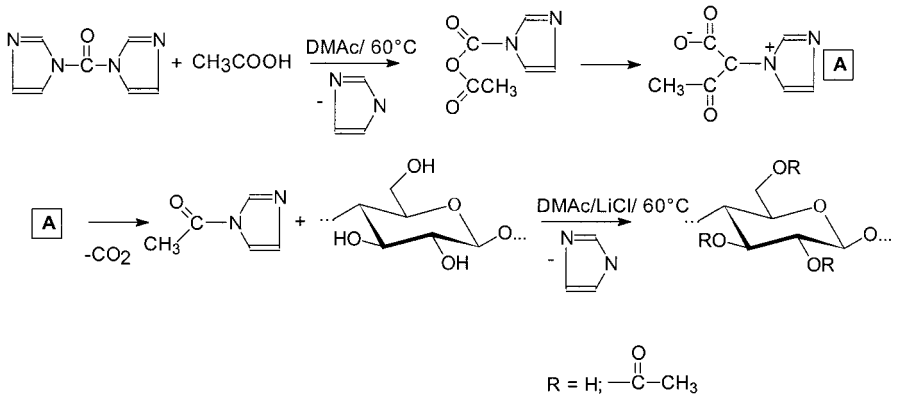


Figure 14. Schematic plot of the reaction via *in situ* activation of carboxylic acids with *1,1'*-carbonyldiimidazole.

For the acetylation of cellulose, the formation of the iminium chloride and the conversion with the acid were carried out with DMF and oxalyl chloride at -20°C. This mixture was added to a solution of cellulose in DMAc/LiCl resulting in gelation. The cellulose ester was isolated simply by filtration from the reaction mixture, washing with methanol and acetone. CA samples with DS values up to 2.4 are accessible but they are collectively insoluble. The solubility behaviour is comparable to products obtained by conversion of cellulose with carboxylic acid/CDI. This finding may be explained by the distribution of the functional groups as discussed in the context of acetylation applying polymeric bases.

New paths for heterogeneous acetylation

Besides the homogeneous esterification, new paths were developed for heterogeneous

processes. This topic is just briefly discussed. All large-scale industrial processes are exclusively carried out heterogeneously (at least at the initial stage of reaction) which, however, is not a topic of this chapter. Comprehensive review articles appeared elsewhere [99].

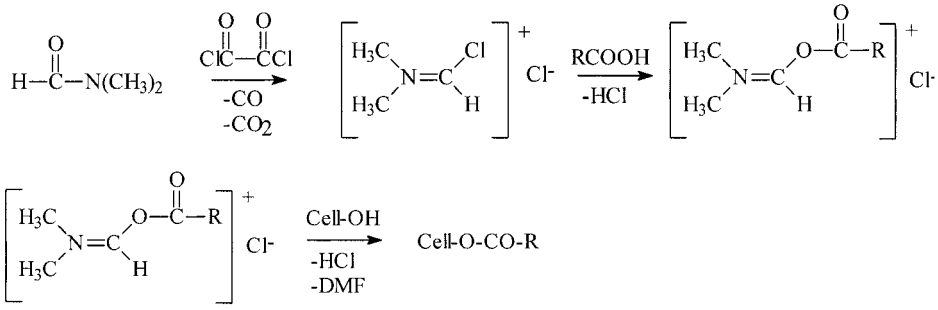


Figure 15. Reaction scheme for the preparation of cellulose esters via iminium chlorides.

A very efficient method for cellulose esterification under heterogeneous reaction conditions is the so-called "impeller" method. The carboxylic acids used are converted to reactive mixed anhydrides during these reactions. Chloroacetyl-, methoxyacetyl-, and most important trifluoroacetyl moieties are used as impellers [100]. Tri-*O*-carboxylic acid esters of cellulose can be obtained in this way, which were part of a series of DSC studies including also regioselectively substituted mixed cellulose esters (e.g. 2,3-di-*O*-acetyl-6-*O*-propionyl cellulose) [101]. A rather drastic decrease in reactivity is observed in the order acetic > propionic > butyric acid anhydride [102]. The reactions succeed almost without chain degradation.

On the other hand, new catalysts were developed, e.g., titanium-(IV)-alkoxid compounds like titanium-(IV)-isopropoxide [103] (Table 17). It was shown that the catalyst could be applied for the preparation of partially esterified cellulose derivatives if an appropriate solvent is used. Furthermore, the esterification of cellulose with acetyl chloride at elevated temperatures and in vacuum using 1,4-dioxan/pyridine as reaction medium is known. Vacuum is applied to remove the liberated HCl during the reaction [104].

The application of solvents and new reagents for the acetylation of cellulose is up to now mostly of academic interest. These alternative paths of acetylation lead to a whole variety of CA

samples with different DS, patterns of substitution and with different morphology. This pool of substances is indispensable for the establishment of structure-property relations as described in chapter 4.2.4. for the solubility behavior of CA. Nevertheless, the homogeneous acetylation of cellulose in DMAc/LiCl with acetic anhydride as well as the conversion via the imidazolide of acetic acid can be of commercial interest for the synthesis of defined CA (defined molecular weights, reproducible DS and substitution pattern) in specific fields of application, e.g. in biotechnology or for the interaction with ionic compounds (see chapter 4.2.6.). Especially for the system DMAc/LiCl/acetic anhydride investigation towards an industrially applicable process, including recovery of the medium, are very promising. DMI can be a reasonable substituent for the thermally more instable DMAc.

Table 17. Long-chain mixed cellulose esters synthesized by titanium (IV) isopropoxide-catalyzed reaction in *N,N*-dimethylacetamide.

Carboxylic acid anhydride	Equivalent per AGU	Time [h]	Temp. [°C]	DS (^{1}H-NMR)	M_w 10^{3} [a] [g/mol]	T_g [°C]
Acetic/Hexanoic	2.00/2.00	9	155	1.91/0.75	164	149
Acetic/Hexanoic	1.00/3.00	9	155	1.38/1.36	113	122
Acetic/Hexanoic	0.00/4.50	6	155	0.12[b]/2.39	245	119
Acetic/Nonanoic	2.00/2.00	11	145	2.03/0.70	177	129
Acetic/Lauric	3.50/1.00	12	140	2.40/0.20	295	165
Acetic/Palmitic	2.00/2.00	12	145	2.06/0.42	125	156
Acetic[c]/Hexanoic	0.00/3.00	7	140	0.00/2.73	61	104
Acetic/Nonanoic	3.00/1.00	8	145	2.44/0.26	220	161
Acetic/Nonanoic	1.00/3.00	13	155	1.59[b]/1.11	182	118
Acetic/Nonanoic	0.00/4.00	13	160	1.11[b]/1.35	200	110

[a] By GPC in NMP.
[b] May results from the reaction of the solvent [103].
[c] *N,N*-Dimethylimidazolidinone (DMI) used as solvent instead of DMAc, AGU = Anhydroglucose unit.

4.2.4. Solubility of cellulose acetate

Although CA has been known for almost a century, an unambiguous description of the solubility depending on the preparation procedure, the partial deacetylation and the resulting functionalization patterns is still not clearly postulated. In this subchapter data known from the literature concerning this issue, is summarized.

Commercial acetylation of cellulose proceeds usually with complete conversion of all accessible hydroxyl functions. Depending on the acetylation procedure, degradation of the

polymer backbone occurs to a different extend resulting in different solubility. Nevertheless, cellulose triacetate (CTA, DP about 300 synthesized from cellulose with DP 800-1600) obtained from the Dreyfus-, the Dormagen-, and the Schering process is generally soluble in chlorinated hydrocarbons, e.g., chloroform, methylene dichloride, tetrachloro ethane, epichlorohydrin and additionally in formic acid, acetic acid, nitro benzene, aniline, and pyridine.

If the synthesis is carried out in a polymeranalogous manner with acetic anhydride/acetic acid in pyridine at 60°C, the CTA obtained is insoluble in common organic solvents like dioxane and THF. The high DP does not cause the insolubility because polymeranalogous regeneration of cellulose from cuoxam and subsequent acetylation under comparable conditions yields soluble CTA [105]. This difference in solubility is due to the existence of two stable polymorphic crystalline structures in cellulose triacetate: CTA I and CTA II (see Chapter 4.1.). In general, CTA I is obtained by the fibrous acetylation of cellulose I. The crystalline structures can be analyzed by means of X-ray diffraction [106] and solid state ^{13}C-NMR spectroscopy [23,107]. Moreover, cellooligosaccharides were studied by means of CPMAS ^{13}C-NMR spectroscopy and X-ray as models for CTA [108].

The effect of temperature, solvent, and concentration on the supramoleculare structure and on the microscopic conformation of CTA was investigated by means of ^{13}C-NMR spectroscopy and two-dimensional nuclear Overhauser exchange spectroscopy (NOESY). It was observed that the polymer derivative exists as 5/4 helix but undergoes an unique transition at 53°C [19]. The formation of mesophases of CTA in different solvents was studied as well [109].

Moreover, it was shown that vapors of solvents, which are capable of forming lyotropic LC phases with cellulose and its derivatives, efficiently affect the processes of structure formation in CA samples and their optical activity. This effect is accompanied by a change not only in the specific optical rotation but also in its sign, thereby suggesting that when exposed to solvent vapors the cholesteric helix of cellulose esters changes so that it rotates the plane of light polarization to the left instead of rotating it to the right [110]. Recently, the interaction of cellulose and CA of different DS values with water, ethanol, and chloroform was studied by the sorption technique. The factors were investigated determining the water-solubility of CA with DS varied in a narrow range [111]. More detailed information on the structure of CA samples in solution is given in Chapter 4.1.3.

4.2.4.1. Adjustment of the solubility of cellulose acetates by defined de-esterification

It is well known that properties of CA samples, e.g. the solubility, change over different periods of time. This is basically due to de-acylation. CA samples may contain about 6% water resulting in hydrolysis. Elevated relative humidity and temperature will accelerate the reaction. The acetic acid formed as a product of degradation may take part in catalyzing further de-acetylation, and the reaction becomes autocatalytic. Thus, this reaction has a slow induction period, wherein the rate of hydrolysis is governed primarily by temperature and relative humidity, and an autocatalytic point, past which the reaction proceeds increasingly rapidly and independently of heat and moisture (they are self-fuelling) [112]. The CA will only begin to smell of acetic acid at this stage. This phenomenon is known as vinegar syndrome. At this point the properties including solubility will be influenced.

Tailored hydrolysis of the cellulose triacetate (primary acetate) to acetone-soluble CA (secondary acetate) is usually carried out with water/H_2SO_4. The de-acetylation starts at the primary functions but during the process these hydroxyl groups can be re-esterified [113]. Controlled de-esterification is also possible with 95% acetic acid at 100°C. The course of reaction, the acetyl contents and the solubility in acetone are summarized in (Table 18).

Table 18. Acetyl content and acetone-solubility of cellulose acetates dependent on the time of treatment with 95% acetic acid at 100°C [114].

Time of treatment [h]	Acetyl content [%]	Solubility in acetone [%]
0	60.6	18.2
1	60.1	36.7
3	59.8	75.2
6	59.4	92.4
9	58.4	100.0
12	57.0	100.0

CA swells or dissolves in various solvents dependent on the DS and the distribution of the functional groups as investigated by Deus *et al.* [17]. Differently prepared CA samples were studied, namely by homogeneous synthesis of cellulose dissolved in *N*-ethylpyridinium chloride (line 2, Figure 16), by acidic hydrolysis of CTA (line 1) and by alkaline hydrolysis of CTA (line

3) as displayed in Figure 16.

It is obvious that a correlation between DS and the polarity of the solvents exists. The solubility shifts to more non-polar solvents with increasing DS. Polymers prepared by acidic hydrolysis with an aqueous mixture of acetic- and sulphuric acid show best solubility (line 1), which is caused by a high degree of degradation.

Especially the solubility of CA in water and in aqueous media depends strongly on the distribution of substituents. Thus, the results shown in line 2 were obtained for CA samples prepared homogenously in *N*-ethylpyridinium chloride, which exhibit a highly pronounced acetylation in position 6. The samples for line 3 were prepared by basic hydrolysis of CTA with ethylene diamine and show an equal substitution on all reactive sites (see Chapter 4.2.5.). The systematic investigation of de-esterification processes focused on the synthesis of regioselectively functionalized CAs especially by basic hydrolysis with amine containing media is discussed in Chapter 4.2.5.

Miyamoto *et al.* studied the dependence of the water-solubility of CA on the distribution of substituents [115]. The DS and distribution of acetyl groups of the water-soluble CA were investigated by means of ^{13}C-NMR spectroscopy. Three different series of acetates with low DS were prepared by:

(1) De-acetylation of cellulose triacetate with aqueous acetic acid,
(2) Reaction of cellulose triacetate with hydrazine, and
(3) Acetylation of cellulose with acetic anhydride in DMAc/LiCl.

The DS values of water-soluble samples range from 0.5 to 1.1. CAs completely soluble in water can be obtained by method 1, only. These products exhibit little difference between the partial DS values at *C*-2, *C*-3 and *C*-6 hydroxyl groups (Table 19). In contrast, samples obtained applying method 2 and 3 revealed a much higher partial DS at the *C*-6 hydroxyl groups compared to those at *C*-2 and 3. Nevertheless, the maximum DS of water-solubility is 1.1 in any case. Aqueous solutions of samples prepared according to method 1 showed no sol-gel transition, even when the temperature was raised to 95°C. X-ray diffraction observations revealed that these samples were essentially non-crystalline in contrast to samples obtained from method 2 and 3.

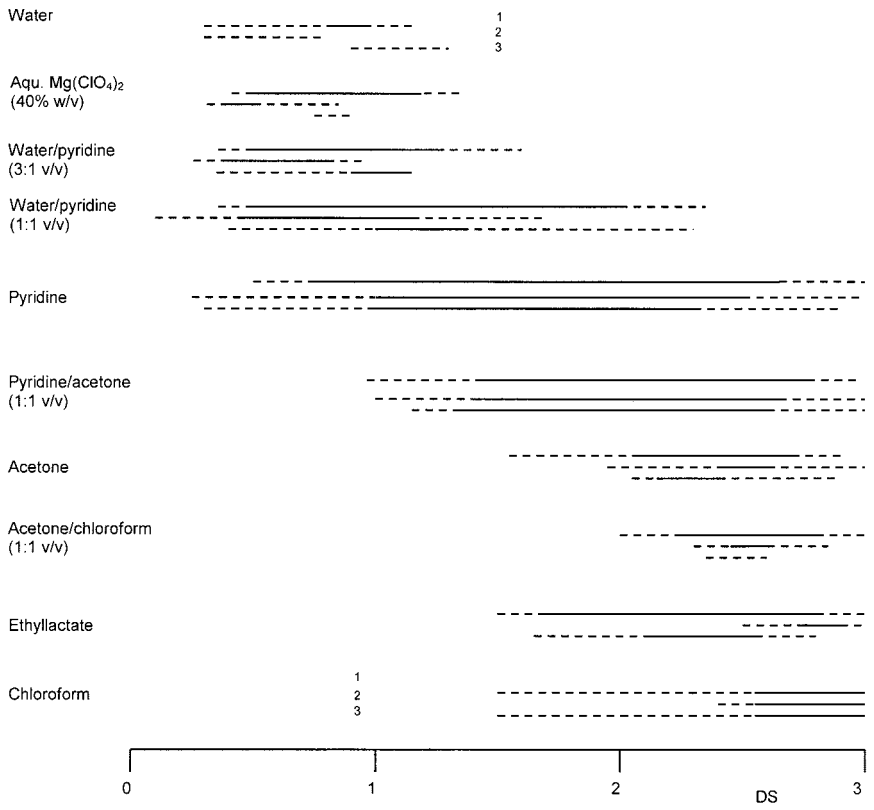


Figure 16. Swelling (dashed line) and solubility (full line) of CA with different DS values and patterns of substitution. Line 1 CA samples obtained by acidic and line 3 by basic hydrolysis of CTA, samples for line 2 were prepared homogenously in *N*-ethylpyridinium chloride (Reproduced with permission from *Makromol. Chem.* **1991**, *192*, 75. Copyright 1991 Wiley-VCH).

A comparable study of solubility of CA prepared by different methods and its correlation with average acetyl group distribution in glucopyranose units was published [11]. In addition to the distribution of substituents on the level of the repeating units, the sequence distribution of substituted and unsubstituted glucopyranose units of water-soluble CA chains were revealed by enzymatic degradation [21]. For this purpose water-soluble samples (DS 0.6-0.9) prepared by

acid-hydrolysis of cellulose diacetate were subjected to enzymatic hydrolysis. The degraded products were fractionated by preparative gel-permeation chromatography (GPC) into 50 and 20 fractions, analyzed by analytical GPC and by ^{13}C-NMR spectroscopy to determine the molecular weight and the DS. The DS value in the degraded products was nearly constant (1.0) and the DP was in the range 1-7. Small portions of water-insoluble components with DS of 2.48 and 2.45, respectively, were determined. They had lower molecular weights than the water-soluble components, indicating the existence of short, highly substituted CA blocks. This result is nicely displayed in a sequence distribution (Figure 17) published in [14].

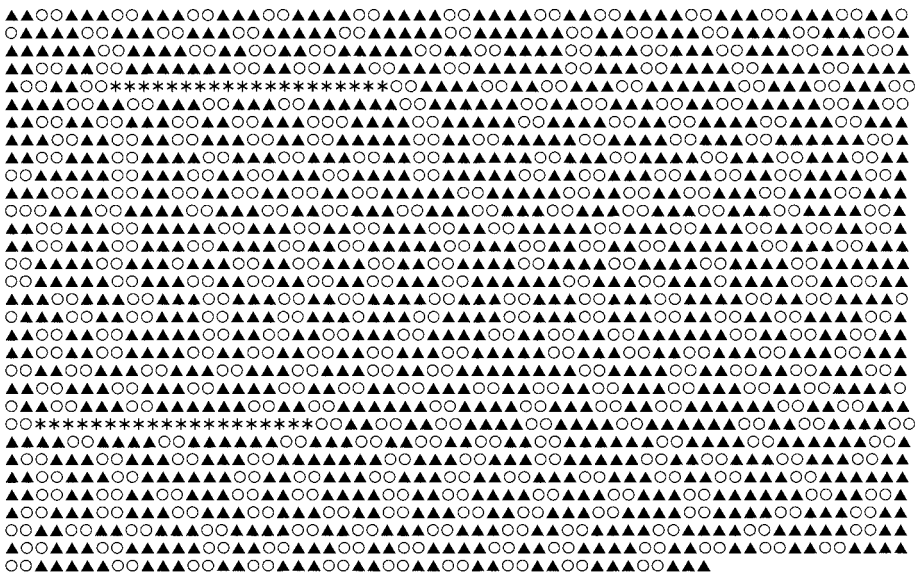


Figure 17. Sequence distribution of differently substituted glucose units along the polymer chain of a water soluble CA with DS 0.64 and DP 96; ○ unsubstituted units; ▲ monosubstituted units; ∗ highly substituted regions (Reproduced with permission from *Macromol. Symp.* **1994**, *83*, 233. Copyright 1994 Wiley-VCH).

Defined procedures for the manufacture of water-soluble CA by acid hydrolysis were developed [116,117]. Thus, cellulose was acetylated using acetic anhydride and H_2SO_4 and the product was hydrolyzed with dilute acetic acid using H_2SO_4 or sodium acetate as hydrolysis

catalyst. The CA obtained was initially soluble in acetone. Water-soluble samples can be obtained when the acetyl content was in the range 18-20%. On increasing the hydrolysis temperature, the hydrolysis rate increased. If sodium acetate is applied as hydrolysis catalyst, water-solubility could not be achieved.

Table 19. Structure analysis of the water-soluble fractions of CA samples prepared via three different methods.

Method[a)]	Total DS[b)]	Degree of acetylation at position[b)]			Water soluble fraction
		2	3	6	[wt.-%]
1	0.49	0.16	0.13	0.20	29
1	0.66	0.23	0.20	0.23	99
1	0.90	0.31	0.29	0.30	93
2	0.73	0.18	0.19	0.36	30
3	1.10	0.33	0.25	0.52	5

[a)] Methods applied: (1) de-acetylation of cellulose triacetate with aqueous acetic acid, (2) reaction of cellulose triacetate with hydrazine, and (3) acetylation of cellulose with acetic anhydride in DMAc/LiCl.
[b)] Determined by ^{13}C-NMR spectroscopy.

The water-soluble product was evaluated as a size for cotton yarn. It's tensile and flex abrasion properties were intermediate between those of starch and polyvinyl alcohol. Degradation and modification of cellulose during acid-catalyzed solvolysis of CA hydrogen sulfate in solution was investigated [118]. The esterification of cotton was carried out with acetic acid and H_2SO_4 in DMF. A water-soluble CA hydrogen sulfate was obtained with a $DS_{HSO4-} > 0.15$. Replacing water by alcohols as solvolysis medium decreases the degradation of the polymer not significantly. A procedure for the manufacture of water-soluble CA fibers was developed [119]. The fibers were prepared by dry-spinning of solutions of CA samples with DS 0.4-1.2. Complete water-solubility was achieved by saponification of the fibers with alkali.

In addition, investigations towards the adjustment of the solubility of CA samples in organic media by de-acetylation were carried out. A sophisticated technique was established for the preparation of CA samples with excellent solubility but low viscosity of concentrated solutions [120]. For this purpose, cellulose was acetylated with acetic anhydride in acetic acid using H_2SO_4 as catalyst. The product was dissolved in DMSO, and partially hydrolyzed to give a CA having DS 2.0, which was then treated with trityl chloride in pyridine, acetylated with acetic anhydride using 4-dimethylaminopyridine (DMAP). The final CA was obtained after treatment

with hydrobromic acid/acetic acid. The CA samples show partial DS in position 2 and 3 of 1.97, and less than 30% in position 6.

Two-stage acetylating processes were investigated to realize CA with a DS values in the range 1.5-2.9 and a uniform distribution of functional groups. Procedures were developed in which CA of DS 0.25 is obtained in the first stage to provide a final product with DS 2.5, which is completely soluble in acetone. This solubility is taken as test of uniformity of acetylation [121].

Products with a DS of 1.70, useful for further derivatization, were obtained at 60°C with 15-34% toluene in the reaction medium of acetic acid/water or without the addition of water [122,123]. The kinetic behavior of toluene-containing systems, dependent on the composition of the reaction medium, as well as on the temperature, was investigated. Reaction systems with 15 and 20% toluene were found to obey a linear relation of $-\ln(DS/DS_0)$ versus time. The hydrolyzed products obtained by the described procedure were soluble in some common organic solvents useful for derivatization, such as DMF, acetic acid, and DMSO.

Solubility of CA samples can also be studied and adjusted by partial fractionation [124]. Acetone-water mixtures were applied for partial fractionation of cellulose diacetate samples. Considerable de-acetylation was observed after long residence times before isolating and drying the fractions. The de-acetylation could be explained in terms of a hydrolytic cleavage of the ester group due to small amounts of acid groups, e.g., sulfate half ester groups left from the manufacture of CA.

4.2.5. Cellulose acetate with defined molecular structures

The application of new reagents and new media for the acetylation of cellulose and the accessible structural features of the CA samples are described in Chapter 4.2.3. Most of these paths lead to a more or less preferred conversion of the primary hydroxyl function. Moreover, there are additionally two basic methods for a control of the regioselectivity. On one hand, the selective deacylation of CA samples and, on the other, the acylation of cellulose after protection may be used to control the functionalization pattern. Most of the work concerning the selective acetylation of cellulose was carried out towards the establishment of structure-property relationships (mostly structure-solubility, see Chapter 4.2.4.). Furthermore, selectively acetylated celluloses were applied for subsequent reactions as briefly discussed in Chapter 4.2.6.

4.2.5.1. Selective de-acylation of cellulose triacetates

Acidic Hydrolysis

Industrial aspects of the hydrolysis, a general mechanism, and relevant literature and patents concerning this process are given in Chapters 3.1.3.1. and 3.2.3. There are a number of publications dealing with the correlation between the hydrolysis procedure and the distribution of substituents but different conclusions were drawn. As early as 1946 the heterogeneous acid and acid-salt hydrolysis of secondary CA (acetyl content of 53.2%) under the influence of HCl, H_2SO_4, HNO_3, HI, H_3PO_4, and HCl containing NaCl, NaBr, KBr, or NaI, or $CaCl_2$ was systematically studied [125]. The results indicate that the rate of hydrolysis falls in the sequence HI, HNO_3, HCl, H_2SO_4, H_3PO_4 and that in the case of HCl, the addition of H_3PO_4 has a retarding effect on the rate of hydrolysis. The salts increase the velocity of hydrolysis in the order Ca^{2+}, Na^+, K^+ for cations and I^-, Br^-, Cl^- for anions.

Among the first reports on the mechanism and the distribution of acetyl functions obtained by acidic hydrolysis of CTA (primary acetate) were publications by Malm *el al.* [113,126,127]. The hydrolysis was carried out with water/H_2SO_4. It starts at the primary functions but during the process these hydroxyl groups can be re-esterified. Controlled de-esterification was also possible with 95% acetic acid at 100°C.

Deus *et al.* [17] studied the distribution of acetyl groups in CA samples prepared in *N*-ethylpyridinium chloride (see Chapter 4.2.3) in comparison to derivatives with different DS obtained by either acidic or basic hydrolysis of CTA (see below). In case of the acidic hydrolysis of CTA to products with DS values down to 2.2, it was found that the rate of de-acetylation in *C*-6 and *C*-2 is comparable. If hydrolysis continues, de-acetylation in *C*-2 is more pronounced, i.e., the acetyl functions in *C*-6 are the most stable. In any case de-acetylation in *C*-3 is the fastest (Figure 18). A different behavior is observed if the hydrolysis with acetic acid/sulfuric acid is carried out directly after the complete functionalization of cellulose. The rate of reaction is comparable for all three reactive sites over the whole range of DS (Figure 18). Thus, CA samples with an even distribution of substituents on the level of the AGU are accessible.

Kowsaka *et al.* describe a comparable functionalization pattern obtained by de-acylation of CA but the higher stability of the acetyl function in *C*-6 was observed in acidic hydrolysis starting from an over-all DS of about 0.8 [128]. An analogous behavior was observed by

Miyamoto *et al.* [115]. Partial DS values for selected samples are shown in Table 18. Defined acidic hydrolysis was applied for the preparation of CA with DS 0.7 – 1.7. Biodegradation, i.e., de-acetylation and de-polymerization can be observed for CA with DS up to 1.5 [133].

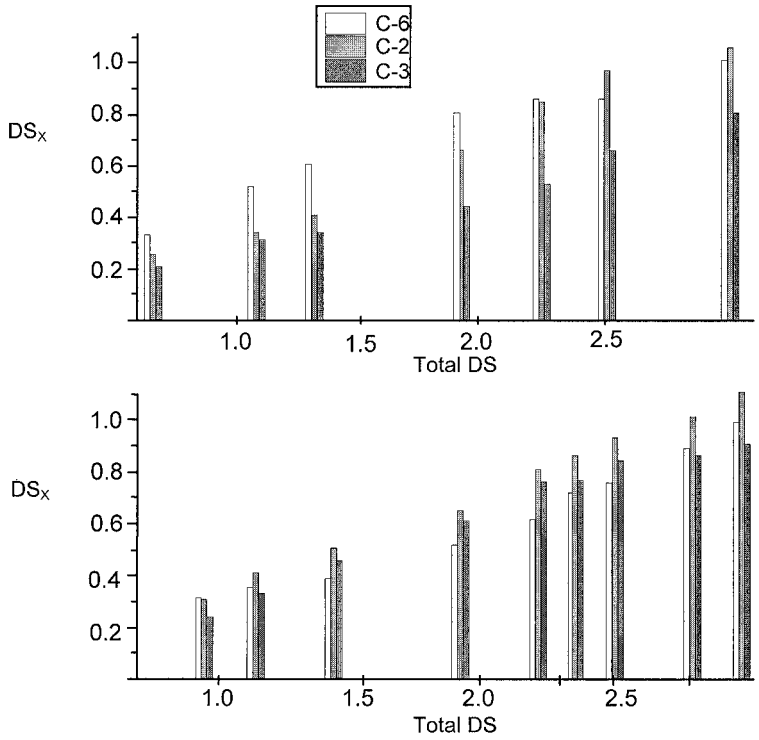


Figure 18. Pattern of substitution of differently prepared CA samples as plot of the partial DS in C-2, C-3 and C-6 (DS_X) versus the over all DS for CA samples prepared via:
Top: acidic de-esterification of cellulose triacetate
Bottom: acidic de-esterification of cellulose triacetate directly after acetylation in *N*-ethylpyridinium chloride (Reproduced with permission from *Makromol. Chem.* **1991**, *192*, 75. Copyright 1991 Wiley-VCH).

Hydrolysis of CA in the presence of organic solvents was studied. Thus, a mixture toluene/acetic acid/water was applied for homogeneous de-acetylation [129]. Products with a low

DS were obtained in shorter times than in the conventional procedure using H_2SO_4/water. Moreover, CA with a high amount of free primary hydroxyl groups was prepared. The degradation of the polymeric chain during hydrolysis is lower in case of short reaction times.

Besides the industrially applied hydrolysis of CTA, the process was used for the selective de-acylation of acetyl-1-^{13}C-labeled CA. Dibutyltin oxide and further different inorganic salts were studied as hydrolysis catalysts, e.g. magnesium acetate tetrahydrate. In addition, the acidic methanolysis was applied. These samples were investigated by means of 2D-COSY and 1D-INAPT techniques (see Chapter 4.2.2.2. [13]).

De-acetylation under basic conditions

Irreversible saponification with alkali is extensively applied for the regeneration of cellulose from CA. For this purpose even acetone containing anhydrous media with NaOMe were studied [1]. The saponification of CA with NaOH and KOH was among the first attempts for a modification of the polymer [130]. Kinetic studies of the saponification of acetone-soluble CA samples with different bases in the presence of alcohols were carried out.

The saponification was applied for adjustment of various properties of CA samples, e.g., water-solubility [119], the hygroscopic character of CA fibers [131], the UV-absorbing property of CA films [132] or the biodegradability [133]. Moreover, the influence of the addition of organic solvents, e.g., acetone during the heterogeneous de-esterification was studied. The irreversible alkaline saponification of acetyl groups in solid CA depends on the accessibility, i.e., the state of swelling as shown in Figure 19 for the decrease in DS on the treatment of CA with 0.1 N NaOH in water/acetone mixtures of increasing acetone content [134]. Nevertheless, according to our knowledge there is no detailed study concerning the distribution of substituents accessible by basic saponification with NaOH or KOH over the whole range of DS.

First attempts for a correlation of the basic hydrolysis of CA with both the DS and the distribution of acetyl groups were carried out by ^{13}C-NMR spectroscopy [115]. De-acetylation of CTA in DMSO was achieved with hydrazine. The relative DS at C-6 hydroxyl groups is very high compared to those at *C*-2 and *C*-3 hydroxyl groups (Table 19). CA with an even more pronounced *C*-6 selectivity can be prepared by de-acetylation in the ternary mixture of DMSO/water/aliphatic amine (e.g., dimethylamine or hexamethylenediamine). Deus *et al.*

observed a very uniform de-acetylation of all three positions of the AGU during a homogeneous aminolysis of CTA by ethylene diamine after dissolution in DMAc under water-free conditions in comparison to other routes of de-acetylation [17].

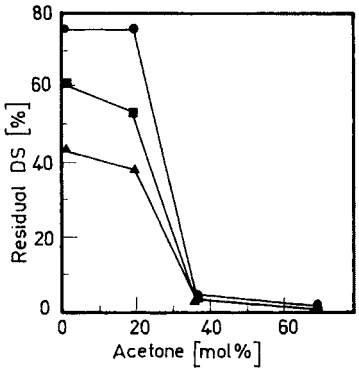


Figure 19. Effect of acetone content and temperature (● 30°C; ■ 40°C; ▲ 50°C) on the course of saponification of CA (DS = 2.9) in 0.1 N NaOH (Adopted from Ref. [134]).

Table 20. Homogeneous de-acetylation of cellulose triacetate in amine-containing (dimethylamine, or hexamethylenediamine) media at 80°C

Amine	Molar ratio	Time	DS[a)]	Pattern of functionalization[b)]		
Example	mol/mol AGU	[h]		*C*-2	*C*-3	*C*-6
NH_2-$(CH_2)_6$-NH_2	2.3	2.5	2.60	0.80	0.80	1.00
		4.5	2.41	0.65	0.75	1.00
		9.0	1.87	0.45	0.55	0.90
		14.0	1.33	0.20	0.45	0.85
		24.0	0.75	0.05	0.10	0.60
$HN(CH_3)_2$	4.5	5.0	2.55	0.75	0.80	1.00
		11.0	2.06	0.50	0.50	1.00
		15.0	1.84	0.35	0.50	0.95
		20.0	1.59	0.30	0.40	0.90
		24.0	1.45	0.20	0.30	0.70

[a)] Determined by saponification and titration.
[b)] Calculated from NMR spectra.

The selectively substituted CA samples obtained were applied for the preparation of cellulose sulfuric acid half esters [135]. The distribution of substituents showed a strong influence on the properties of the products, e.g., solubility, membrane formation and separation behavior,

and interaction with human blood. In addition, manufacture of CA phosphate with definite molecular structure was described [136]. The mixed esters with phosphate moieties mainly in the position 2 and 3 are manufactured by de-acetylation of CTA for 0.5-72 h at 20-100°C with an amine and subsequent phosphorylation in an aprotic solvent (e.g., DMF) with polyphosphoric acid in the presence of tributyl amine. Thus, the de-acetylation of CA of DS 2.90 with dimethylamine in aqueous DMSO gives a product with DS 0.85 and partial DS of *C*-2 = 0.05, *C*-3 = 0.15, and *C*-6 = 0.7, which was phosphated for 6 h at 120°C with polyphosphoric acid in DMF in the presence of tributyl amine. CA phosphate with DS_{Ac} 0.83 and DS_P 1.20, which was de-acetylated by treatment with ethanolic NaOH to yield cellulose phosphate with DS_P 0.96 and partial degrees of phosphation of *C*-2,3 = 0.77 and *C*-6 = 0.19.

An alternative to the de-acetylation of CTA is the preparation of partially acetylated cellulose in DMAc/LiCl with pyridine/acetic anhydride leading to a CA with a preferred substitution at *O*-6. In a subsequent step, the CA was carefully de-acetylated at 30°C in DMSO with 80 wt-% aqueous solution of hydrazine monohydrate yielding a polymer with functionalization at position 6 only (DS 0.6). For such a sample with a DP of 96, it was possible to determine the sequence distribution of substituted AGUs along the polymer chain by means of ^{13}C-NMR spectroscopic studies ([14], see Figure 17).

4.2.5.2. Regioselective esterification

For the synthesis of CA with a preset, well-defined structure, the polymeranalogous regioselective esterification of the secondary hydroxyl groups is approached by protection of the primary function with the bulky triphenylmethyl moiety. The conversion of 6-*O*-triphenylmethyl cellulose with acetic anhydride in pyridine yields 2,3-di-*O*-acetyl-6-*O*-triphenylmethyl cellulose, which can be selectively detritylated with gaseous hydrogen chloride in dichloromethane [14] (Figure 20) or more preferred with hydrogen bromide/acetic acid [137]. The correlation of properties, e.g., solubility with the molecular structure was investigated [14].

Subsequent acylation of the generated free hydroxyl groups with propionic anhydride leads to a completely modified 2,3-di-*O*-acetyl-6-mono-*O*-propionyl cellulose. Starting with the propionylation, a product with an inverse pattern of functionalization, i.e., 6-mono-*O*-acetyl-2,3-di-*O*-propionyl cellulose is accessible. These esters were utilized as model compounds for NMR

spectroscopic studies [137]. Full assignment of their NMR signals by applying the high-sensitivity 2D-heteronuclear multiple-bond connectivity (HMBC) technique together with the conventional 2D-NMR techniques was reported. Moreover, DSC studies on regioselectively substituted cellulose esters, e.g., propionate diacetate-, butanoate diacetate-, acetate dipropanoate-, acetate dibutanoate of cellulose, in comparison with cellulose triester were carried out [54]. Based on the results a strong correlation between the melting point and the length of the acyl groups at the secondary OH moieties was shown.

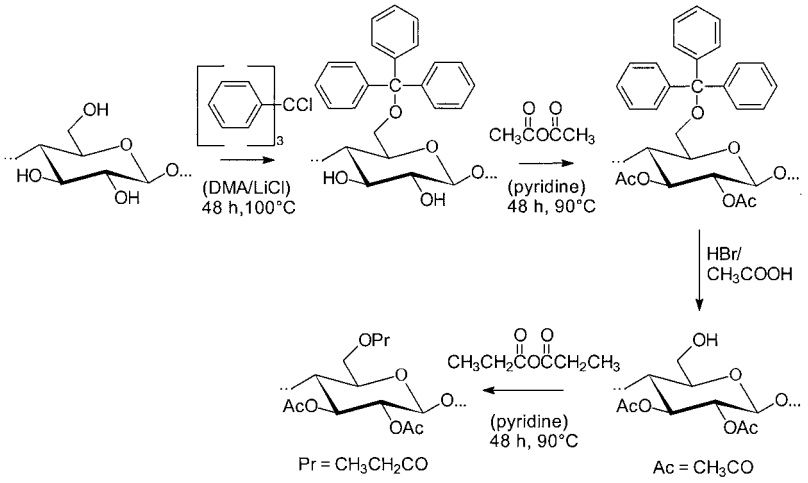


Figure 20. Reaction schema of the regioselective acylation of cellulose

In addition, direct imaging of single crystals of regioselectively substituted cellulose esters by Atomic Force Microscopy was possible (Figure 21, [138]). A close relationship between the observed thickness of both single crystals (29 nm for 2,3-di-*O*-acetyl-6-mono-*O*-propionyl cellulose and 45 nm for 6-mono-*O*-acetyl-2,3-di-*O*-propionyl cellulose) and the calculated lamellar thickness based on the fiber repeat distance and DP indicates that chain-folding at their lamellar surfaces have not occurred in both single crystals. Furthermore, the dynamic structures formed in polar solvents of regioselectively substituted CA samples were compared with those of

commercial products where the distribution of hydroxy- and acetyl groups was nearly random in the chain. It was found that the difference in the chain architecture induces a large difference in the chain conformation, the solubility, and the clustering mechanism and structures [139,140].

Figure 21. Atomic Force Microscopy-image of single crystals of 2,3-di-*O*-acetyl-6-*O*-propanoyl cellulose (Reproduced with permission from *Macromolecules* **1997**, *30*, 6683. Copyright 1997 Am. Chem. Soc.).

A fairly new method for the protection of the primary hydroxyl groups and hence the preparation of regioselectively substituted cellulose esters in positions 2 and 3 is the introduction of tert.-butyldimethylilyl- and thexyldimethylsilyl functions (Table 21) [141,142]. Depending on the reaction conditions the selectivity can be adjusted (Figure 22). Thus, selective protection of the position 6 or selective protection of positions 6 and 2 can be achieved in different reaction media. By reacting tert.-butyldimethylsilyl- or thexyldimethylsilyl cellulose with acetyl chloride in the presence of a tertiary amine such as triethyl amine the secondary OH groups can be peracetylated [143]. In addition, acetylation with acetic anhydride in the presence of pyridine yields 2,3-di-*O*-acetyl-6-mono-*O*-thexyldimethylsilyl cellulose.

Structural evidence was gained by means of ^{1}H-NMR and ^{1}H/^{1}H COSY-NMR spectroscopy (Figure 23, [144]). Derivatization, de-silylation and subsequent acetylation can be

applied for the preparation of 6-mono-*O*-acetyl-2,3-di-*O*-methyl cellulose, 3-mono-*O*-methyl-2,6-di-*O*-acetyl cellulose, or 3-mono-*O*-allyl-2,6-di-*O*-acetyl cellulose [145]. $^{1}H/^{1}H$ and $^{1}H/^{13}C$ correlated NMR spectra were recorded (Figure 24).

Table 21. Silylation of cellulose with tert.-butyldimethylilyl chloride (t-BDMSC) and thexyldimethylsilyl chloride (ThxDMSC) in DMAc/LiCl[a].

Chlorosilane (mol/mol AGU)		DS_{Si}	Solubility		
t-BDMSC	ThxDMSC		DMF	THF	$CHCl_3$
1.0	-	0.67	+	-	-
1.5	-	0.96	+	-	-
3.0	-	1.53	-	+	+
-	1.0	0.71	+	-	-
-	1.5	0.92	+	-	-
-	3.0	1.43	-	+	+

[a] 5% Cellulose, 8% LiCl, 1.1 mol pyridine/mol chloro silane.

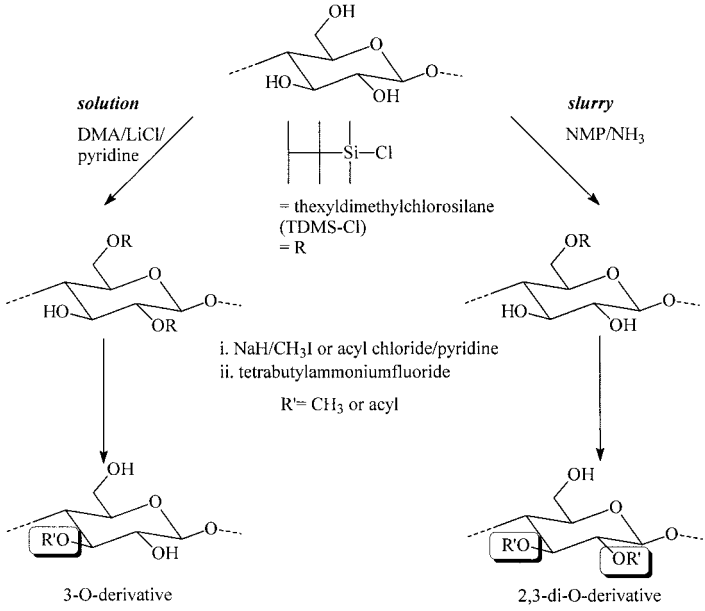


Figure 22. Schematic plot of the different paths yielding cellulose acetates selectively functionalized at position 3 only or at 2 and 3 after protection with thexyldimethylsilyl moieties.

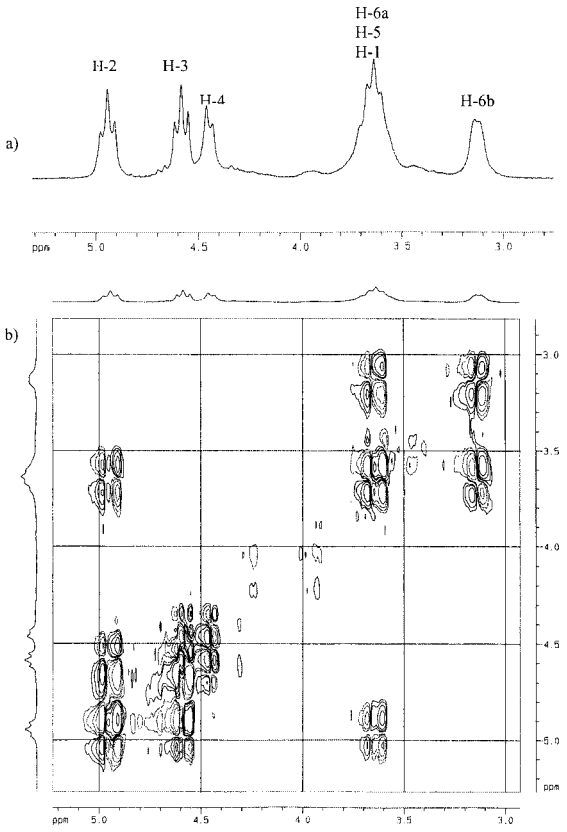


Figure 23. ^{1}H-NMR spectrum (a) and ^{1}H/^{1}H correlated NMR spectrum (b) of 2,3-di-*O*-acetyl-6-mono-*O*-thexyldimethylsilyl cellulose. (Reproduced with permission from *Cellulose* **2003**, *10*, 251. Copyright 2003 Kluwer).

An interesting approach towards the synthesis of regioselectively functionalized CA samples and mixed derivatives is the ring opening polymerization of modified sugars. Six possible regioselectively methylated CA samples, namely acetylated 3,6-di-, 2,6-di-, and 2,3-di-*O*-methyl cellulose, 6-mono-, 3-mono-, and 2-mono-*O*-methyl cellulose were prepared from chemically synthesized cellulose derivatives obtained by cationic ring-opening polymerization and analyzed by means of ^{1}H- and ^{13}C-NMR spectroscopy. The chemical shifts of ring protons

and carbons are influenced by substituents (methyl or acetyl) and clearly reflect the pattern of functionalization of the AGU. The data may conveniently be used for the determination of the pattern of substitution of methyl cellulose and for the elucidation of the structure-property relationship [146].

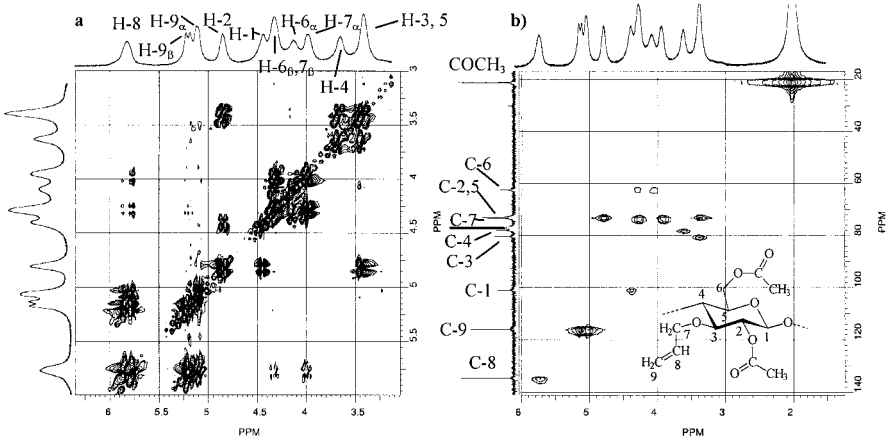


Figure 24. $^{1}H/^{1}H$ (left) and $^{1}H/^{13}C$ (right) correlated NMR spectrum (b) of 3-*O*-allyl-2,6-di-*O*-acetyl cellulose. (Reproduced with permission from *Macromol. Biosci.* **2001**, *1*, 49. Copyright 2003 Wiley-VCH).

4.2.6. Derivatives of cellulose acetate

There is a huge variety of derivatives of CA obtained directly by the conversion of cellulose with different reagents (both one-step reactions and subsequent reactions) or synthesized by subsequent conversion of isolated CA. It is not possible to give a comprehensive summary of all reactions and chemical structures, which were prepared. Consequently, the subsequent products will be grouped according to the specific field of application they were synthesized for and an overview will be given of basic approaches for different problems. The following subsequent reactions were carried out on CA samples for:

- analytical reasons
- the establishment of structure-property relations (regioselective functionalization)
- the adjustment of properties

- the interaction with inorganic compounds or for the immobilization of enzymes

Moreover, CA is an interesting intermediate in cellulose functionalization. A summary of reactions exploited for the analysis of CA and the corresponding structures obtained is given in Figure 25.

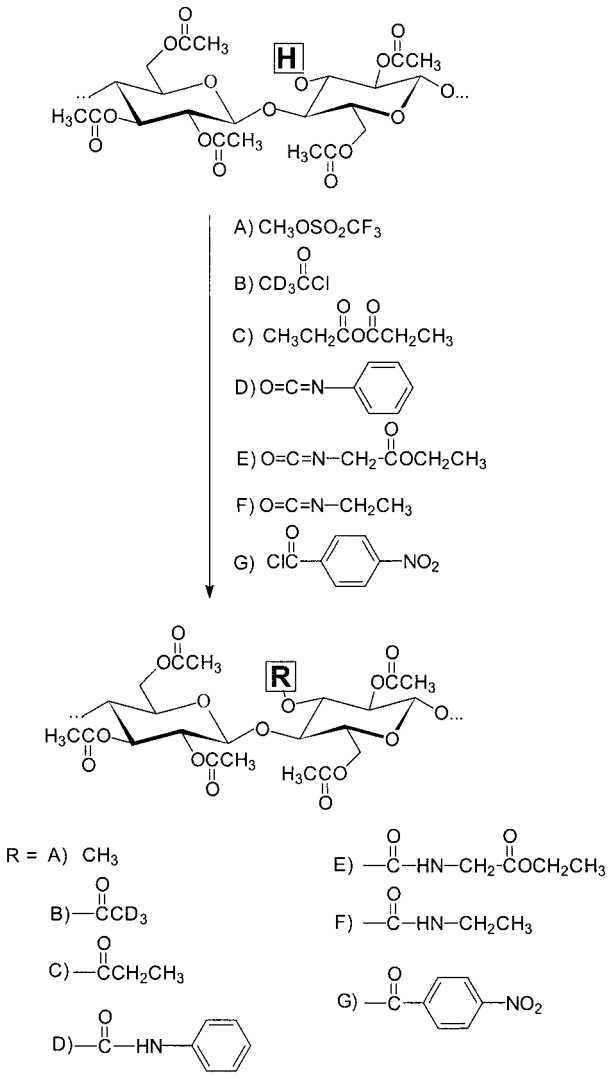
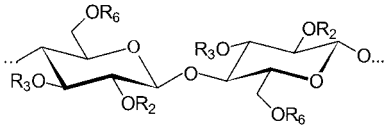


Figure 25. Summary of reactions exploited for the analysis of CA (exemplified for DS 2.5) and the corresponding structures obtained.

For detailed discussion on the reaction conditions, the analytical strategies and the chromatographic as well as the spectroscopic data see Chapter 4.2.2.

Regioselectively functionalized CA and derivatives of CA useful as model compounds and for the establishment of structure-property relations were accessible by protective group techniques or by cationic ring-opening polymerization. This subject is discussed in detail in Chapter 4.2.5. Thus, regioselectively substituted mixed CA propionates and acetate butyrates prepared via 6-*O*-triphenylmethyl cellulose (Figure 26) were utilized as model compounds for NMR spectroscopic studies, in DSC measurements and for the direct imaging of single crystals by AFM (see Figure 21). Furthermore, the dynamic structures formed in polar solvents of regioselectively substituted CA samples were compared with those of commercial products [137,138]. Differences in the chain conformation, solubility, and clustering mechanism were found [139,140].

Tert.-butyldimethylsilyl- and thexyldimethylsilyl functions (Figure 26, [141,142]) were applied for the protection of cellulose as well. Synthesis of 6-mono-*O*-acetyl-2,3-di-*O*-methyl cellulose, 3-mono-*O*-methyl-2,6-di-*O*-acetyl cellulose, and 3-mono-*O*-allyl-2,6-di-*O*-acetyl cellulose has been achieved after protection with thexyldimethylsilyl functions [144,145]. The preparation of all types of selectively functionalized methylated CA samples was possible via cationic ring-opening polymerization. However, the DP of the products synthesized via this path is in the rang of 10 - 40 only [146].



2,3-Di-O-acetyl-6-mono-O-triphenylmethyl cellulose

$R_{2,3}$= $\overset{O}{\overset{\|}{C}}CH_3$; R_6 = C 

2,3-Di-O-acetyl-6-mono-O-propionyl cellulose

$R_{2,3}$= $\overset{O}{\overset{\|}{C}}CH_3$; R_6 = $\overset{O}{\overset{\|}{C}}CH_2CH_3$

6-Mono-O-acetyl-2,3-di-O-propionyl cellulose

R_6 = $\overset{O}{\overset{\|}{C}}CH_3$; $R_{2,3}$ = $\overset{O}{\overset{\|}{C}}CH_2CH_3$

Figure 26. Structure of the intermediate 2,3-di-*O*-acetyl-6-mono-*O*-triphenylmethyl cellulose and the regioselectively substituted mixed CA propionates.

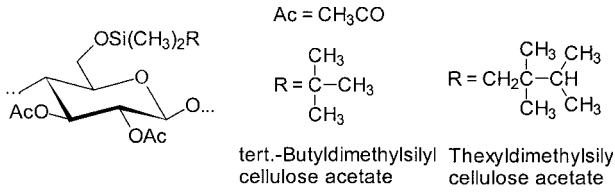


Figure 27. Structure of 2,3-di-*O*-acetyl-6-mono-*O*-tert.-butyldimethylsilyl and 2,3-di-*O*-acetyl-6-mono-*O*-thexyldimethylsilyl cellulose.

4.2.6.1. Modification of cellulose acetates for tailored properties

Recently, Edgar *et al.* nicely reviewed this topic [147]. The starting polymers used were not only pure CA but also mixed esters such as acetate propionates (CAP) and acetate butyrates (CAB). The derivatives described were mainly used for controlled release applications, as radiation curable coatings, and as waterborne coatings (Figure 28).

CA, CAP, CAB, CA phthalates (CAPht, **9**, Figure 28) were applied for sustained release of actives, including highly water-soluble drugs [148-150]. They can also be employed as so-called elementary osmotic pump delivery system [151-153] and for the controlled release of pesticides or herbicides in agriculture [154]. Conversion of CA, CAP and CAB with cyclic anhydrides yields pH-sensitive esters (compounds **9-13**) for enteric coatings [155]. The goal of an enteric coating is to permit an oral dosage form to survive the harsh environment of the stomach intact, but to release the actives quickly and completely to be absorbed in the intestines. Modified CA has found application not only in the pharmaceutical field and in agriculture, but also in controlled release of polymer additives [156] and fragrances.

Besides the subsequent functionalization of CA for controlled release applications, a major stimulation for the modification of CA was the search for radiation curable coatings. The introduction of pendant branches that provide cross-linkable functionality to a cellulose ester aids in the formation of a hard, scratch-resistant, and solvent-resistant surface following radiation curing. For this purpose CA was modified with unsaturated isocyanates to give the corresponding CA urethane (**1,** [157,158]) and with cyclic anhydrides to give carboxycellulose esters (**9-13,** [159]). The carboxycellulose esters can be esterified at the carboxylate functionality with glycidyl acrylate or glycidyl methacrylate (e.g. compound **2**). The synthesis of β-alkylamino esters (**3**) was

possible via α,β-unsaturated cellulose esters (**4,** [160]). A more simple and versatile cellulose ester for radiation curable coatings has been prepared by alkali-catalyzed maleation of CAP (**5**, [161-164]). Synthesis paths were developed for silyl ether derivatives containing thiol functionality that can function as chain-transfer/cross-linking (**6**, [165]). Acrylamidomethyl derivatives (**8,** [166,167]) are commercially available under the trade name Jaylink™. A more complex radiation curable cellulose ester (**4** and **7**, [168,169]) was obtained by reacting an acrylic anhydride and *m*-isopropenyl-α,α-dimethylbenzyl isocyanate with the cellulose esters. It should be mentioned that cross-linking of CA samples could also be achieved with pyromellitic dianhydride (PMDA, [170]).

A new strategy for the preparation of waterborne coatings on the basis of CA has been the introduction of carboxylic acid functions. This can be achieved by conversion with dicarboxylic anhydrides. Examples are CA phthalates (**9**, [171]) and succinates (**11**, [172]). Comparable approaches are carboxymethylated cellulose esters. The carboxymethyl cellulose esters [173] are soluble in a wide range of solvents, are compatible with a number of resins, and are readily dispersed in water. Structures accessible by oxidation of CA, CAP and CAB with ozone are shown in Figure 29. Besides the introduction of carboxylic acid functions this treatment also produces pendant peroxide groups [174].

In addition to the oxidation of CA samples, the acetylation of oxidized cellulose was investigated [175]. Thus, oxidized CA samples (OCA), with a DS value ranging between 1.1 and 2.3 and a free carboxylic acid group content of 20% (w/w), have been prepared by reacting oxidized cellulose with a mixture of acetic acid/acetic anhydride and sulfuric acid as a catalyst. Oxidation of CA with $NaIO_4$ was exploited for the activation of porous cellulose acetate. The derivative was used as beads for amyloglucosidase immobilization [176].

The manufacture of long-chain alkyl-containing CA ethers, e.g., CA cetyl ether was applied to prepare derivatives useful as materials for water-repellent papers and protein adsorbents [177].

4.2.6.2. Application of cellulose acetate as intermediate in cellulose fuctionalization

Partially hydrolyzed CA was used as intermediate for the sulfation and phosphation of cellulose (see Chapter 4.2.5.1. [134,135]). The preparation of sulfoacetate derivatives of cellulose

was possible by direct esterification. The location of the sulfate groups and the rheological properties of the cellulose sulfoacetates were studied [178-180].

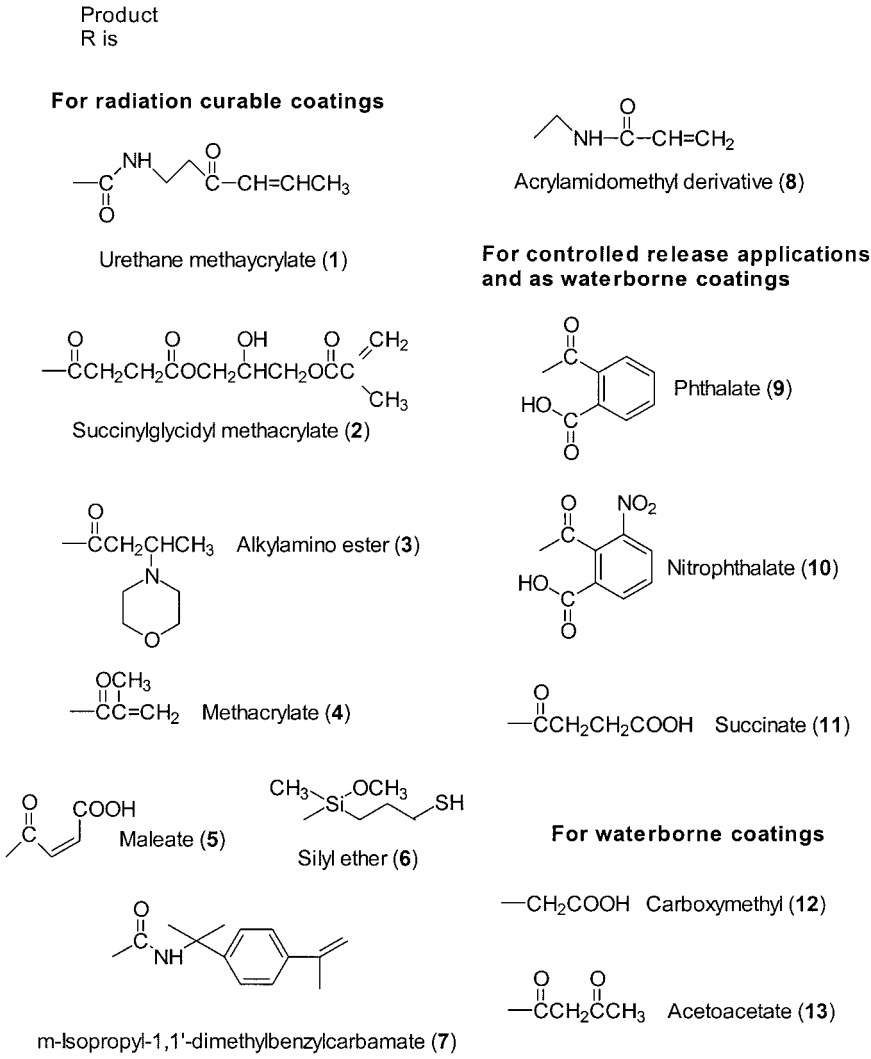


Figure 28. Examples of subsequently functionalized CA, CAP and CAB (R = additional function) used for controlled release, as radiation curable coatings, and as waterborne coatings.

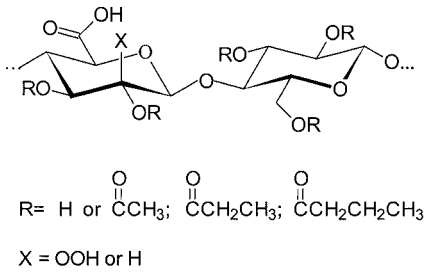


Figure 29. Polymers accessible by oxidation of CA, CAP and CAB with ozone, which can be used as waterborne coatings.

CTA was extensively used as starting compound for the *in situ* regeneration of highly activated cellulose, e.g., for the synthesis of triphenylmethyl cellulose (see Figure 26, [181,182]). Tri-*O*-isopentyl cellulose was prepared from CTA with aqueous sodium hydroxide and 3-methylbutyl bromide. The derivative was applied for the construction of ultrathin layers [183]. Furthermore, different methyl celluloses (MC) were prepared from CTA. The CTA was partially deacetylated under homogeneous conditions. In a subsequent reaction the CA samples with DS values in the range 0.7-1.9 were methylated with sodium naphthalene and methyl iodide. The pure MC samples were obtained by complete deacetylation with aqueous ammonia. The water-solubility and the thermally reversible sol-gel transition of these MC samples in correlation with the DS and the functionalization pattern were investigated [184]. It was observed that aqueous solutions of MC samples with an even distribution of substituents on the basis of the AGU (prepared via CA) do not show precipitation upon heating in contrast to commercial MC samples with a preferred methylation in position 6 and 2.

An interesting approach for the synthesis of cellulose ethers with a non-statistic distribution of substituents along the polymer chain can be realized starting from solutions of CA (DS 0.8) in DMSO. These solutions were treated with solid, water-free NaOH particles and the so-called "cellulose in reactive microstructure" is formed (Figure 30).

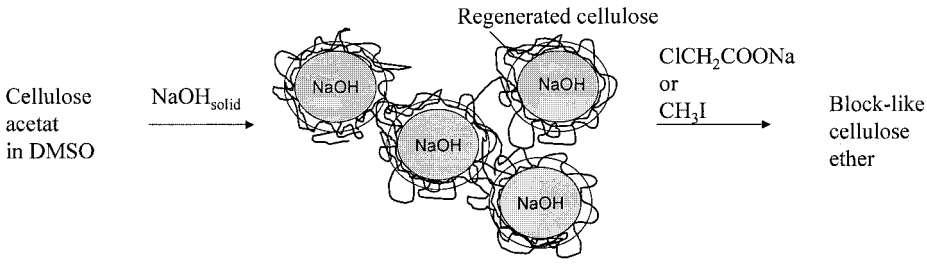


Figure 30. Schematic plot of the preparation of unconventional cellulose ethers (block-like derivatives) prepared via "cellulose in reactive microstructure". The "reactive microstructure" was obtained by conversion of cellulose acetate with solid NaOH particles.

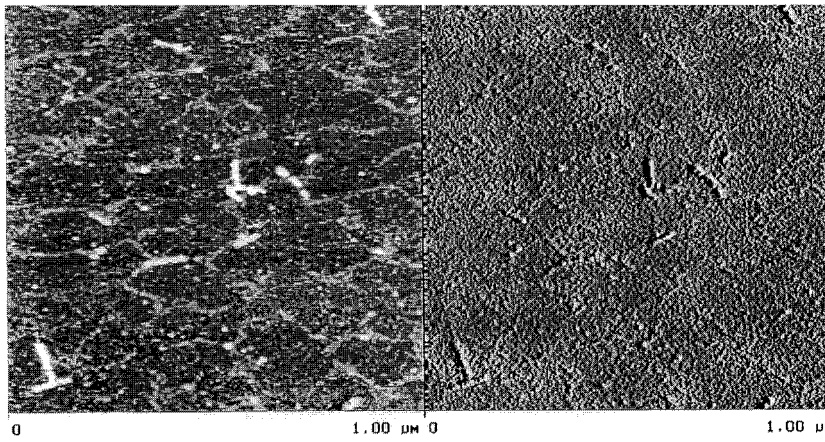


Figure 31. Atomic force microscopy image (on mica under butanol appling tapping mode; left: topographic image, right: amplitude image.) of carboxymethyl cellulose (degree of substitution = 1.72) prepared via "cellulose in reactive microstructure" (Reproduced with permission from *Biomacromol.*, **2001**, *2*, 1124. Copyright 2001 Am. Chem. Soc.).

This "reactive microstructure" can be transformed with methyl iodide or sodium monochloroacetate to give unconventional MC or carboxymethyl cellulose. These derivatives show an unconventional pattern of substitution along the polymer chain as determined by HPLC measurements after complete de-polymerization and comparison of the values obtained with

statistic calculations [185]. A block-like distribution of the substitutents along the polymer chain was determined by enzymatic degradation of the polymers. The ethers exhibit new superstructures [186]. In contrast to commercial derivatives with an even distribution of substituents along the polymer chain, which built up "fringed micelle", a network-like structure was determined by atomic force microscopy (AFM, Figure 31). A remarkable influence of the functionalization along the chain of the polymer and the resulting suprastructure on the polymer properties was found. Thus, the new cellulose derivatives stabilize colloidal dispersions, e.g., colloidal $BaSO_4$ and show unusual interaction with polycations during titration of aqueous solutions, which can be attributed to the formation of more compact polyelectrolyte complexes with significantly smaller dimensions and higher particle density [187].

4.2.6.3. Miscellaneous modifications of cellulose acetate

Besides the use of CA samples as starting material for the defined degradation, e.g., with supercritical water and alcohols [188] pivaloylysis of CTA (Figure 32, [189]) was exploited as a new degradation method for the preparation of cellulose oligomers. These oligomers can be applied as starting material in organic synthesis.

Immobilization of enzymes

CA was widely applied as carrier material and for different immobilization reactions. Thus, cholesterol oxidase (COD) was immobilized on a CA membrane. The membranes exhibit high catalytic activity and can be applied in biosensors [190]. Urease was immobilized on CA membrane by entrapment. The activity, yield, and stability of urease immobilized membrane were investigated in catalyzing hydrolysis of urea [191]. Moreover, alcohol oxidase (alcohol: oxygen oxireductase; EC 1.1.3.13) and glucose oxidase (D-glucose: oxygen 1-oxireductase; EC 1.1.3.4) were covalently linked to CA membranes. In case of the more hydrophobic membranes, obtained from CAB, a reduction of the activities but better storage stability was observed [192]. As mentioned above, attachment of amyloglucosidase on porous CA beads was achieved after activation of CA by oxidation with $NaIO_4$ [176].

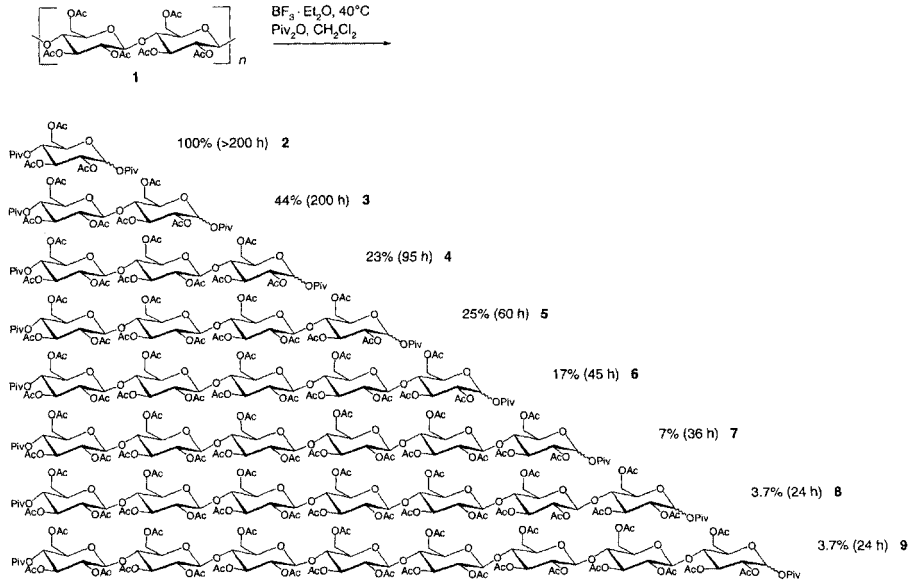


Figure 32. Degradation of cellulose triacetate by pivaloylysis. (Reproduced with permission from *Cellulose* **2003**, *10*, 75. Copyright 2003 Kluwer).

A new concept for the immobilization of enzymes is the formation of composite gel fibers from CA with transition metal compounds and entrapment of the enzyme. Entrap-immobilization of β-galactosidase [193] as well as invertase [194] on the fiber consisting of CA and zirconium tetra-n-butoxide was described. The gel is formed by the coordination of OH- and C=O groups of the cellulose derivative to zirconium, taking six coordination numbers around the zirconium. The activity of the immobilized β-galactosidase increased as the fiber diameter decreased. These findings indicated that lactose hydrolysis took place in the vicinity of the fiber surface. The immobilized β-galactosidase had a higher thermal stability than the native type. β-Galactosidase may also be entrapped in a gel fiber of CA and titanium iso-propoxide. The fiber shows amphoteric adsorption properties depending on pH. However, it had no adsorption property for a pyrogen endotoxin [195]. Glucose oxidase was entrapped in the same material. This immobilization can be easily and simply carried out under mild conditions. The fiber is stable in common solvents, high ionic solutions and over the wide pH range of 3-10 [196,197].

Enantioselective esterification of racemic ibuprofen was possible in isooctane by immobilized lipase on cellulose acetate-titanium iso-propoxide gel fiber [198]. For this purpose lipase (*Candida rugosa*) was entrap-immobilized on CA-titanium iso-propoxide gel fiber by a sol-gel method. The immobilized lipase was used for the direct synthesis of (S)-ibuprofen ester from racemic ibuprofen. The activity of the immobilized lipase was decreased to about 10-20% in comparison to a native lipase. However, the reaction was more enantioselective compared to that with native lipase. A comparable fiber containing lipase (EC 3.1.1.3) was applied for the esterification of n-butyric acid with n-butyl alcohol. In addition, enantioselective acylation of (R, S)-phenylethanol using vinyl acetate as an acyl donor was possible with this system [199].

An interesting approach towards a fructose biosensor was published recently. The sensor is based on D-fructose dehydrogenase immobilized on a ferrocene-embedded CA membrane [200]. The prevention of ferrocene leakage from an electrode by retention of mediator in a CA membrane matrix is reported. The membranes prepared, including a CA membrane without ferrocene, were much more resistant to ascorbate interference in comparison to an uncovered glassy carbon electrode. With increasing amounts of ferrocene, a decreasing ability of the membrane to retain mediator was observed. Ferrocene-embedded membranes were successfully applied in the construction of a fructose biosensor by immobilization of PQQ-dependent fructose dehydrogenase. A biosensor with a membrane containing 20.0% of ferrocene in the matrix exhibited the lowest detection limit, the shortest response time (45 s) and the highest sensitivity.

Interaction with transition metal ions

A variety of papers were published concerning the interaction of CA with transition metal ions. The preparation and characterization of secondary CA complexes with chromium(III), copper(II), cobalt(II), nickel(II), and UO_2^{2+} was published [201,202]. CA acts as a uninegatively charged bidentate ligand and reacts with the metal ion via the oxygen atom of the secondary unacetylated hydroxyl group in the glucose subunit of the polymer, plus the oxygen atom of the vicinal ester group, to form a five-membered chelate ring (Figure 33). In addition, the thermal properties of the CA-transition metals complexes were investigated [203]. TGA and DTA of CTA and its complexes with Ni(II), Co(II), Cu(II) and Cr(III) chlorides were studied from room temperature to 550°C. The TGA curves obtained show that these samples degrade thermally in 3

steps. The complexing of CA with metal ions increased its thermal stability. The calculated activation energies varied in the following sequence: CTA-Cu > CTA-Ni > CTA-Co > CTA-Cr > CTA. This observation was attributed to the electronegativity of the metal ion and the strength of the bond between the CA and the metal ion.

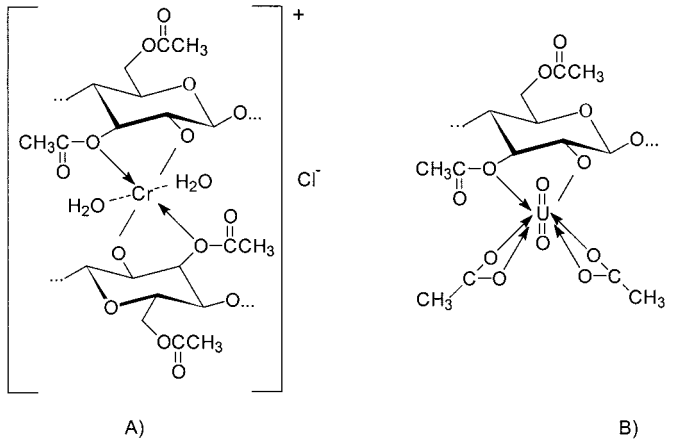


Figure 33. Structure of cellulose acetate complexes with chromium(III) (A), and UO_2^{2+} (B). (Reproduced with permission from *Transition Metal Chem.* **1994**, *19*, 340. Copyright 1994 Kluwer).

Furthermore, spectroscopic characterization of CA membranes containing Cu(1,3-butadiene) trifluoromethanesulfonate (OTf) was carried out [204]. The polymer-metal complexes have been successfully applied to facilitate olefin transport membranes for the olefin/paraffin separation. The reversible solid-state interactions of Cu^+ ions with CA and olefins have been studied using FT-IR- and UV spectroscopy. FT-IR spectroscopy clearly shows that the Cu^+ ions in the Cu-CA membrane are coordinated by the carbonyl groups of CA. Upon incorporation of Cu(1,3-butadiene) OTf into CA, the carbonyl stretching frequency of CA at 1753 cm^{-1} shifts to a lower frequency at around 1702 cm^{-1} and the degree of coordination increases with increasing amounts of Cu(1,3-butadiene)OTf. The Cu^+-carbonyl interaction is found to be significantly affected by the coordination of an olefin, suggesting that the olefin and carbonyl group compete with each

other for the coordination to Cu^{+} ions. Reversible olefin coordination to Cu^{+} ions in the Cu-CA membranes has been observed by FT-IR and UV studies. Treatment of the Cu-CA membrane with propylene, ethylene, or 1,3-butadiene produces a corresponding olefin-coordinated membrane in which the coordinated olefin is easily replaced by another olefin.

The description of the chemical characteristics of CA clearly indicates that the biopolymer-based product is well-known and well-understood. Considering its abundant resource and the degree of refinement of its manufacturing process, as well as alternative pathways for preparation and new techniques for detailed structure analysis, it will be a material for the future and will contribute to the sustainable development. For a detailed discussion see Chapter 6.

Abbreviations

AFM	atomic force microscopy
AGU	anhydroglucose units
CA	cellulose acetate
CAP	cellulose acetate propionate
CAB	cellulose acetate butyrate
CDA	cellulose diacetate
CDI	N,N'-carbonyldiimidazole
CI	chemical ionization
CTA	cellulose triacetate
CF	cellulose formate
CMC	carboxymethyl cellulose
COSY	correlated spectroscopy
CTFA	cellulose trifluoroacetate
DCC	N,N-dicyclohexylcarbodiimide
DEA	diethylamine
DMAc	N,N-dimethylacetamide
DMAP	N,N-dimethylaminopyridine
DMF	N,N-dimethylformamide
DMI	1,3-dimethyl-2-imidazolidinone
DMSO	dimethyl sulfoxide
DP	degree of polymerization
DS	degree of substitution; DS is the average number of functional groups per anhydroglucose repeating unit arriving at a level of three after complete functionalization of all hydroxyl groups.
DSC	differential scanning calorimetry
EI	electron impact
Et	ethyl

FTIR	Fourier transform infra-red spectroscopy
glc	glucose
GLC	gas liquid chromatography
GLC-MS	gas liquid chromatography-mass spectroscopy
GPC	gel permeation chromatography
HMBC	heteronuclear multiple-bond connectivity
HPLC	high performance liquid chromatography
INEPT	insensitive nuclei enhancement by polarization transfer
IR	infra-red spectroscopy
MC	methyl cellulose
Me	methyl
m.p.	melting point
NMMNO	N-methylmorpholine-N-oxide
NMP	N-methyl-2-pyrrolidone
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser exchange spectroscopy
OCA	oxidized cellulose acetate
OTf	trifluoromethanesulfonate
PF	paraformaldehyde
PP	4-pyrrolidinopyridine
TBAF	tetrabutylammonium fluoride trihydrate
TDMS	texyldimethylsilyl
TEA	triethylamine
TFA	trifluoroacetic acid
Tg	glass transition temperature
THF	tetrahydrofuran
TMS	trimethylsilyl
TMSC	trimethylsilyl cellulose
Tos-Cl	p-toluenesulfonyl chloride
Tos-OH	p-toluenesulfonic acid
Triflat	trifluoromethanesulfonic acid ester
Trityl	triphenylmethyl

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4.2.7. References

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