Interactions of Ionic Liquids with Polysaccharides 1. Unexpected Acetylation of Cellulose with 1-Ethyl-3-methylimidazolium Acetate

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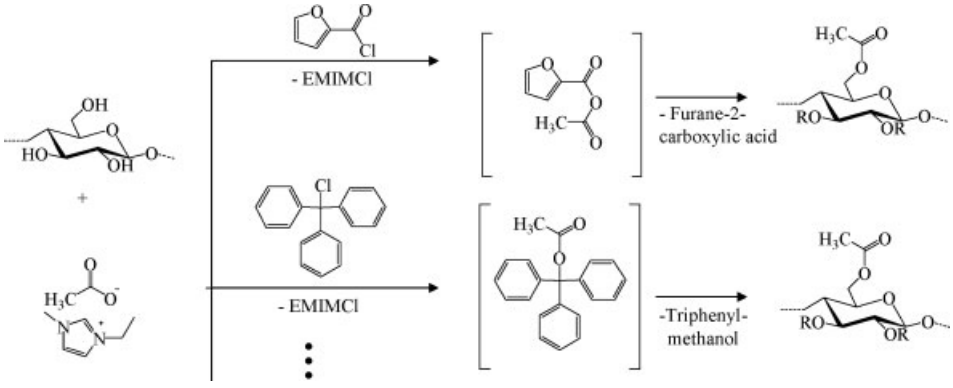
The homogeneous conversion of cellulose in the ionic liquid 1-ethyl-3-methylimidazolium acetate with 2-furoyl chloride, *p*-toluenesulfonyl chloride, and triphenylmethyl chloride yields surprisingly pure cellulose acetate samples in any case. From NMR spectroscopic studies, it may be concluded that during the homogeneous functionalization reactive intermediates including furane-2-carboxylic acid/acetic acid anhydride and acetic acid triphenylmethyl ester are formed leading to the cellulose acetates with DS values in the range from 0.55 to 1.86.



Introduction

Starting with the work of Rogers and coworkers the interest in organic salt melts as media for dissolution, regeneration, and chemical modification of cellulose was revived.[1] Although comparable systems were already investigated in the 1930s by Graenacher[2] and in the 1960s by Husemann and Siefert,[3] the new interest is fueled both by the experiences with solvents on the basis of reactive melts such as *N*-methylmorpholine-*N*-oxide[4] and by the commercial availability of a whole variety of such compounds now referred to as ionic liquids (ILs). During the last four years, the number of publications related to the use of ILs as solvent and reaction medium for different carbohydrates and cellulose in particular increased dramatically. In the beginning, the most popular solvent was 1-butyl-3-methylimidazolium chloride (BMIMCl).[5] A large amount of work has been carried out to evaluate the potential of this solvent for the homogeneous chemical modification of cellulose. It was

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demonstrated that the acylation of cellulose with different anhydrides and chlorides as well as the carbanilation succeeds with remarkable efficiency.[6–8]

These findings are of tremendous impact, because it was demonstrated that chemical modification of cellulose may be carried out under homogeneous conditions using ILs in a commercial scale for the first time. It has to be mentioned that this homogeneous path could significantly broaden the number of commercially relevant, high-value cellulose derivatives and could thereby significantly increase the amount of the cellulose used as renewable feedstock.

Besides the regeneration of cellulose and the chemical modification, there were preliminary attempts for the description of the state of dissolution of cellulose in this solvent. From $^{35/37}$Cl NMR spectroscopy it was concluded that the chloride counterion is essential for the dissolution of the polysaccharide.[9] Nevertheless, new results show that ILs with other counterions are also able to dissolve the biopolymer.[10] Especially, 1-ethyl-3-methylimidazolium acetate (EMIMAc) is well suited as a cellulose solvent.[11] In addition to the fact that this solvent is in liquid state at room temperature, it shows a much higher capability for cellulose dissolution. Moreover, EMIMAc is less toxic than comparable chlorides and is even biodegradable.[12] These features make it a desirable solvent for shaping and homogeneous chemical functionalization of cellulose.

In this communication, investigations concerning the homogeneous conversion of cellulose in EMIMAc with acid chlorides, trityl chloride and tosyl chloride are discussed. The surprising result is that in any case pure cellulose acetates are obtained. Here we present for the first time the possible mechanisms for these remarkable side reactions on the cellulose backbone.

Experimental Part

Solvents and Reagents

Microcrystalline cellulose (Fluka, Avicel® PH-101) dried at 105 °C for 2 h was used. 2-Furoyl chloride (FC), triphenylmethyl chloride (trityl chloride), *p*-toluenesulfonyl chloride (tosyl chloride), and EMIMAc (≥98%) were supplied by Fluka and Merck. Imidazole was obtained from Alfa Aesar. All chemicals were used as received.

Measurements

^{1}H NMR spectra were measured in DMSO-d_6 (50 mg · mL^{-1} for the cellulose derivative, 0.49 mol · L^{-1}, equimolar, for the determination of the reactive intermediate) with a Bruker Avance 250 spectrometer running at 250 MHz at room temperature. 16 scans were accumulated.

^{13}C NMR spectra were recorded in DMSO-d_6 (100 mg · mL^{-1} for the cellulose derivative, 0.49 mol · L^{-1}, equimolar, for the determination of the reactive intermediate) with a BRUKER AVANCE 250 or 400 spectrometer running at 62 or 100 MHz, at room temperature. 10 000–16 000 scans were accumulated.

FTIR spectra were recorded on Nicolet Avatar 370 DTGS spectrometer with the KBr technique.

The elemental analysis was performed by CHNS 932 Analyzer (Leco).

Dissolution of Cellulose

The biopolymer was mixed with the molten IL up to 12 h at 70 °C under stirring in air to guarantee complete dissolution. An optically clear solution was obtained.

Reaction of Cellulose with FC in EMIMAc

For a typical conversion, 1.25 mL (15.4 mmol) of pyridine and 1.51 mL (15.4 mmol) of FC were added carefully to a solution of 0.5 g microcrystalline cellulose dissolved in 4.5 g EMIMAc and stirred for 3 h at 65 °C in the absence of light. The homogeneous reaction mixture was precipitated into 150 mL of ethanol and the polymer was collected by filtration. After washing five times with 50 mL of ethanol and drying at 45 °C under vacuum, product **1** was obtained.

Yield: 0.73 g (98.5%).

DS (determined by ^{1}H NMR spectroscopy after perpropionylation): 1.86.

Elemental analysis: Calcd. C 56.66, H 3.60; Found C 55.73, H 3.75, N 0.06.

IR (KBr): 3 487 ν(OH), 2 948 ν(CH), 2 901 ν(CH$_2$), 1 750 ν(C=O ester), 1 234 cm^{-1} ν(O–C–O ester) cm^{-1}.

^{13}C NMR (DMSO-d_6): δ = 169.9 (CO acetate), 102.2 (C-1), 99.2 (C-1′), 79.7–71.1 (C-2$_s$-5), 62.3 (C-6$_s$), 60.0 (C-6), 20.3 (CH$_3$ acetate).

^{1}H NMR (of the perpropionylated derivative in DMSO-d_6): δ = 5.1–3.5 (cellulose backbone, H ester), 2.2 (CH$_2$ propionate), 2.1–1.9 (CH$_3$ acetate), 1.2–0.9 (CH$_3$ propionate).

Reaction of Cellulose with Triphenylmethyl Chloride in EMIMAc

Trityl chloride (10.3 g, 37 mmol) was added to a solution of 2 g cellulose in 65 g EMIMAc and stirred for 24 h at 70 °C. The homogeneous reaction mixture was precipitated into 600 mL methanol and the polymer was collected by filtration. After washing two times with 100 mL of a 9:1 v/v mixture of methanol/water and drying at 60 °C under vacuum, product **2** was obtained.

Yield: 2.29 g (95.9%).

DS (determined by ^{1}H NMR spectroscopy after perpropionylation): 0.75.

Elemental analysis: Calcd. C 46.51, H 5.94; Found C 43.4, H 6.16, N 0.03.

IR (KBr): 3 339 ν(OH), 2 889 ν(CH$_2$), 1 728 ν(C=O ester), 1 237 cm^{-1} ν(O–C–O ester).

^{13}C NMR (DMSO-d_6): δ = 170.6–169.5 (CO acetate), 103.1 (C-1), 80.4–72.5 (C-2$_s$-5), 63.6 (C-6$_s$), 60.9 (C-6), 20.9 (CH$_3$ acetate).

^{1}H NMR (of the perpropionylated derivative in CDCl$_3$): δ = 5.1–3.5 (cellulose backbone, H$_{ester}$), 2.4–2.2 (CH$_2$ propionate), 2.1–1.7 (CH$_3$ acetate), 1.2–0.9 (CH$_3$ propionate).

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Reaction of Cellulose with *p*-Toluenesulfonyl Chloride in EMIMAc

Imidazole (2.1 g, 30.9 mmol) was added to a solution of 1 g of cellulose dissolved in 32 g EMIMAc and stirred for 12 h at 25 °C. The temperature was decreased to 7 °C and 2.3 g (12.3 mmol) tosyl chloride was carefully added. The homogeneous reaction mixture was stirred for 5 h and then precipitated into 300 mL of ethanol and the polymer was collected by filtration. After washing three times with 100 mL of a 4:1 v/v mixture of ethanol/water and drying at 60 °C under vacuum, product **3** was obtained.

Yield: 1.13 g (93.0%).

DS (determined by ^{1}H NMR spectroscopy after perpropionylation): 0.55.

Elemental analysis: Calcd. C 42.11, H 6.43; Found C 43.95, H 6.63, N 0.08, no Cl.

IR (KBr): 3 409 ν(OH), 2 889 ν(CH_2), 1 726 ν(C=O ester), 1 232 cm^{-1} ν(O–C–O ester).

^{13}C NMR (of the perpropionylated derivative in DMSO-d_6): δ = 170.2–169.2 (CO), 100.3 (C-1), 75.8–71.7 (C-2_s-5), 62.0 (C-6), 20.7 (CH_3).

^{1}H NMR (of the perpropionylated derivative in $CDCl_3$): δ = 5.1–3.5 (cellulose backbone, H_{ester}), 2.4–2.2 (CH_2 propionate), 2.1–1.9 (CH_3 acetate), 1.2–1.0 (CH_3 propionate).

Perpropionylation (Typical Procedure)

A mixture of 6 mL pyridine and 6 mL propionic acid anhydride was added to 0.3 g of cellulose furoate (product **1**). After 24 h at 55 °C in the absence of light, the reaction mixture was cooled to room temperature and precipitated in 50 mL of ethanol. The product was reprecipitated from chloroform into 50 mL of ethanol, filtered, washed with 50 mL of ethanol three times, and dried under vacuum at room temperature.

Yield: 0.31 g (99%).

DS_{Ac} = 1.86, DS_{Prop} = 1.14 (determined by ^{1}H NMR spectroscopy).

FTIR (KBr): no ν(OH), 2 943 ν(CH), 2 901 ν(CH_2), 1 751 ν(C=O ester), 1 234 cm^{-1} ν(O–C–O ester).

^{1}H NMR (in DMSO-d_6): δ = 5.1–3.5 (cellulose backbone, H ester), 2.2 (CH_2 propionate), 2.1–1.9 (CH_3 acetate), 1.2–0.9 (CH_3 propionate).

Results and Discussion

The homogeneous reaction of cellulose with triphenylmethyl chloride (trityl chloride), *p*-toluenesulfonyl chloride (tosyl chloride) and FC in EMIMAc was studied. Surprisingly, the organosoluble cellulose derivatives obtained were in any case cellulose acetates with degrees of substitution (DS) in the range of 0.55–1.86 (Figure 1, Table 1) as can be revealed by ^{13}C NMR spectroscopy. Figure 2 shows the typical spectrum for product **1** obtained with FC and cellulose dissolved in EMIMAc.

In the ^{13}C NMR spectrum no signals for the furane ring were present. Furthermore, a signal at 171.0 ppm for the carbonyl moiety and a signal at 22.2 ppm for the methyl moiety of the acetyl group were determined confirming the formation of pure cellulose acetate. The C-6 position of the anhydroglucose unit is completely acetylated. Comparable spectra are acquired for products formed by conversion of cellulose dissolved in EMIMAc with trityl chloride and tosyl chloride, i.e., cellulose acetate is formed.

Thus, we investigated the reactions in detail. The goal was to gain information about the mechanisms behind these conversions and to elucidate the general tendency of this IL toward different side reactions by chemical modifications of cellulose in EMIMAc. A reasonable explanation for the acetylation of cellulose in EMIMAc during the conversion with FC would be the formation of the reactive mixed furane-2-carboxylic acid/acetic acid anhydride that is known from the literature.[13] The existence of the proposed anhydride can be confirmed by ^{13}C NMR spectroscopic characterization of a mixture of EMIMAc, FC, and pyridine in DMSO-d_6 (Figure 3). Especially the appearance of new signals for a carbonyl moiety at 166.9 ppm and for a methyl function at 21.5 ppm indicates the formation of the mixed anhydride. This intermediate

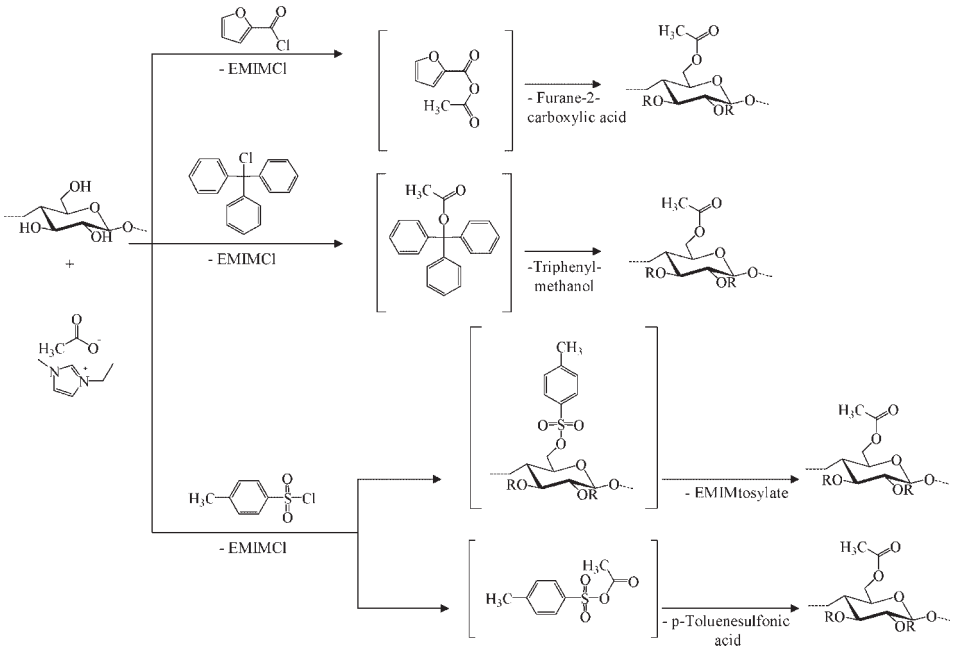

Figure 1. Overview of the synthesis path leading to cellulose acetates in EMIMAc/cellulose (R = acetyl group or H depending on the degree of substitution) during conversion with FC, triphenylmethyl chloride and *p*-toluenesulfonyl chloride.

Table 1. Results of homogeneous acetylation of cellulose in EMIMAc with different reagents (Rg).

Reaction conditions				Cellulose acetate	
Reagents	**Molar ratio AGU[a]:Rg:Base**	**Time**	**Temperature**	**No.**	**DS[d]**
		h	**°C**		
FC	1:3:3[b]	3	65	**1**	1.86
trityl chloride	1:3:0	24	70	**2**	0.75
tosyl chloride	1:2.1:5[c]	5	25	**3**	0.55

[a]Anhydroglucose unit; [b]Pyridine as base; [c]Imidazole as base; [d]Degree of substitution, determined by ^{1}H NMR spectroscopy after perpropionylation.

yields pure cellulose acetate (**1**) with DS 1.86 (see Figure 2). It should be mentioned that this type of reaction also occurs with low molecular weight alcohols such as methanol.

In addition, the conversion of acetyl chloride with EMIMAc was applied as model reaction to study the generality of this process. As expected, the symmetric acetic acid anhydride was obtained. A signal at 2.2 ppm, corresponding to the CH_3 protons of the acetic acid anhydride, was found in the ^{1}H NMR spectrum of the mixture of acetyl chloride and EMIMAc. The ^{1}H NMR spectrum of the mixture of acetic anhydride and EMIMAc shows identical signals.

Treatment of cellulose dissolved in EMIMAc with trityl chloride (**2**; Table 1) yields cellulose acetate with a DS value of 0.75. Again, the reactive intermediate was synthesized and studied by means of ^{13}C NMR spectroscopy. New peaks for a carbonyl moiety at 168.7 ppm (C-2), for C atoms of the phenyl ring at 148.3 ppm (C-4) and 130.0–127.0 ppm (C-5-7), for the triphenyl substituted methyl moiety at 89.0 ppm (C-3), and for the methyl function of the converted acetyl group at 22.5 (C-1) ppm were observed (Figure 4). These chemical shifts and the splitting pattern correspond to the formation of reactive trityl acetate during the reaction of trityl chloride with EMIMAc. Obviously, the reactive ester of the voluminous triphenyl carbinol is well suited for transesterification reactions toward cellulose acetate.

In contrast, acetylation by means of the reaction of tosyl chloride with cellulose dissolved in EMIMAc may succeed via two different reaction pathways. One possibility may be the formation of the cellulose tosylate and subsequent nucleophilic displacement reaction with the acetate anion[14] of the ionic liquid. The behavior of cellulose tosylate (DS 1.33), dissolved in EMIMAc at 70 °C, was investigated by FT-IR of samples taken after different time

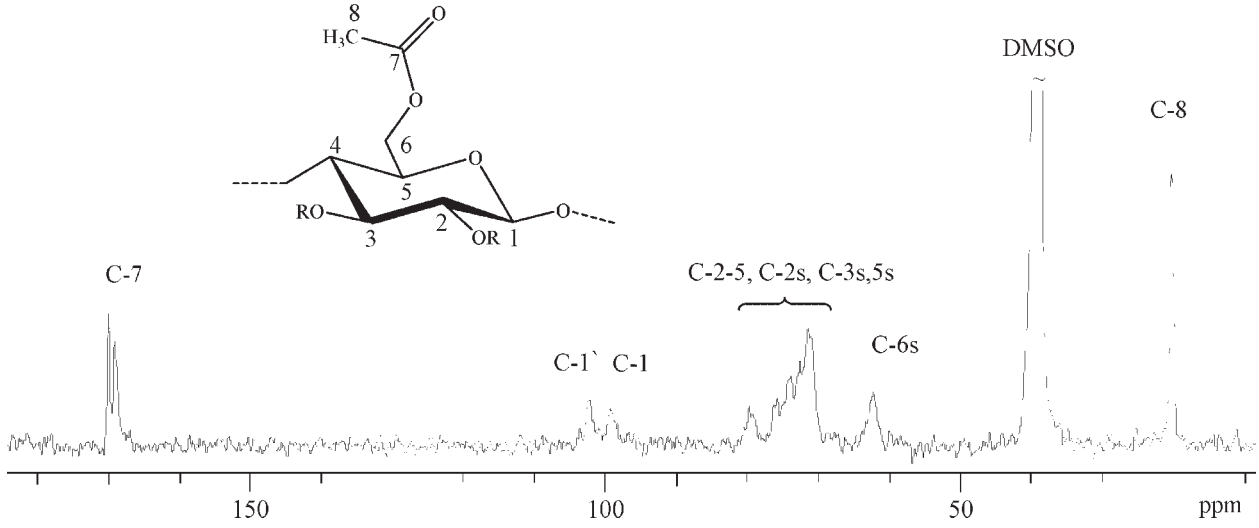

Figure 2. ^{13}C NMR spectrum (DMSO-d_6) of a cellulose acetate (degree of substitution = 1.86) obtained by conversion of cellulose with FC in EMIMAc.

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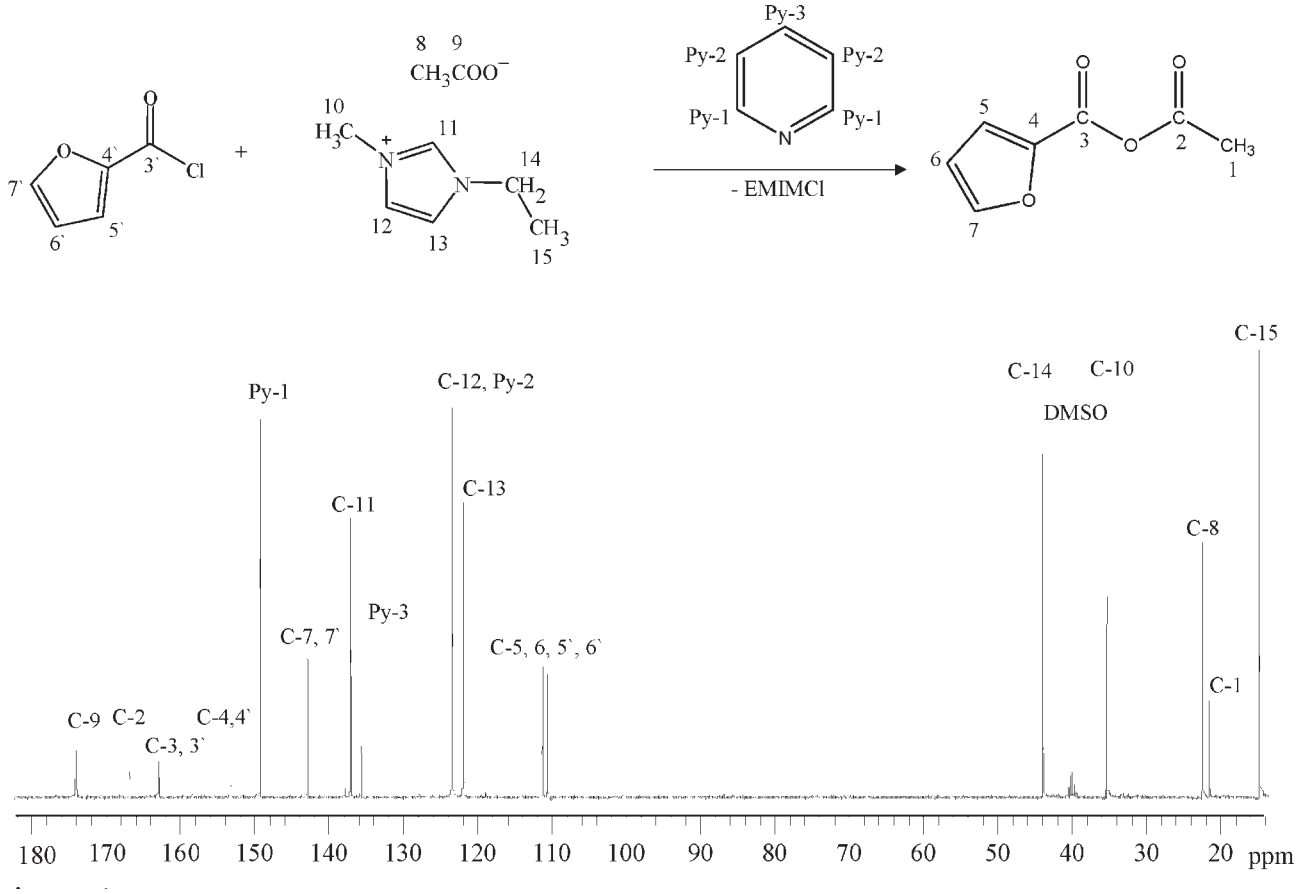

Figure 3. ^{13}C NMR spectrum of the mixture EMIMAc/FC/pyridine in DMSO-d_6 showing the mixed furan-2-carboxylic acid/acetic acid anhydride.

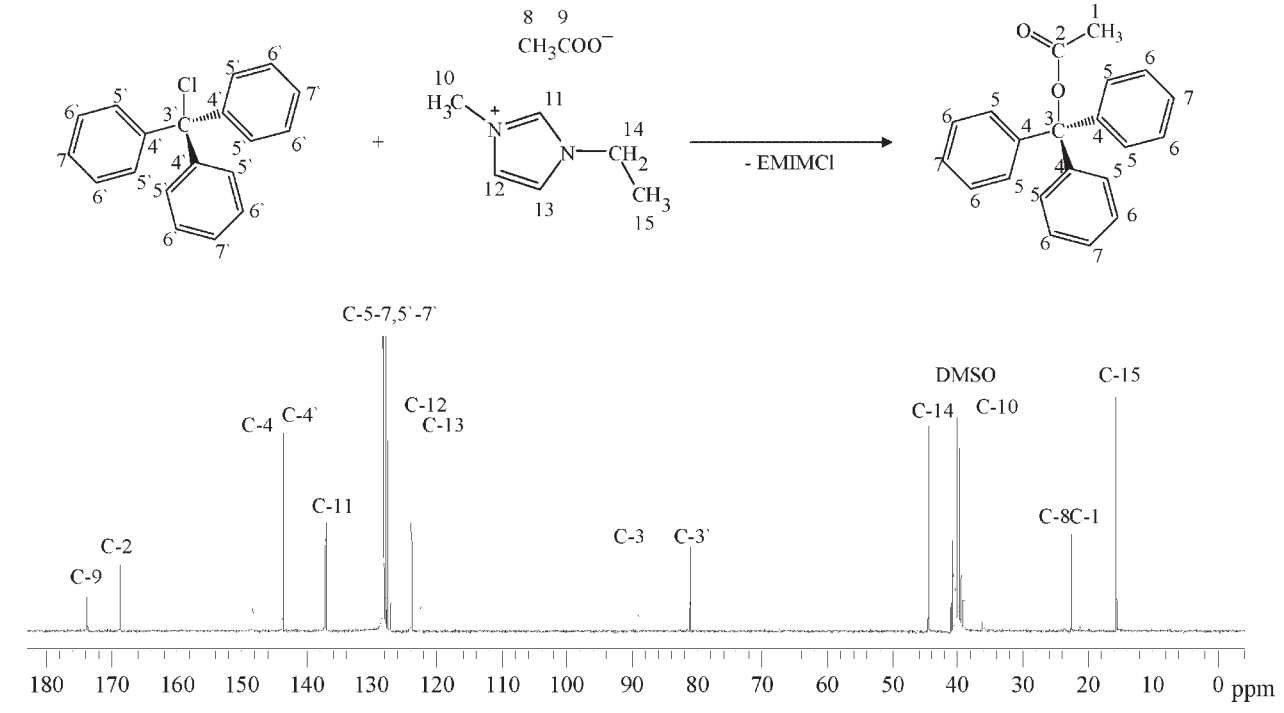

Figure 4. ^{1}H NMR spectrum of the mixture EMIMAc/trityl chloride in DMSO-d_6 showing the formation of trityl acetate.

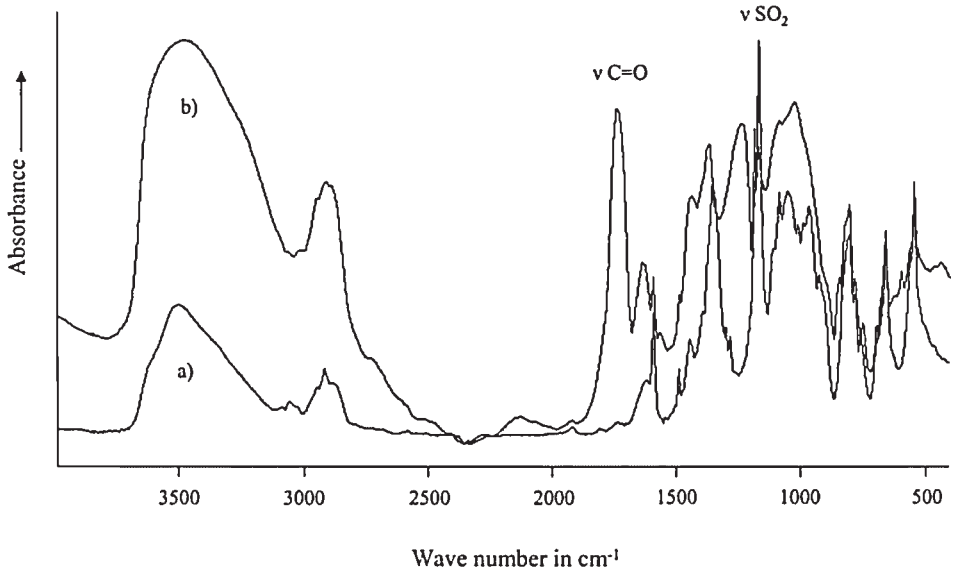

Figure 5. IR spectra of (a) cellulose tosylate (degree of substitution = 1.33) and (b) cellulose acetate obtained by dissolution of cellulose tosylate in EMIMAc for 4 h at 70 °C.

intervals. A decrease in DS of tosyl moieties down to 0.14 after 4 h was observed, on one hand. On the other, the introduction of acetyl moieties was determined with DS values even exceeding the starting tosyl DS, which is the subject of ongoing investigations. The nucleophilic displacement was also revealed by FTIR spectroscopy. An increase in the signals for the carbonyl of the acetate group at 1734 cm^{-1} and a decrease of signals for the tosyl function at 1176 cm^{-1} was observed [Figure 5(b)]. The nitrogen content of the cellulose acetate isolated was 0.08% showing the absence of EMIMAc in the product.

The alternative reaction pathway may run through a mixed *p*-toluenesulfonic acid/acetic acid anhydride formed from tosyl chloride and EMIMAc (see Figure 1). ^{13}C NMR spectroscopic investigations give a first hint that the anhydride is relevant as concluded from the appearance of new signals for a carbonyl moiety of 167.4 (C-6) ppm and for a methyl moiety of the acetyl group at 22.4 ppm (C-7, Figure 6). Even peaks

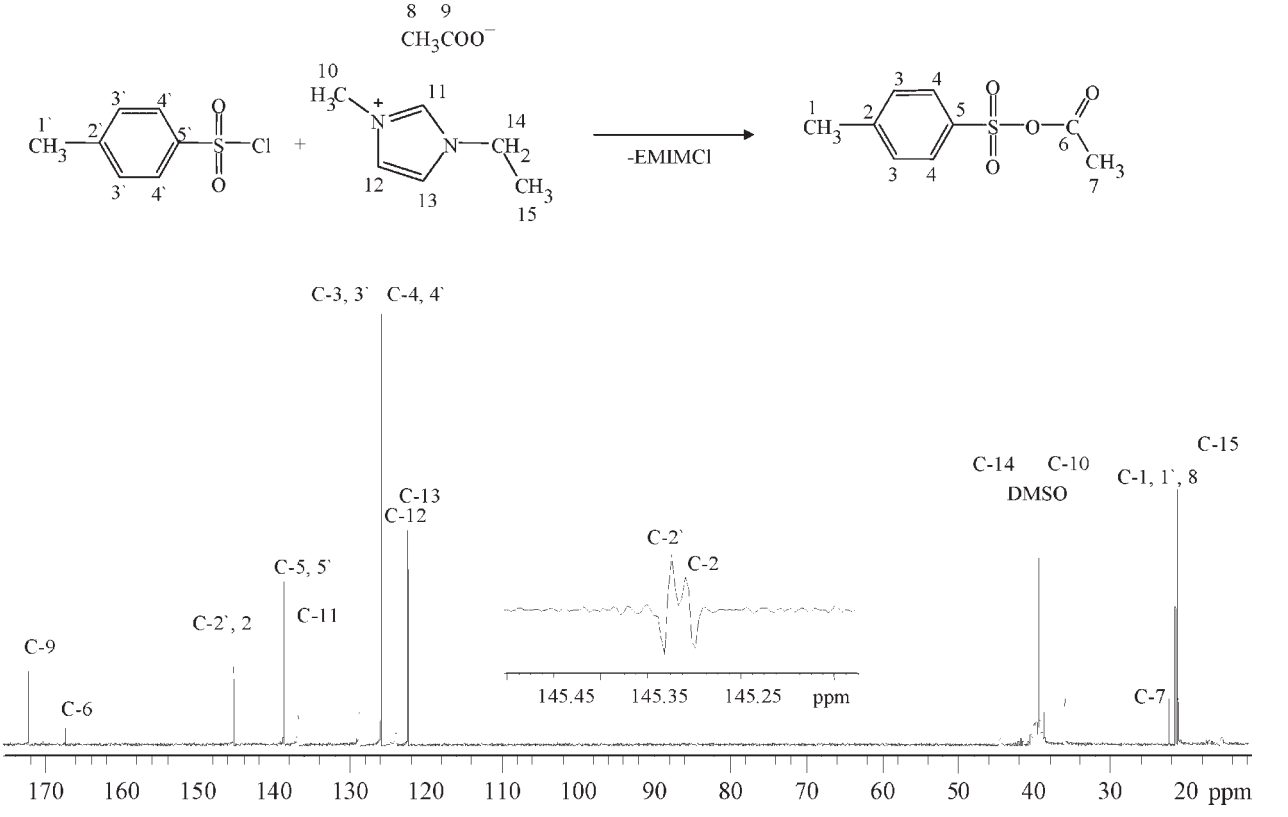

Figure 6. ^1H NMR spectrum of the mixture EMIMAc/tosyl chloride in DMS-d_6 showing the formation of *p*-toluensulfonic acid/acetic acid anhydride.

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for the aromatic carbon atoms of the mixed anhydride can be detected using a typical squared sinusoidal window function for transforming the FID data.[15] Applying this technique, separate signals of these carbon atoms may be found, e.g., for C-2 (see inset, Figure 6) at 145.31 ppm supporting the assumed reaction path. Consequently, the acetylation caused by the conversion with tosyl chloride could be a combination of both mechanisms, i.e., acetylation by nucleophilic displacement and reaction with the mixed anhydride formed.

Conclusion

It is shown that EMIMAc may not exclusively act as a solvent during the modification of cellulose but also as a reagent. The reaction of FC, *p*-toluenesulfonyl chloride and triphenylmethyl chloride with EMIMAc results in the formation of mixed anhydrides and triphenylmethyl acetate. The conversion with cellulose does not yield the expected cellulose derivative, but the corresponding acetate of the biopolymer. The results indicate that the formation of the mixed anhydride applying FC proceeds faster than the formation of the intermediates from *p*-toluenesulfonyl chloride and triphenylmethyl chloride, which will be studied by kinetic experiments applying NMR spectroscopy. Furthermore, the consumption of the IL (exchange of the anion) is a matter of interest, in particular with regard to reuse of the IL.

Attempts are now under progress to use this type of side reaction as a synthesis tool toward products hardly obtainable by direct conversion of cellulose. Thus, the synthesis of cellulose trifluoroacetate, which is a hydrolytically unstable cellulose intermediate, is now under investigation using a commercially available 1-ethyl-3-methylimidazolium trifluoroacetate in combination with acetyl chloride. Via this path, the introduction of the more reactive trifluoroacetyl function would be possible without the presently used highly corrosive and low boiling trifluoroacetic acid and trifluoroacetic anhydride.[16]

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