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Studies on the tosylation of cellulose in mixtures of ionic liquids and a co-solvent

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ABSTRACT

The tosylation of cellulose in ionic liquids (ILs) was studied. Due to the beneficial effect of different co-solvents, the reaction could be performed at 25 °C without the need of heating (in order to reduce viscosity) or cooling (in order to prevent side reactions). The effects of reaction parameters, such as time, molar ratio, and type of base, on the degree of substitution (DS) with tosyl- and chloro-deoxy groups as well as on the molecular weight were evaluated. Products with a $DS_{tosyl} \leq 1.14$ and $DS_{Cl} \leq 0.16$ were obtained and characterized by means of NMR- and FT-IR spectroscopy in order to evaluate their purity and distribution of functional groups within the modified anhydroglucose unit (AGU). Tosylation of cellulose in mixtures of IL and a co-solvent was found to result in predominant substitution at the primary hydroxyl group. Size exclusion chromatography (SEC) revealed only a moderate degradation of the polymer backbone at a reaction time of 4–8 h. Finally, the nucleophilic displacement (S_N) of tosyl- and chloro-deoxy groups by azide as well as recycling of the ILs was studied.

1. Introduction

The *p*-toluenesulfonic acid ester of cellulose, commonly referred to as tosyl cellulose (TOSC), is a versatile intermediate for the preparation of various cellulose derivatives. The tosyl moiety is an excellent leaving group in nucleophilic displacement (S_N) reactions and can for instance be substituted by halogens, azide, or amines yielding the corresponding deoxy-cellulose compounds. (Berlin, Klemm, Tiller, & Rieseler, 2000; Heinze et al., 2011; Heuser, Heath, & Shockley, 1950; Liebert, Hänsch, & Heinze, 2006; Liu & Baumann, 2002) In lab-scale, tosylation of cellulose is usually carried out at low temperatures (8–10 °C) in *N*,*N*-dimethylacetamide (DMA)/LiCl as reaction medium (McCormick, Dawsey, & Newman, 1990; Rahn, Diamantoglou, Klemm, Berghmans, & Heinze, 1996). The homogeneous reaction course enables efficient control of the degree of substitution (DS), guarantees a uniform distribution of tosyl moieties along the polysaccharide chain, and leads to a predominant conversion of primary hydroxyl groups at DS values up to 1.

Taking into account the role of TOSC as key-intermediate for highly engineered cellulose derivatives, there is increasing interest in the use of novel reaction media for the homogeneous preparation of TOSC. Recycling of the cellulose solvent and the possibility to omit energy consuming cooling or heating operations especially need to be addressed for efficient synthesis.

In this context, ionic liquids (ILs) received much interest in recent years as novel cellulose solvents (El Seoud, Koschella, Fidale, Dorn, & Heinze, 2007; Liebert & Heinze, 2008; Pinkert, Marsh, Pang, & Staiger, 2009). Although it has to be pointed out that ILs possess some specific limitations, they bear huge potential as reaction media for the chemical modification of cellulose and have been applied for the synthesis of various cellulose derivatives, mainly esters of organic and inorganic acids (Gericke, Fardim, & Heinze, 2012). Preliminary results on the preparation of a TOSC with a DS of 0.84 by tosylation of microcrystalline cellulose (MC) in the IL 1-allyl-3-methylimidazolium chloride (AMIMCl), at 10 °C have been presented (Granström et al., 2008). However, due to very high viscosity, the reaction conditions were found to be not suitable especially when celluloses of high molecular weights were applied.

The present work is a comprehensive study on the homogeneous preparation of TOSC in ILs. The aim was to provide detailed information on the tosylation in ILs with respect to the effect of different reaction conditions on the product properties, in order to enable efficient preparation of cellulose derivatives. Thus,

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tosylation in different mixtures of ILs and co-solvents was studied, which ensured efficient mixing during the reaction and yielded well defined products. It was demonstrated that co-solvents and bases for tosylation of cellulose can be chosen based on their solvatochromic parameters (Gericke, Liebert, El Seoud, & Heinze, 2011).

2. Materials and methods

2.1. Materials

Cellulose (Cellunier F, dissolving pulp, $[\eta]_{cuen}$ = 289 ml/g) was purchased from Rayonier Inc., USA, and microcrystalline cellulose (MC, Avicel PH 101) was obtained from Fluka. Cellulose was dried for 3 h at 100 °C in vacuum prior to use. 1-Butyl-3-methylimidazolium chloride (BMIMCl, >99%, Lot.: H00720.1), 1-allyl-3-methylimidazolium chloride (AMIMCl, >98%, Lot.: G00110.1.4), and 1-ethyl-3-methylimidazolium diethyl phosphate (EMIMDEP, >98%, Lot.: G00713.1.1) were purchased from IoLiTec GmbH, Germany, sealed, and stored in a desiccator. Anion exchanger Purolite A500 (chloride loaded, 1.15 eq/l, 0.7 kg/l) was obtained from Purolite Deutschland GmbH, Germany. All other solvents, bases, and chemicals were obtained in anhydrous grade from Sigma Aldrich and used without pretreatment.

2.2. Measurements

NMR spectra were recorded at 25 °C in deuterated dimethylsulfoxide (DMSO-d_6) with a Bruker Avance 250 MHz spectrometer. For ^{1}H NMR spectra of ionic liquids (ILs), 20 mg sample were dissolved in 1 ml solvent and 16 scans were acquired. ^{13}C NMR spectra of cellulose derivatives were recorded with at least 10,000 scans and a sample concentration of 85 mg/ml. A CHNS 932 analyzer (Leco) was used for elemental analyses and chlorine content was determined by titration. The degrees of substitution (DS) of the tosyl- and chloro-deoxy moieties were calculated from the elemental composition (based on the average values from three measurements) according to the following formulas (see supplementary data for derivation of the formulas and for DS_{azide} calculation):

$$DS_{tosyl} = \frac{(S\%/100\%) \cdot 162.1 \cdot 35.5}{32.1 \cdot 35.5 - (S\%/100\%) \cdot 35.5 \cdot 154.1 - (Cl\%/100\%) \cdot 32.1 \cdot 18.5}$$

$$DS_{Cl} = \frac{(Cl\%/100\%) \cdot (162.1 + DS_{tosyl} \cdot 154.1)}{35.5 - 18.5 \cdot (Cl\%/100\%)}$$

Based on the found DS values, theoretical elemental composition was calculated. Size exclusion chromatography (SEC) was performed on an Agilent 1200 series LC system (isocratic pump G1310A, G1362A refractive index detector) with a PSS Gram 30 and a PSS Gram 1000 column in series. *N*,*N*-Dimethylacetamide (DMA) with 0.21 wt.% LiCl was used as eluent (40 °C, flow rate: 1 ml/min) and pullulan as calibration standard. Tosyl celluloses (TOSC) were directly dissolved in the eluent (10 mg/ml) whereas cellulose solutions were prepared according to a literature procedure (Meiland, Liebert, & Heinze, 2011). In brief, the polysaccharide was dissolved in DMA/8% LiCl and the solution obtained was diluted with DMA to match the eluent and give a final cellulose concentration of 10 mg/ml.

2.3. Synthesis

2.3.1. Tosylation in mixtures of BMIMCl and pyridine, typical example (TOSC **16**)

2.0 g cellulose (12.34 mmol anhydroglucose units/AGU) were mixed with 18 g BMIMCl and stirred with a mechanical stirrer at 80 °C for 16 h. The solution obtained was cooled to 25 °C and 10 ml pyridine were added. 7.06 g tosyl chloride (3 mol per mol AGU) were dissolved in 10 ml pyridine and after 15 min stirring at 25 °C the solution was added dropwise to the cellulose/BMIMCl/pyridine solution within 5 min. After stirring the reaction mixture at 25 °C for 8 h, it was precipitated into 350 ml of ethanol. The product obtained was separated by filtration, washed with ethanol, water, again three times with ethanol (100 ml each), and finally dried in vacuum at 60 °C. The filtrate was retrieved for recycling of BMIMCl. Experiments using other ILs or other co-solvents than pyridine were carried out according to the same procedure. One half of the total amount of co-solvent was added, followed by the bases, and finally tosyl chloride, dissolved in the remaining co-solvent.

Yield (TOSC **16**): 3.16 g (11.08 mmol modified AGU, 90% of the theoretical yield)

$DS_{tosyl} = 0.79$, $DS_{Cl} = 0.11$

Elemental analysis found: C% 48.21, H% 5.08, N% 0.0, S 8.84, Cl% 1.39; calculated: C% 48.43, H% 5.82, N% 0.0, S 8.83, Cl% 1.39

FT-IR (KBr): 3482 (O—H), 3066 (ν C—$H_{aromatic}$), 2895 (ν C—$H_{aliphatic}$), 1598 (ν C=$C_{aromatic}$), 1360 (ν_{as} SO_2), 1176 (ν_s SO_2) 832 (δ C—$H_{aromatic}$), 815 (ν S—O—C) cm^{-1}

^{13}C NMR (250 MHz, DMSO-d_6): δ (ppm) = 145.4, 132.7, 130.6, 128.5 ($C_{aromatic}$), 101.9 (C-1), 78.5 (C-4), 73.9, 73.2, 72.2 (C-2, C-3 and C-5), 69.6 (C-$6_{tosylated}$), 69.6 (C-$6_{non\text{-}substitued}$), 21.6 ($CH_3$).

2.3.2. Tosylation in AMIMCl (TOSC **7**), according to Granström et al. (2008)

1.0 g MC (6.17 mmol AGU) were mixed with 10 g AMIMCl and stirred with a mechanical stirrer at 80 °C for 16 h. The solution obtained was cooled to 10 °C and 3.53 g tosyl chloride (3 mol per mol AGU), dissolved in 2.9 ml pyridine (6 mol per mol AGU), were added within 30 min. The viscous, inhomogeneous reaction mixture was stirred at 10 °C for 48 h and then poured into 200 ml ice water. The resulting precipitant was separated, washed two times with water and ethanol (100 ml each), and was finally dried in vacuum at 60 °C. The crude product (TOSC **7**) was mixed with 60 ml DMSO and the resulting solution, which contained solid residues, was filtered. The dissolved part was dialyzed for 3 days against water and subsequently isolated by freeze drying (TOSC **7a**). The DMSO insoluble fraction was washed with ethanol and finally dried in vacuum at 60 °C (TOSC **7b**).

Crude product (TOSC **7**): yield: 1.20 g

DS values, determined from different spots of the sample: $DS_{tosyl\ 1}$ = 0.76, $DS_{Cl\ 1}$ = 0.03; $DS_{tosyl\ 2}$ = 0.48, $DS_{Cl\ 2}$ = 0.02

Elemental analysis found: $C\%_1$ 46.09, $H\%_1$ 5.69, $N\%_1$ 0.0, $S\%_1$ 6.48, $Cl\%_1$ 0.36; $C\%_2$ 48.02, $H\%_2$ 5.50, $N\%_2$ 0.0, S_2 8.72, $Cl\%_2$ 0.42 calculated: $C\%_1$ 47.52, H_1 6.28, $N\%_1$ 0.0, $S\%_1$ 6.49, $Cl\%_1$ 0.36; $C\%_2$ 48.60, $H\%_2$ 5.90, $N\%_2$ 0.0, $S\%_2$ 8.74, $Cl\%_2$ 0.42

DMSO soluble part (TOSC **7a**): yield: 0.66 g

$DS_{tosyl} = 1.08$, $DS_{Cl} = 0.04$

Elemental analysis found: C% 49.47, H% 5.10, N% 0.0, S% 10.51, Cl% 0.43; calculated: C% 49.47, H% 5.60, N% 0.0, S% 10.53, Cl% 0.43

DMSO insoluble part (TOSC **7b**): yield: 0.36 g

$DS_{tosyl} = 0.05$, $DS_{Cl} = 0.00$

Elemental analysis found: C% 44.07, H% 6.43, N% 0.0, S% 0.89, Cl% 0.0; calculated: C% 44.89, H% 7.25, N% 0.0, S% 0.89, Cl% 0.0.

2.3.3. Tosylation in DMA/LiCl (TOSC **1**–**3**), adapted from Rahn et al. (1996)

A mixture of 1.0 g cellulose (6.17 mmol AGU) and 30 ml of DMA was stirred with a mechanical stirrer at 130 °C for 2 h. About 5 ml of DMA were removed under reduced pressure together with traces

of water. Afterwards, the mixture was cooled to 100 °C and 1.80 g LiCl were added. The mixture was allowed to cool to 25 °C over night, upon which cellulose dissolved. 2.57 ml triethylamine (3 mol per mol AGU) were added to the solution followed by 1.77 g tosyl chloride (1.5 mol per mol AGU), dissolved in 3 ml DMA. After 4, 8, and 24 h, parts of the reaction mixture were precipitated into 50 ml of ethanol and purified as described for the tosylation in BMIMCl/pyridine.

Reaction time 4 h (TOSC **1**): yield: 0.25 g

$DS_{tosyl} = 0.84, \quad DS_{Cl} = 0.04$

Elemental analysis found: C% 47.67, H% 5.30, N% 0.0, S% 9.25, Cl% 0.54; calculated: C% 48.82, H% 5.81, N% 0.0, S% 9.24, Cl% 0.54

Reaction time 8 h (TOSC **2**): yield: 0.22 g

$DS_{tosyl} = 0.84, \quad DS_{Cl} = 0.07$

Elemental analysis found: C% 47.76, H% 5.14, N% 0.0, S% 9.23, Cl% 0.80; calculated: C% 48.75, H% 5.80, N% 0.0, S 9.23, Cl% 0.80

Reaction time 24 h (TOSC **3**): yield: 0.83 g

$DS_{tosyl} = 0.72, \quad DS_{Cl} = 0.18$

Elemental analysis found: C% 46.95, H% 5.06, N% 0.0, S% 8.37, Cl% 2.28; calculated: C% 48.00, H% 5.84, N% 0.0, S 8.36, Cl% 2.28.

2.3.4. Preparation of 6-azido-6-deoxy cellulose (AZC **1**), according to Liebert et al. (2006)

0.50 g TOSC **19** (1.78 mmol modified AGU, $DS_{tosyl} = 0.74$, $DS_{Cl} = 0.16$) were dissolved in 10 ml DMF and 0.58 g NaN_3 (8.92 mmol) were added. After 24 h stirring with a mechanical stirrer at 100 °C, the reaction mixture was cooled to room temperature and poured into 50 ml water. The resulting precipitant was separated, washed five times with water and ethanol (25 ml each), and finally dried in vacuum at 60 °C.

Yield: 0.25 mg (1.33 mmol modified AGU, 73% of the theoretical yield)

$DS_{azide} = 0.90, \quad DS_{tosyl} = 0.02, \quad DS_{Cl} = 0.01$

Elemental analysis found: C% 37.60, H% 5.42, N% 20.11, S% 0.38, Cl% 0.26; calculated: C% 39.26, H% 4.90, N% 20.11, S% 0.39, Cl% 0.26.

2.4. Recycling of ILs

After precipitation in ethanol and filtration of the TOSC, the ethanol filtrates from different tosylation reactions containing the same IL, base, and co-solvent were collected. Ethanol and volatile compounds were removed by evaporation under reduced pressure and the crude ILs were used for different recycling trials.

BMIMCl/pyridine was purified according to the following procedure: 10 ml crude IL were mixed with 10 ml of 2% aqueous $NaHCO_3$ solution and the solution was neutralized with solid $NaHCO_3$. Water was removed under reduced pressure and 25 ml chloroform were added. The precipitating solid was separated by filtration. Chloroform together with residues of pyridine were removed from the filtrate under reduced pressure. The obtained product was dissolved in 25 ml water and 15 ml anion exchanger (chloride loaded) were added. After 24 h stirring at room temperature, the ion exchanger was removed by filtration and water was evaporated under reduced pressure to yield the purified IL.

BMIMCl from reactions with 1,3-dimethyl-2-imidazolidinone (DMI) was purified according to a similar procedure: 10 ml crude IL were neutralized as described above. After precipitating inorganic salts in chloroform and subsequent removal of the volatile hydrocarbon, the crude IL was dissolved in 20 ml water and extracted with 50 ml toluene in order to remove the organic bases. The extraction was performed five times in case of 1-butylimidazole (BuIM) and three times in case of 1-benzyl-2-methylimidazole (BenzMIM). The extracts were collected and toluene was removed under reduced pressure. Afterwards, anion exchange was performed as described above.

3. Results and discussion

3.1. Tosylation in N,N-dimethylacetamide/LiCl and ionic liquids

Usually, tosyl cellulose (TOSC) is prepared by homogeneous conversion of cellulose, dissolved in *N,N*-dimethylacetamide (DMA)/LiCl, with tosyl chloride in the presences of triethylamine as base for 24 h (Rahn et al., 1996). Degrees of substitution (DS) around 0.8–1 are favored in order to guarantee a predominant tosylation of the primary hydroxyl group. Uniform products can be obtained in a subsequent nucleophilic displacement (S_N) of the tosyl groups with other moieties (Fig. 1). On the contrary, Walden inversion at the asymmetric carbon atoms (positions 2 and 3) would occur during the S_N2 substitution of secondary tosylated hydroxyl groups. A complex mixture of different polysaccharide derivatives with a varying amount of modified glucose-, manose-, altrose-, and allose repeating units would be the consequence. Moreover, the reactivity of secondary tosylated hydroxyl groups in S_N substitution is lower, i.e., no or only partial substitution would occur depending on the nucleophilicity of the reagent applied. Residual tosyl moieties in the final product may have a negative impact on water solubility.

S_N substitution may already occur during the tosylation. Chloride ions, present in the reaction media, can react with TOSC to yield chloro-deoxy cellulose (McCormick et al., 1990). Chlorinated organic compounds are in general undesired, especially in processes of technical scale, due to the difficulties and safety issues in waste disposal. A tosylated AGU may also react with hydroxyl groups of the same or another cellulose chain, which would result in cross-linking and thus insoluble products. In order to prevent these side reactions, temperature is usually kept around 8–10 °C.

From an economical point of view, reactions at room temperature are strongly favorable because cooling is an energy consuming and technically challenging process. Consequently, one aim of the present work was to facilitate tosylation at 25 °C. Moreover, it was of great interest to gain efficient control of the DS_{tosyl}. For a comparison of results obtained using ionic liquids (ILs) as solvents, tosylation was performed in DMA/LiCl (Table 1) in the presence of triethylamine as base. After a reaction time of 4 h, the isolated TOSC **1** possessed a DS_{tosyl} of 0.84. An increase to 8 h showed no effect on the amount of tosyl groups, however, after 24 h a significant decrease to $DS_{tosyl} = 0.72$ was observed. The DS_{Cl} increased from 0.04 (4 h) to 0.07 (8 h) and finally to 0.18 (24 h). The overall DS, remained nearly constant, meaning that prolongation of the reaction time did not favor the tosylation of hydroxyl groups but the conversion into chloro-deoxy moieties. Tosylation is not only influenced by the reaction time but also by the type of base. While the strong base triethylamine ($pK_a = 10.68$) gave excellent results within short reaction time, no tosylated products could be obtained in DMA/LiCl at 25 °C when the moderate base pyridine ($pK_a = 5.37$) was applied (samples **4**–**6**).

The tosylation of cellulose was studied in different imidazolium based ILs with chloride or diethyl phosphate as counter ions (Fig. 2). First experiments were carried out according to a procedure described in the literature (Granström et al., 2008). Microcrystalline cellulose (MC) with a weight average degree of polymerization (DP_W) of 330 was dissolved in 1-allyl-3-methylimidazolium chloride (AMIMCl) and converted with tosyl chloride at 10 °C in the presence of pyridine as a base. However, no reproducible results could be obtained. As a result of the very high viscosity, stirring and mixing during the reaction proved to be insufficient

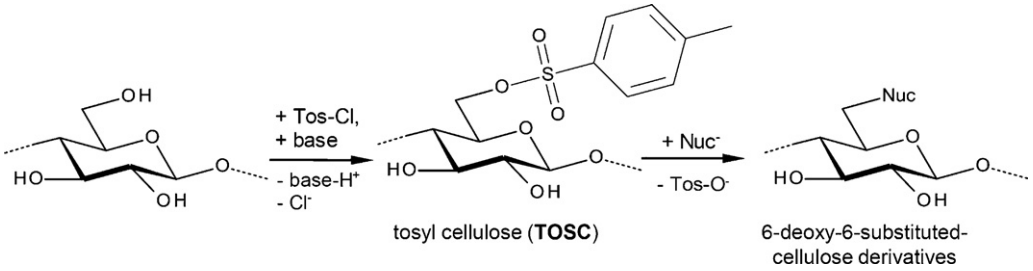

Fig. 1. Scheme for the reaction of cellulose with tosyl chloride (Tos-Cl) and the subsequent conversion of tosyl cellulose with a nucleophile (Nuc^-).

Table 1
Results of the tosylation of cellulose in different solvents under different reaction conditions, reaction temperature 25 °C.

Sample	Reaction conditions					Product[a]						
	Solvent[b]	Base[c]		Tosyl chloride	Time, h	Overall		DMSO soluble part			Insoluble part	
		Type	Ratio[d]	Ratio[d]		DS_{tosyl}	DS_{Cl}	Content, %	DS_{tosyl}	DS_{Cl}	DS_{tosyl}	DS_{Cl}
1	DMA/LiCl	Et_3N	3	1.5	4	0.84	0.04	100	0.84	0.04	–	–
2	DMA/LiCl	Et_3N	3	1.5	8	0.84	0.07	100	0.84	0.07	–	–
3	DMA/LiCl	Et_3N	3	1.5	24	0.72	0.18	100	0.72	0.18	–	–
4	DMA/LiCl	Pyridine	3	1.5	4	0.00	0.00	0	–	–	0.00	0.00
5	DMA/LiCl	Pyridine	3	1.5	8	0.00	0.00	0	–	–	0.00	0.00
6	DMA/LiCl	Pyridine	3	1.5	24	0.00	0.07	0	–	–	0.00	0.07
7	AMIMCl[e]	Pyridine	6	3	48	0.48[f]	0.02[f]	65	1.08	0.04	0.05	0.00
						0.76[f]	0.03[f]	65	1.08	0.04	0.05	0.00

[a] Degrees of substitution (DS) are given for the overall product as well as the individual parts that are soluble/insoluble in dimethylsulfoxide (DMSO).
[b] DMA: *N*,*N*-dimethylacedamide, AMIMCl: 1-allyl-3-methylimidazolium chloride.
[c] Et_3N: triethylamine.
[d] mol per mol anhydroglucose units.
[e] Reaction temperature: 10 °C.
[f] DS values were determined for different parts of sample **7**.

(see Fig. 1 in supporting information) and resembled a heterogeneous conversion due to the limited diffusion of the reagent. The product obtained (TOSC **7**, Table 1) possessed a very inhomogeneous composition. Elemental analyses of different parts of the same sample yielded largely differing DS_{tosyl} values of 0.48 and 0.76. Moreover, the product could be separated into a tosylated product (TSOC **7a**, DS_{tosyl} = 1.08, DS_{Cl} = 0.04) and almost unmodified cellulose (TSOC **7b**, DS_{tosyl} = 0.05, DS_{Cl} = 0.0). Sample **7a** made up 65% of the non-fractionated reaction product and readily dissolved in dimethylsulfoxide (DMSO) whereas **7b** was insoluble.

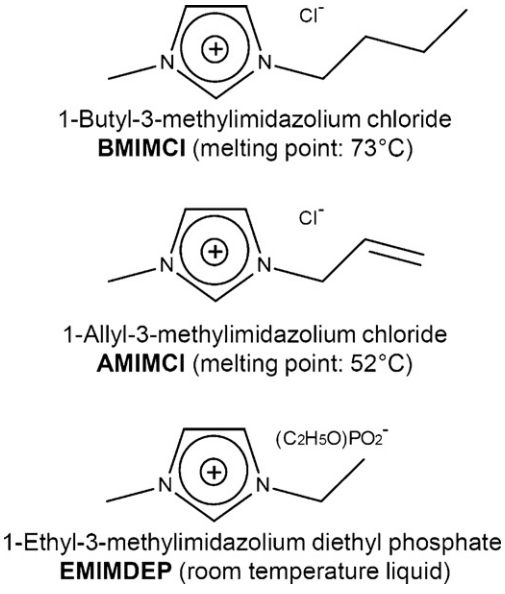

Fig. 2. Molecular structure of ionic liquids used in this study.

Mixing difficulties became even more pronounced if a commercially interesting pulp with a higher DP_W was applied due to the significantly higher viscosity. For cellulose solutions (10%, at 20 °C) in 1-ethyl-3-methylimidazolium acetate (EMIMAc), an increase in DP comparable to the present case has been described to result in a tenfold increase in viscosity from about 100 to 1000 Pa s (Gericke, Schlufter, Liebert, Heinze, & Budtova, 2009). Consequently, tosylation of the cellulose pulp at 10 °C with a high DP was not attempted.

3.2. Tosylation of cellulose in mixtures of 1-butyl-3-methylimidazolium chloride and a co-solvent

It has been demonstrated that the viscosity of cellulose/IL solutions rapidly increases with decreasing temperature showing a strong deviation from the typical Arrhenius-like behavior of polymer solutions at temperatures < 40 °C (Gericke, Schlufter, et al., 2009; Sescousse, Le, Ries, & Budtova, 2010). Thus, an increase from 10 °C to 25 °C, the desired reaction temperature, does not yield a reaction medium that can be efficiently mixed. Much higher temperatures of at least 60–80 °C would have been necessary to overcome these difficulties, which would have been accompanied by an increase in DS_{Cl}, a higher energy consumption, and most likely pronounced degradation of the polymer chain.

Addition of organic solvents to cellulose/IL solutions is an efficient way to reduce viscosity that decreases exponentially with the amount of co-solvent. It has been demonstrated that homogeneous sulfation can be performed in mixtures containing equal parts of *N*,*N*-dimethylformamide (DMF) and cellulose/IL solution (Gericke, Liebert, & Heinze, 2009). Addition of pyridine induces also a viscosity decrease (Vitz, Yevlampieva, Rjumtsev, & Schubert, 2010). Consequently, tosylation of cellulose in mixtures of ILs with pyridine (without additional base) or with the dipolar aprotic co-solvents 1,3-dimethyl-2-imidazolidinone (DMI) and DMF (in the presence of different bases) was studied.

Table 2
Normalized empirical polarity (E_T^N), miscibility with ionic liquids (ILs), and pK_a values of co-solvents and bases used in this study.

Compound[a]	E_T^N	Miscible with ILs	pK_a
BIM	0.35[b]	+	7.18[c]
BenzMIM		+	6.68[d]
DMA	0.38[e]	+	
DMAP		+	9.87[f]
DMF	0.39[e]	+	
DMI	0.37[e]	+	
Et_3N	0.04[e]	–	10.68[g]
MIM	0.40[b]	+	7.12[c]
Pyridine	0.30[e]	+	5.37[f]

[a] BIM: 1-butylimidazole, BenzMIM: 1-benzyl-2-methylimidazole, DMA: *N*,*N*-dimethylacetamide, DMAP: 4-(dimethylamino)pyridine, DMF: *N*,*N*-dimethylformamide, DMI: 1,3-dimethyl-2-imidazolidinone, Et_3N: triethylamine, MIM 1-methylimidazole.
[b] Calculated from $E_T(30)$ values given by Mellein, Aki, Ladewski, and Brennecke (2006), according to $E_T^N = (E_T(30) - 30.7\,kcal/mol)/32.4\,kcal/mol$.
[c] S. Cassidy, Reinhardt, Cleland, and Frey (1999).
[d] pK_a in water has been extrapolated to a value of 6.68 by Avdeef, Comer, and Thomson (1993).
[e] Reichardt (1994).
[f] Castro, Cubillos, Aliaga, Evangelisti, and Santos (2004).
[g] Frenna, Vivona, Consiglio, and Spinelli (1985).

General guidelines for the handling of various co-solvents have been advanced based on the solvatochromic parameters of the individual compounds as well as the mixtures of co-solvents with ILs (Gericke et al., 2011; Rinaldi, 2011). As an example, cellulose/IL solutions are only miscible with compounds having normalized empirical polarity (E_T^N) above 0.25, which enables prediction of the miscibility of the reaction mixture with potential co-solvent or bases (Gericke et al., 2011). E_T^N values for co-solvents and bases discussed in this study are given in Table 2 together with pK_a values of the bases used. Among these compounds, only triethylamine is immiscible with the ILs used to dissolve cellulose as a result of its low polarity ($E_T^N = 0.04$).

Pyridine is likewise a moderate base and an efficient co-solvent for polysaccharide chemistry. Cellulose/BMIMCl solutions have been found to tolerate up to 3 weight equivalents before precipitation occurs (Gericke et al., 2011). Co-solvents may be applied in a 1 to 1 weight ratio, which corresponds to 20 mol pyridine per mol AGU. No additional base was utilized for tosylation of cellulose in BMIMCl/pyridine (Table 3). Only minor conversion was observed in BMIMCl/pyridine using 1 mol tosyl chloride per AGU (sample **8**); doubling the amount of tosyl chloride yielded TOSC with DS_{tosyl} values between 0.29 (4 h, TOSC **9**) and 0.50 (24 h, TOSC **11**) depending on the reaction time. Using 3 or 4 mol tosyl chloride per mol AGU resulted in higher DS values up to 1.03 (TOSC **22**, 24 h). At 5 mol per mol AGU almost the same results were obtained ($DS_{tosyl} = 0.97$, TOSC **25**, 24 h). As will be demonstrated below, a reasonable explanation is the comparably low reactivity of the secondary hydroxyl groups towards tosylation in ILs thus only the primary hydroxyl group was converted.

TOSCs have been prepared also by heterogeneous tosylation in pyridine (Heuser et al., 1950). However, a tenfold excess of tosyl chloride was required in order to obtain DS values comparable to the derivatization in BMIMCl/pyridine. Thus, the reactivity of cellulose towards conversion with tosyl chloride was significantly improved by the homogeneous reaction course. Moreover, the heterogeneously prepared products showed a relatively high content of tosylated secondary hydroxyl groups even at $DS < 1$.

In addition to tosylation in BMIMCl/pyridine, derivatization in mixtures of BMIMCl and dipolar aprotic co-solvents was studied with different bases commonly used (Table 3). Experiments were carried out in BMIMCl/DMF, which proved to be an efficient reaction medium for the sulfation of cellulose (Gericke, Liebert, et al., 2009). Although triethylamine is favored for the tosylation of cellulose in DMA/LiCl, it could not be applied for homogeneous tosylation of cellulose in ILs because the base neither dissolved in the undiluted IL nor in mixtures of IL with a co-solvent. Almost no tosylation occurred in the heterogeneous system formed (sample **26**). Pyridine and 4-(dimethylamino)pyridine (DMAP) gave homogeneous mixtures with cellulose/BMIMCl/DMF solutions but shortly after the addition of tosyl chloride, the systems became turbid and heterogeneous. Considerable conversion was only observed in the presence of DMAP (TOSC **28**, $DS_{tosyl} = 0.29$, $DS_{Cl} = 0.05$).

It appeared that co-solvents for tosylation in ILs are not only required for lowering viscosity but also for keeping the tosylated product soluble, as it becomes increasingly hydrophobic with increasing DS. 1,3-Dimethyl-2-imidazolidinone (DMI), in combination with LiCl, has been utilized to dissolve cellulose and shows higher dissolution power than DMA/LiCl (Tamai, Tatsumi, & Matsumoto, 2004). Moreover, DMI has a slightly lower E_T^N value (0.37) than DMF ($E_T^N = 0.39$) and DMA ($E_T^N = 0.38$) and was found to be more suitable to prevent phase separation, so was consequently utilized in the following experiments. Tosylation in the presence of pyridine turned to a heterogeneous reaction in BMIMCl/DMF after 0.5 h (sample **27**) but remained completely homogeneous in BMIMCl/DMI over the whole reaction time of 24 h (TOSC **30**). A tosylated product could be obtained in the latter case although the DS_{tosyl} (0.14) was relatively small as result of the only moderate basicity of pyridine. It has been reported that in the presence of pyridine, amides and lactams can form Vilsmeier-adducts with tosyl chloride, which interfere with the tosylation of cellulose by directly reacting with the polysaccharide to yield iminium derivatives (McCormick et al., 1990; McCormick & Dawsey, 1990; Zarth, Koschella, Pfeifer, Dorn, & Heinze, 2011). In the present study, the tosylated products were obtained in high yield (around 90%). Neither NMR spectroscopy nor elemental analysis (nitrogen content < 0.1%) indicated that iminium substituents were introduced in considerable amount during conversion of cellulose with tosyl chloride in BMIMCl/DMI in the presence of pyridine or with any other base used, which might be due to the fact that reaction temperature and amount of tosyl chloride were relatively low compared to the cited references.

Tosylation of cellulose in BMIMCl/DMI in the presence of DMAP as a stronger base ($pK_a = 9.87$) gave products with DS_{tosyl} of 0.38 (TOSC **31**, molar ratio of 2 to 1) and 0.86 (TOSC **32**, molar ratio of 3 to 1) within 4 h. In these cases, phase separation occurred with DMI as co-solvent as well after 1–3 h reaction time upon increasing derivatization. It should be noted that DMAP is a solid, which further complicated its dissolution in the reaction mixture. It is reasonable to assume that at a certain stage, the amount of compounds with rather low polarity (i.e., tosylated cellulose, excess tosyl chloride, and base) exceeded the limit that can be solubilized by the rather polar IL/co-solvent system.

Finding a suitable base was the key issue for an efficient homogeneous preparation of TOSC. The base should: (i) possesses a higher pK_a values than pyridine, and (ii) be (unlike triethylamine and DMAP) well miscible with the rather polar ILs. 1-Methylimidazole ($pK_a = 7.12$) is a much stronger base than pyridine and possesses a relatively high E_T^N value of 0.43, i.e., it is also miscible with ILs. In general, it should be an excellent base for derivatization of cellulose in mixtures of IL and co-solvents but the adverse effect of high polarity on the tosylation reaction has already been pointed out. Moreover, less polar bases are favorable in terms of subsequent recycling because removal from aqueous BMIMCl solutions by extraction with hydrophobic solvents (e.g., toluene as will be shown below) would be feasible. Thus, 1-butylimidazole (BIM) was applied as a base in the present study (Table 3, entries **33**–**40**). It is well miscible with the ILs, possesses a comparably high basicity ($pK_a = 7.18$) and a lower polarity ($E_T^N = 0.35$)

Table 3
Conditions for and results of the tosylation of cellulose in mixtures of ionic liquid and a co-solvent, reaction temperature 25 °C.

Sample	Reaction conditions							Product					
	Ionic liquid[a]	Co-solvent[b]	Base[c]		Tosyl chloride	Time, h	Reaction course[d]	DS_{tosyl}	DS_{Cl}	Solubility[e]			
			Type	Ratio[f]	Ratio[f]					DMSO	DMF	DMA	Pyridine
8	BMIMCl	Pyridine	Pyridine	20	1	24	hom	0.07	0.01	–	–	–	–
9	BMIMCl	Pyridine	Pyridine	20	2	4	hom	0.29	0.01	+	–	–	–
10	BMIMCl	Pyridine	Pyridine	20	2	8	hom	0.43	0.02	+	+	+	–
11	BMIMCl	Pyridine	Pyridine	20	2	24	hom	0.50	0.07	+	+	+	+
12	BMIMCl	Pyridine	Pyridine	20	3	1	hom	0.23	0.01	+	–	–	–
13	BMIMCl	Pyridine	Pyridine	20	3	2	hom	0.34	0.00	+	–	–	–
14	BMIMCl	Pyridine	Pyridine	20	3	4	hom	0.49	0.02	+	+	+	–
15	BMIMCl	Pyridine	Pyridine	20	3	8	hom	0.62	0.12	+	+	+	+
16	BMIMCl	Pyridine	Pyridine	20	3	16	hom	0.79	0.11	+	+	+	+
17	BMIMCl	Pyridine	Pyridine	20	3	24	hom	0.77	0.08	+	+	+	+
18	BMIMCl	Pyridine	Pyridine	20	3	32	hom	0.76	0.09	+	+	+	+
19	BMIMCl	Pyridine	Pyridine	20	3	48	hom	0.74	0.16	+	+	+	+
20	BMIMCl	Pyridine	Pyridine	20	4	4	hom	0.68	0.02	+	+	+	+
21	BMIMCl	Pyridine	Pyridine	20	4	8	hom	0.87	0.07	+	+	+	+
22	BMIMCl	Pyridine	Pyridine	20	4	24	hom	1.03	0.11	+	+	+	+
23	BMIMCl	Pyridine	Pyridine	20	5	4	hom	0.68	0.02	+	+	+	+
24	BMIMCl	Pyridine	Pyridine	20	5	8	hom	0.86	0.03	+	+	+	+
25	BMIMCl	Pyridine	Pyridine	20	5	24	hom	0.97	0.08	+	+	+	+
26	BMIMCl	DMF	Et_3N	2.5	2	4	het	0.00	0.01	–	–	–	–
27	BMIMCl	DMF	Pyridine	6	3	4	hom > het (0.5 h)	0.01	0.02	–	–	–	–
28	BMIMCl	DMF	DMAP	4	2	4	hom > het (0.5 h)	0.29	0.05	+	–	–	–
29	BMIMCl	DMI	Et_3N	3	2	4	het	0.02	0.00	–	–	–	–
30	BMIMCl	DMI	Pyridine	6	3	24	hom	0.14	0.01	–	–	–	–
31	BMIMCl	DMI	DMAP	3	2	4	hom > het (3 h)	0.38	0.02	+	–	–	–
32	BMIMCl	DMI	DMAP	4.5	3	4	hom > het (1 h)	0.86	0.10	+	+	+	+
33	BMIMCl	DMI	BIM	4	2	4	hom	0.59	0.02	+	+	+	+
34	BMIMCl	DMI	BIM	4	2	8	hom	0.62	0.03	+	+	+	+
35	BMIMCl	DMI	BIM	4	2	24	hom	0.62	0.06	+	+	+	+
36	BMIMCl	DMI	BIM	6	3	2	hom	0.84	0.01	+	+	+	+
37	BMIMCl	DMI	BIM	6	3	4	hom	0.95	0.02	+	+	+	+
38	BMIMCl	DMI	BIM	6	3	6	hom	1.01	0.03	+	+	+	+
39	BMIMCl	DMI	BIM	6	3	8	hom	1.02	0.04	+	+	+	+
40	BMIMCl	DMI	BIM	6	3	24	hom	1.14	0.08	+	+	+	+
41	BMIMCl	DMI	BenzMIM	4	2	4	hom	0.19	0.01	–	–	–	–
42	BMIMCl	DMI	BenzMIM	4	2	8	hom	0.18	0.01	–	–	–	–
43	BMIMCl	DMI	BenzMIM	4	2	24	hom	0.16	0.02	–	–	–	–
44	BMIMCl	DMI	BenzMIM	6	3	2	hom	0.51	0.01	+	+	+	+
45	BMIMCl	DMI	BenzMIM	6	3	4	hom	0.55	0.02	+	+	+	+
46	BMIMCl	DMI	BenzMIM	6	3	8	hom	0.60	0.03	+	+	+	+
47	BMIMCl	DMI	BenzMIM	6	3	24	hom	0.73	0.06	+	+	+	+
48	AMIMCl	Pyridine[g]	Pyridine	16	3	4	het > hom (0.5 h)	0.16	0.00	–	–	–	–
49	AMIMCl	Pyridine[g]	Pyridine	16	3	24	het > hom (0.5 h)	0.72	0.05	+	+	+	+
50	EMIMDEP	DMF	Pyridine	6	3	24	het	0.00	0.00	–	–	–	–
51	EMIMDEP	DMI	DMAP	4.5	3	24	het	0.04	0.00	–	–	–	–
52	EMIMDEP	DMI	BuIM	6	4	24	het	0.06	0.02	–	–	–	–
53	EMIMDEP	Pyridine	Pyridine	20	3	4	het	0.01	0.00	–	–	–	–

[a] BMIMCl: 1-butyl-3-methylimidazolium chloride, AMIMCl: 1-allyl-3-methylimidazolium chloride, EMIMDEP: 1-ethyl-3-methylimidazolium diethyl phosphate.
[b] 1 ml co-solvent per g cellulose solution, DMF: *N*,*N*-dimethylformamide, DMI: 1,3-dimethyl-2-imidazolidinone.
[c] Et_3N: triethylamine, DMAP: 4-(dimethylamino)pyridine, BIM: 1-butylimidazole, BenzMIM: 1-benzyl-2-methylimidazole.
[d] hom: homogeneous, het: heterogeneous/two phases, hom > het: transition from homogeneous to heterogeneous, het > hom: transition from heterogeneous to homogeneous, time required for phase transition is indicated in parentheses.
[e] +: soluble, –: insoluble.
[f] mol per mol anhydroglucose units.
[g] 0.8 ml co-solvent per g cellulose solution.

than 1-methylimidazole due to the longer aliphatic alkyl chain. 1-Benzyl-2-methylimidazole (BenzMIM) was tested as a base as well (Table 3, entries **41**–**47**). It is miscible with BMIMCl but immiscible with water. Thus, it could be separated easily from IL/water mixtures by extraction.

Tosylation of cellulose in BMIMCl/DMI with both 1-alkylimidazoles proceeded completely homogeneously from the beginning and no precipitation or phase separation occurred even after 24 h reaction time. In contrast to reactions in BMIMCl/DMI with the weaker base pyridine, samples with a considerable DS_{tosyl} of about 0.60 (TOSC **33**–**35**) could be obtained with a twofold excess of tosyl chloride. The reaction was completed within 4 h and almost no differences were observed upon increasing the reaction time from 4 to 24 h (Fig. 3), which is comparable to conversion in DMA/LiCl. At a molar ratio of 3 mol tosyl chloride per mol AGU (TOSC **36**–**40**), the reaction showed a certain time dependence. The DS_{tosyl} increased from 0.84 after 2 h to 0.95 after 4 h and finally to 1.14 after 24 h reaction time. Chloride is present in the reaction medium in high concentration due to the fact that it represents the IL's anion. Moreover, derivatization with tosylchloride generates additional chloride as a second reaction product (see Fig. 1). Nevertheless, all products showed only small $DS_{Cl} \leq 0.04$, when the reaction time was 8. Even after 24 h and a high $DS_{tosyl} > 1$, the tendency towards introduction of chlorine was less pronounced compared to the tosylation in DMA/LiCl (compare TOSC **3** and TOSC **39**). This finding correlates well with

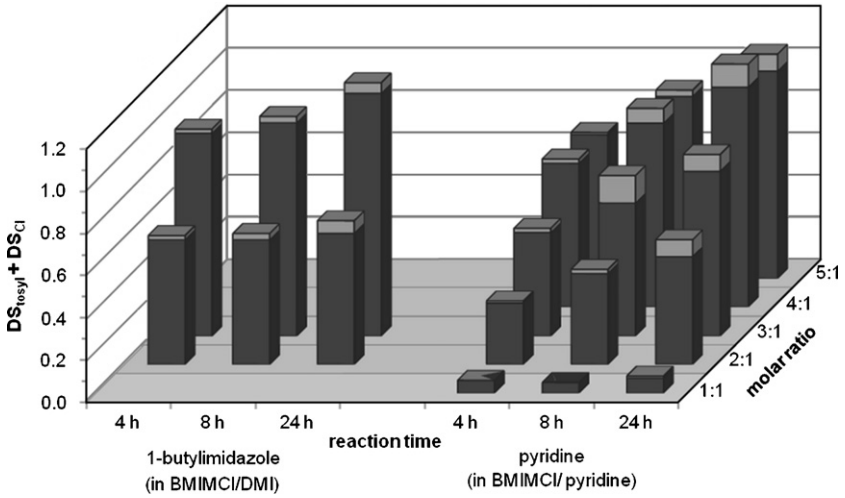

Fig. 3. Overall degree of substitution (DS) of tosyl celluloses obtained in 1-butyl-3-methylimidazolium chloride (BMIMCl)/1,3-dimethyl-2-imidazolidinone (DMI) in the presence of 1-butylimidazole (left side) or in BMIMCl/pyridine without an additional base (right side) at different reaction conditions. Individual contributions of DS_{tosyl} (dark areas) and DS_{Cl} (bright areas) are highlighted.

the fact that the nucleophilicity of chloride is reduced in ILs due to strong hydrogen bonding with the imidazolium cation, in comparison to dipolar aprotic solvents that are weak hydrogen bond donors (Chiappe & Pieraccini, 2004). The second-order rate constant for the S_N2 substitution of methansulfonate by chloride has been found to decrease by a factor of 5 when the reaction was performed in an IL instead of DMSO (Betti, Landini, & Maia, 2008). Finally, tosylation of cellulose in BMIMCl/DMI in the presence of BenzMIM yielded products of lower DS applying the same molar ratio (Table 3, samples **41**–**47**) due to the lower basicity of BenzMIM.

For the tosylation of cellulose in BMIMCl/DMI in the presence of BIM as a strong base, only small differences were observed between 4 and 8 h reaction time (Fig. 3). Even an increase of the reaction time to 24 h yielded only a slight increase in DS_{tosyl}. Conversions in BMIMCl/pyridine required longer reaction time to reach constant DS values. A successive increase in reaction time from 1 to 16 h resulted in an increasing DS_{tosyl} from 0.23 to 0.79 (TOSC **12**–**16**). Further prolonging of the reaction time to 24 or 48 h had almost no effect on the tosylation but the DS_{Cl} increased (TOSC **19**). In both reaction media, DS_{tosyl} did not significantly exceed a value of 1 even by using an excess of tosyl chloride (TOSC **23**–**25**). Compared to the tosylation in BMIMCl/DMI with BIM as base, tosylation in BMIMCl/pyridine yielded lower DS values applying the same molar ratios. Moreover, the content of chloro-deoxy groups was higher at same reaction times. Nevertheless, BMIMCl/pyridine is a promising reaction medium for the homogeneous preparation of TOSC due of the ease of recycling the IL after the reaction.

3.3. Tosylation of cellulose in mixtures of co-solvents with other ionic liquids

AMIMCl has been applied frequently as solvent and reaction medium for cellulose mainly because of its lower melting point and viscosity compared to BMIMCl. Consequently, it was included in the present studies. In general, solutions of cellulose in AMIMCl have been found to tolerate much lower amounts of co-solvents than those in BMIMCl (Gericke et al., 2011). Precipitation of the polysaccharide occurred already at a ratio of 0.8 g pyridine per g cellulose solution; therefore, modification of the experimental conditions was necessary. Moreover, upon the addition of the tosyl chloride, dissolved in pyridine, the reaction mixture became turbid forming a heterogeneous system because the local concentration of co-solvent at the drop-in zone exceeded the maximum limit. After 30 min reaction time, a clear solution was obtained. The DS values of the product isolated were comparable to values of products obtained by the reactions in BMIMCl/pyridine.

1-Ethyl-3-methylimidazolium diethyl phosphate (EMIMDEP), in combination with different co-solvents and bases, was also studied as reaction medium for tosylation because it has the advantage of having a lower viscosity and being liquid at room temperature (samples **50**–**53**). However, cellulose/EMIMDEP/co-solvent solutions became heterogeneous immediately after the addition of tosyl chloride and no considerable conversion was observed. In this context it has to be noted that also EMIMAc, another room temperature liquid IL, is not suitable for the preparation of TOSC. It has been demonstrated that the acetate ions, present in the reaction medium in high concentration, finally led to the formation of cellulose acetate instead of the desired derivative (Köhler et al., 2007). Thus, BMIMCl is currently the preferred IL for tosylation of cellulose.

3.4. Characterization of tosyl celluloses

On the contrary to the heterogeneous tosylation of cellulose in AMIMCl (without co-solvent), TOSCs prepared in BMIMCl with DMI or pyridine as co-solvent were completely soluble in DMSO even at low DS of 0.23 (TOSC **12**). In addition, all samples dissolved in DMF and DMA at $DS \geq 0.43$ (TOSC **10**) and in pyridine at $DS \geq 0.50$ (TOSC **11**), indicating uniform, not cross-linked products and an even distribution of tosyl moieties along the polymer chains. The FT-IR spectra of TOSCs clearly indicate the introduction of tosyl groups into the polysaccharides (Fig. 4). With increasing DS_{tosyl}, different signals emerged that can be attributed to the sulfonic acid ester group and to the *p*-substituted toluene ring (Cabassi, Casu, & Perlin, 1978; Freeman & Hambly, 1957; Rahn et al., 1996).

As can be concluded from the ^{13}C NMR spectra of different TOSCs (Fig. 5), the tosylation of cellulose in mixtures of ILs and co-solvents occurs predominantly at position 6 up to a DS of about 0.8–1. With increasing DS_{tosyl}, a new peak of increasing intensity emerged around 69 ppm, which indicates a tosylation of the primary hydroxyl group, whereas the intensity of the signal corresponding to an unmodified C-6 atom (61 ppm) decreased. This signal disappeared almost completely in the background noise for TOSC **19** despite the fact that DS_{tosyl} was only 0.74. However, as a result of the high DS_{Cl} of 0.16, an additional peak occurred around 45 ppm that is attributed to a 6-chloro-6-deoxy moiety. Thus, only 9% of

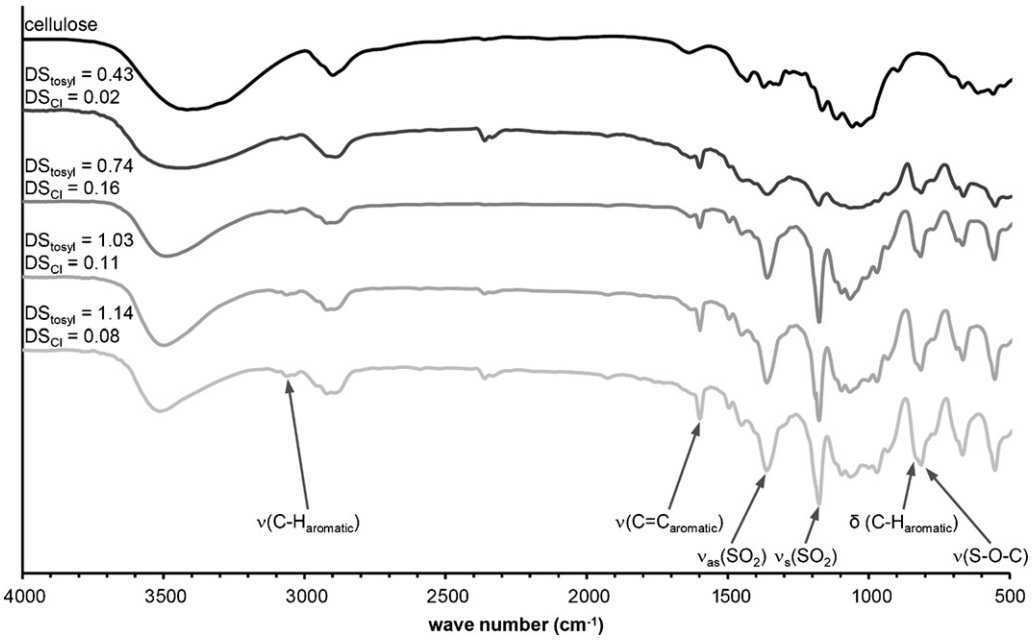

Fig. 4. FT-IR spectra of cellulose and tosyl celluloses **10**, **19**, **22**, and **40** with different degrees of substitution (DS). Bands that are characteristic for vibrations associated with the tosyl group are highlighted.

the primary hydroxyl groups remained unmodified, which explains the low intensity of the signal corresponding to C-6 with non-substituted hydroxyl groups. A signal at 45 ppm also occurred with a lower intensity in the spectrum of TOSC **22** (DS$_{Cl}$ = 0.11). Assignment of those peaks to a chlorinated position 6 is in accordance to NMR spectroscopic studies that has been performed for 3,6-di-chloro-3,6-di-deoxy monosaccharides, present in the repeating unit of highly chlorinated cellulose, as well as for 6-chloro-6-deoxychitosan (Furuhata et al., 1994; Tseng, Takechi, & Furuhata, 1997). In previous publications on the tosylation of cellulose in DMA/LiCl and AMIMCl, it has incorrectly been stated that signals corresponding to the C-6$_{Cl}$ atom would occur around 60 ppm (Granström et al., 2008; Rahn et al., 1996).

Based on the relatively high intensities of the C-6 related signals in correlation to the DS values, it can be concluded that no significant tosylation occurred at the secondary hydroxyl groups. Thus, DS$_{tosyl}$ did not significantly exceed a value of 1 even by using an excess of tosyl chloride (TOSC **23**–**25**). The reactivity of the secondary hydroxyl groups towards homogeneous tosylation in BMIMCl/pyridine and BMIMCl/DMI appears to be lower than that of the primary one. Finally, no residual IL was traceable in the TOSC by means of NMR spectroscopy or elemental analysis. It has been demonstrated for water insoluble cellodextrin (DP = 7) that the imidazolium cation may react with the reducing end-group (Liebert & Heinze, 2008). Although the influence of the end-groups diminishes rapidly with increasing chain length, the same modification could be detected for cellulosic samples of considerable DP as well by

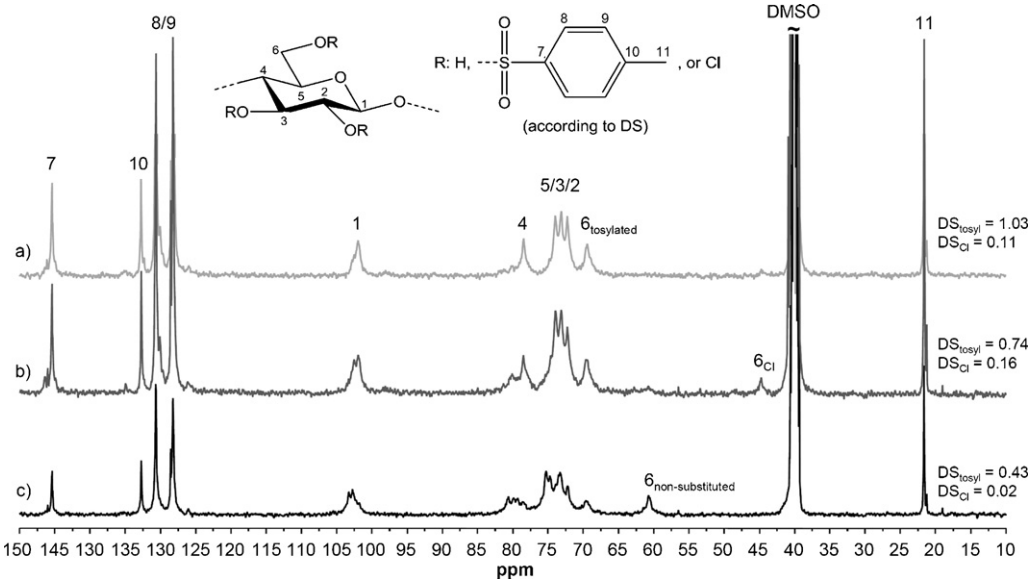

Fig. 5. ^{13}C NMR spectra of tosyl celluloses **22** (a), **19** (b), and **10** (c), recorded at 25 °C in DMSO-d_6.

Table 4
Results of size exclusion chromatography (SEC) of celluloses and tosyl celluloses (TOSC) obtained in 1-butyl-3-methylimidazolium chloride/pyridine after different reaction times; eluent: *N*,*N*-dimethylacetamide with 0.21 wt.% LiCl.

Sample	Reaction time, h	SEC results[a]	
		DP_W	PDI
Microcrystalline cellulose	–	330	3.7
Cellulose (Cellunier F)	–	1544	3.9
TOSC **14**	4	1101	7.4
TOSC **15**	8	972	7.8
TOSC **17**	24	928	5.8
TOSC **18**	32	903	7.5
TOSC **19**	48	876	6.4

[a] DP_W: weight average degree of polymerization, PDI: polydispersity index.

using ILs labeled with ^{13}C or a fluorescent probe (Ebner, Schiehser, Potthast, & Rosenau, 2008). Thus, additional analytic tools might be required to verify the purity in "ppm-scale", which is for instance required for products applied in medical applications.

Size exclusion chromatography (SEC) was performed with TOSCs prepared in BMIMCl/pyridine at different reaction times (Table 4). DMA with 0.21% LiCl was used as eluent for cellulose and for tosylated samples (Meiland et al., 2011). DP_W decreased from 1544 to 1101 within 4 h of tosylation. A further increase in reaction time to 8 h (DP_W = 972) and finally 48 h (DP_W = 896) led to a less pronounced degradation of the polymer backbone. A certain decrease in DP by slight hydrolysis of the polysaccharide in the reaction medium is often observed during derivatization of cellulose, in particular in case of high molecular weight starting materials and when relatively acidic compounds are present, e.g., pyridinium hydrochloride. Compared to the starting cellulose, the polydispersity index (PDI) increased upon tosylation, which could not fully be explained in the present study. As described above, all TOSC of appropriate DS readily dissolved in organic solvents meaning that significant cross-linking during tosylation is unlikely. However, TOSC might form some looses aggregates when dissolved in DMA/LiCl, e.g., by interaction of the aromatic moieties (Berlin et al., 2000). The SEC curves of TOSC samples show a small shoulder at high molecular weights (see Fig. 2 in supporting information), which might indicate such aggregation and thus explain the broader molecular weight distribution (Sjöholm, Gustafsson, Eriksson, Brown, & Colmsjo, 2000). For the sake of completeness it should be noted that an increase in PDI might also indicate that hydrolysis of TOSC is not occurring randomly over the whole chain, which would result in PDI converting to 2, but preferably takes place near the end (Guaita, Chiantore, & Luda, 1990). As concluding remark, TOSC, cellulose, and pullulan that was used as calibration standard are likely to have different hydrodynamic radii, which makes quantitative discussion without additional input difficult. For a detailed discussion, further studies, including mechanistic studies of the hydrolysis and static light scattering experiments for absolute determination of the M_W of TOSCs and their conformation in DMA/LiCl, are required. Nevertheless, the SEC results demonstrate that only moderate degradation of the polysaccharide backbone occurred during tosylation in ILs with co-solvents at 25 °C.

3.5. Nucleophilic displacement reaction with tosyl cellulose

TOSC is a key intermediate for the preparation of 6-deoxy-6-substituted-cellulose derivatives by nucleophilic displacement reaction. In the present work, conversion with azide ions was studied as a typical example. The resulting 6-azido-6-deoxy cellulose (AZC) can be converted into a vast number of tailored polysaccharide derivatives by 1,3-dipolar cycloaddition (Huisgen reaction) as shown in various publications (Heinze, Schöbitz, Pohl, & Meister, 2008; Koschella, Hartlieb, & Heinze, 2011; Liebert et al., 2006). Moreover, the azido group can be reduced to an amino moiety using $LiAlH_4$ (Liu & Baumann, 2002).

TOSC **19** with a rather high chlorine content (DS_{tosyl} = 0.74, DS_{Cl} = 0.16) was allowed to react with sodium azide to tested whether small amounts of 6-chloro-6-deoxy groups disturb the S_N reaction or if the overall DS is determining the outcome of the reaction. The resulting product (AZC **1**) showed a high DS_{azide} of 0.90 that resembled the overall amount of tosyl- and chloro-deoxy substituent in the starting material. Consequently, both groups likewise acted as good leaving groups for the S_N reaction and were displaced almost quantitatively (AZC **1**; remaining DS_{tosyl} = 0.02, DS_{Cl} = 0.01). It has been reported that also 6-chloro-6-deoxy celluloses with high DS_{Cl} can been applied for the preparation of amino-deoxy and azido-deoxy cellulose derivatives (da Silva Filho, de Melo, & Airoldi, 2006; Eyley & Thielemans, 2011; Nakamura, Amano, Saegusa, & Sato, 1992).

3.6. Ionic liquid recycling

Reutilization of solvents, including IL, is an important ecological as well as economical aspect. Thus, studies were carried out to characterize major impurities and enable recycling of the IL and the co-solvents. After the tosylation in BMIMCl/pyridine, the cellulose derivatives were removed from the reaction mixture by precipitation in ethanol and filtration. One of the most prominent features of ILs is their low volatility. Consequently, ethanol could be removed from the filtrate and afterwards reutilized for precipitation by evaporation at reduced pressure. By further decreasing the pressure, also a certain amount of pyridine was collected. Although no further evaporation of volatile compounds under vacuum (10 mbar, 60 °C) was observed, the crude IL still contained residual pyridine, most likely as hydro chloride, as well as toluene sulfonic acid (Fig. 6c). To purify the crude IL further, it was dissolved in water and neutralized with $NaHCO_3$. Subsequently, water was removed under reduced pressure and the IL was dissolved in chloroform. Inorganic salts precipitated by this treatment and were separated by filtration. After evaporation of chloroform and residual pyridine (Fig. 6b), tosylate anions were removed by treating the IL in aqueous solution with a chloride loaded anion exchanger (Fig. 6a). The recycled IL was found to be free of residues that might affect the tosylation of cellulose.

For the tosylation in BMIMCl/DMI, the recycling procedure was slightly modified. After neutralization and precipitation of inorganic compounds with chloroform, the 1-alkyl-imidazoles could not be removed by evaporation, as it was possible for pyridine, but by extraction of aqueous IL solutions with toluene. BenzMIM is immiscible with water and thus already formed a separate phase in these mixtures. It could be removed completely by extracting the system three times with toluene. In case of BIM, 5 extraction steps were performed. DMI has a rather high boiling point of around 225 °C and was consequently not removed (see Fig. 3 in supporting information for NMR spectrum). Nevertheless, the purified IL/co-solvent solution, obtained by the recycling process, can be used directly for the dissolution of cellulose (Rinaldi, 2011).

Recycling of ILs used for dissolution and chemical modification of cellulose is one of the main issues that need to be addressed in order to apply these solvents in considerable scale. Several techniques, including "salting-out", pervaporation, nanofiltration, reverse osmosis, and utilization of "distillable ILs", are currently evaluated for that task (Gericke et al., 2012). Based on the knowledge gained in the present study, regarding the major impurities that need to be removed, the recycling of ILs used for tosylation of cellulose might be improved further.

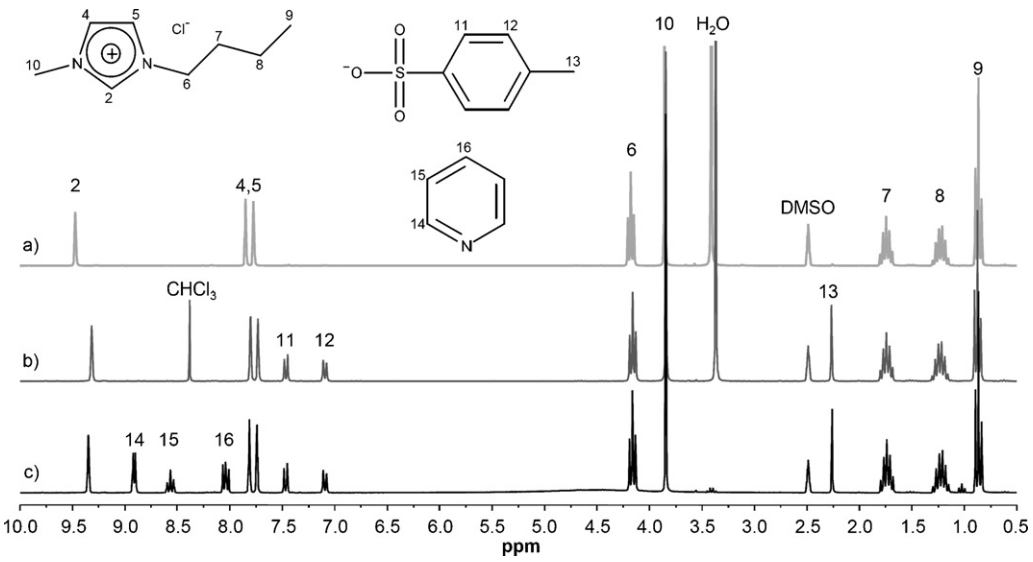

Fig. 6. ^{1}H NMR spectra of 1-butyl-3-methylimidazolium chloride that was recycled after tosylation with pyridine as co-solvent and base, recorded in DMSO-d_6: (c) crude ionic liquid, (b) after removal of pyridine, and (a) after removal of residual tosylate.

4. Conclusion

Mixtures of ILs with a co-solvent turned out to be efficient media for the homogeneous tosylation of cellulose. It was demonstrated that co-solvents as well as bases, suitable for this derivatization reaction, can be chosen based on solvatochromic parameters. The amount of tosyl- and 6-chloro-6-deoxy moieties in the products obtained can be controlled by the reaction parameters in order to obtain tailored products for subsequent conversion into various promising cellulose derivatives. Moreover, extensive cooling, usually applied during tosylation of cellulose in DMAc/LiCl, was not required. The reaction could be performed at 25 °C, which is energy efficient and allowed shortening of the reaction time from 24–48 h to 8–16 h. Utilization of pyridine as base and co-solvent simplifies the recycling procedure. On the other hand, application of DMI as co-solvent and 1-butylimidazole as base increases the reactivity.

Further studies are currently performed in order to compare the benefit of the developed tosylation procedures with the conversion in DMA/LiCl at 25 °C. A promising approach to improvement is certainly the design of novel ILs with tailored properties. Based on the results gained in the present study, two major findings appear to be important. The miscibility of the IL with non-polar compounds should be improved, which would prevent phase separation with increasing DS of the derivative formed. Furthermore, reducing the viscosity of the IL will enable better mixing and stirring during the reaction. In this context, the diversity of ILs, which is gained by combination of numerous potential anions and cations, must be pointed out. However, a deeper understanding of the interaction of cellulose and ILs and the parameters that determine solubility or insolubility is required.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carbpol.2012.03.040.

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