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Side reaction of cellulose with common 1-alkyl-3-methylimidazolium-based ionic liquids

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ABSTRACT

Ionic liquids with 1-alkyl-3-methyl-imidazolium cations react at C-2 with cellulose at its reducing end, forming a carbon–carbon bond. The reaction is strongly catalyzed by bases, such as the commonly present impurities in ILs, imidazole, and 1-methylimidazole. The direct reaction was verified by means of ^{13}C-isotopical labeling and with the help of an IL that carried a fluorescence label which was transferred to cellulose upon the reaction. In solutions of cellulose in alkylmethylimidazolium ILs, both the ionic liquid and the cellulose are evidently not inert.

Within the past several years, ionic liquids (ILs) have attracted much interest in cellulose chemistry as dissolution[1,2] and derivatization media,[3–5] and research to use ILs for high-quality cellulosic fiber production is going on.[6,7] It has been realized that the integrity of the cellulose chain during dissolution and derivatization in ILs is largely dependent on the purity of these solvents and of the absence of IL-derived byproducts. We recently observed that cellulose after dissolution in imidazolium-based ILs and reprecipitation showed less fluorescence with the carbonyl-selective fluorescence label CCOA[8] than the starting cellulose labeled directly. This seemed to indicate a reaction between the ILs and carbonyl groups of the cellulose. These carbonyls are present in the form of a hemiacetal at the reducing end of the cellulose chain, and as keto (C-2, C-3) or aldehyde (C-6) groups along the cellulose chain, which are the result of random oxidation during cellulose processing and aging.

In the literature, there is one interesting report on side reactions of imidazolium-based ionic liquids in base-catalyzed Baylis–Hillman reactions.[9] It was shown that under basic conditions butylmethylimidazolium (BMIM) ionic liquids are deprotonated at C-2 to give species capable of reacting with electrophiles, such as benzaldehyde. Here, we would like to communicate our studies on the reaction of alkylmethylimidazolium ILs with the reducing ends of cellulose and aldopyranose model compounds, demonstrating that BMIM-type ILs do not behave as inert solvents to cellulose.

To simulate the reactivity of the reducing end of celluloses we used a simple but fitting model compound D-glucose, present as natural mixture of α- and β-glucopyranoside, which was ^{13}C-labeled at C-1 (>99%, **2**). The intensity gain roughly by the factor 100 in ^{13}C NMR would allow to reliably detect also minor side reactions at this position: If 10% of the glucopyranose in a 10% solution in alkylmethylimidazolium ILs form a byproduct, the corresponding signal would still be in the same intensity order as those of the solvent and thus be readily distinguishable. Figure 1a shows the ^{13}C NMR spectrum of the butylmethylimidazolium acetate (BMIM–OAc, **1**), and of 5% 1-^{13}C-D-glucose (**2**) in this IL immediately after dissolution (Fig. 1b). The resonances at approx. 99 ppm and 93 ppm correspond to the β-D-glucopyranose and α-D-glucopyranose form, respectively.[10] After 7 days of storage under inert atmosphere at room temperature, clearly two new signals (at approx. 65 ppm and 67 ppm) had developed (Fig. 1c), which originate from the addition products **3a** and **3b**, formed by electrophilic attack of C-2 of the imidazolium at the anomeric carbon of **2**. The same outcome was observed already after 2h in the presence of catalytic amounts of triethylamine (TEA, additional small resonances at 11.7 ppm and 45.7 ppm) at rt, see Figure 1d. In both cases, about 15–20% of the glucopyranose were converted into the corresponding addition product by reaction with

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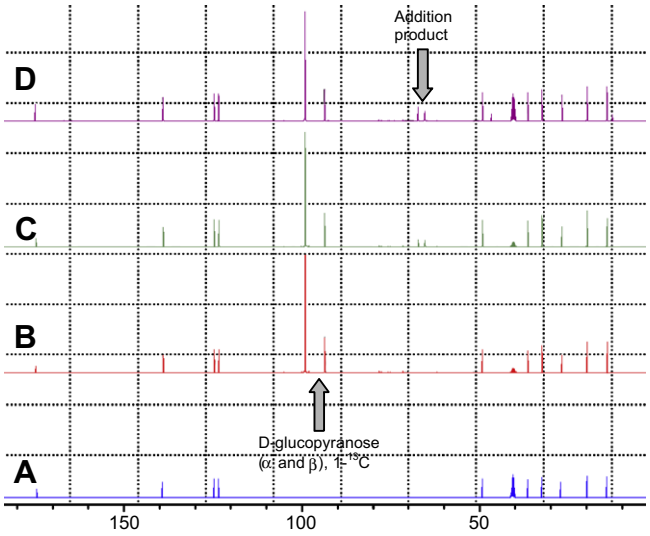
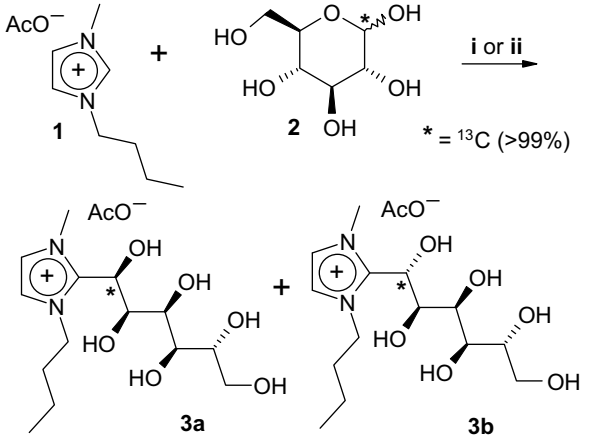


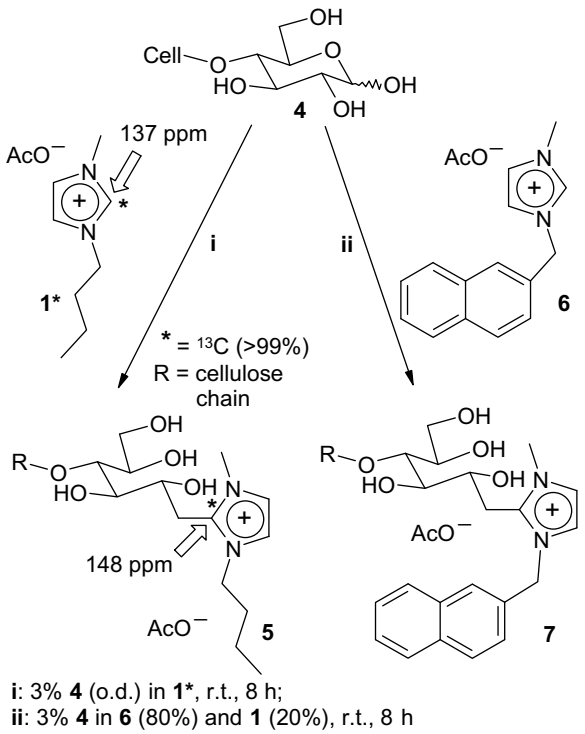
Figure 1. ^{13}C NMR spectra (ppm). (A) BMIM–OAc (**1**); (B) BMIM–OAc (**1**) and 5% 1-^{13}C-D-glucose (**2**, 5%, w/w), spectrum acquired immediately after dissolution; (C) composition as in (B), measured after 7 d at rt, (D) BMIM–OAc (**1**), 5% 1-^{13}C-D-glucose (**2**, 5%, w/w), and 3% TEA (w/w), spectrum acquired after 2 h.

BMIM–OAc (**1**), see Scheme 1. It was evident that the IL reacted with the glucopyranose both at longer reaction times and upon base catalysis.

Assuming a similar reaction under similar conditions (rt, 7 d or rt, 2 h, 3% TEA), the amount of IL bound to cellulose (**4**) is actually rather small. At a DP of 500, there is per 500 glucopyranose units one reducing glucopyranose end, of which possibly not all would react. This small amount of derivatized reducing ends is impossible to be traced down by NMR, and is also within the error limits of microanalysis (N-content). However, when we used isotopically labeled ionic liquid (2-^{13}C-BMIM–OAc, **1***), the NMR resonance intensity of the coreacting center in the IL is multiplied by 100, and thus approaches the detectable range. Indeed, cellulose dissolved in **1*** for 7 d, then precipitated, and finally measured by NMR in DMAc-d_9/LiCl (2.5%, w/w) shows a weak but clearly discernible resonance at 147.8 ppm, corresponding to C-2 in the imidazolium moieties of the endwise-derivatized cellulose (**5**), see Scheme 2.



Scheme 1. Reaction of butylmethylimidazolium IL **1** with 1-^{13}C-D-glucopyranose (**2**) to the isomeric addition products **3a** and **3b**.



Scheme 2. Reaction of ^{13}C-labeled butylmethylimidazolium IL **1*** and of (2-naphthylmethyl)methylimidazolium IL **6** with cellulose at its reducing end to derivative **5** with ^{13}C NMR-detectable cellulose-IL linkage, and to fluorescent derivative **7,** respectively.

C-2 in **1** resonates at 137 ppm. This resonance was absent in isolated **3** and in the precipitated derivatized cellulose **5**. However, after addition of base to the addition products, non-derivatized IL (**1**) re-appears, showing that the initial addition products are unstable under basic conditions and undergo a reversal of the addition reaction (a retro-aldol type cleavage). This is in line with observations on the reversible addition of butylmethylimidazolium IL to benzaldehyde.[9] The finding implies that cellulose in butylmethylimidazolium ILs becomes derivatized at the reducing end according to Scheme 2, but loses the IL moiety over time in a reversal of the addition process. Due to the negligible vapor pressure of the ILs, the released IL, although present in minute amounts only, cannot leave the cellulosic material and will accumulate there, which should be kept in mind as a possible problem for medical and physiological application scenarios.

To conclusively prove the derivatization of cellulose by ILs based on 1-alkyl-3-methyl-imidazolium, we used 1-(2-naphthylmethyl)-3-methyl-imidazolium acetate (NapMIM, **6**) instead of BMIM–OAc. Having otherwise similar reactivity, **6** carries a UV- and fluorescence-active moiety, which can be used to report the IL moiety in derivatives. While the reaction product of BMIM with cellulose (**5**) has no fluorescence, the analogous NapMIM-cellulose derivative (**7**) is strongly fluorescent. This property can be used to verify by size exclusion chromatography (SEC)[11] whether indeed an IL-based moiety is covalently attached to cellulose after dissolution of cellulose in this ionic liquid. In the case of IL being only adsorbed or adherent to cellulose, fluorescence would occur only in the exclusion peak (long retention times), but not along the molecular weight distribution of the cellulose. If, on the contrary, the IL was covalently bound to the cellulose, there would be a discernible fluorescence signal also along the molecular weight distribution, indicating the endwise derivatization of the cellulose chains by the IL.

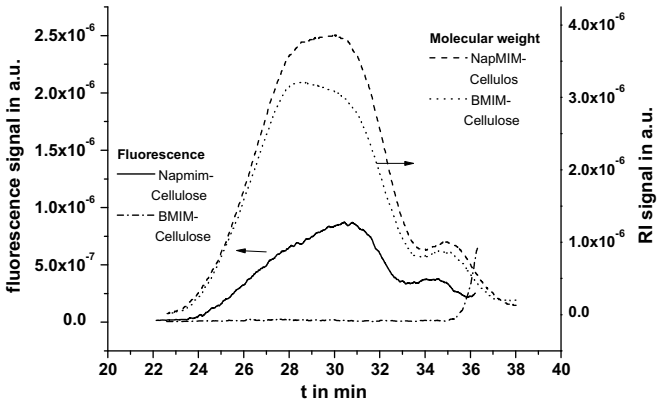


Figure 2. Molecular weight distributions (right *y*-axis) and fluorescence signals (left *y*-axis) of BMIM-derivatized and NapMIM-derivatized cellulose. No fluorescence was detectable in the case of BMIM (dash-dot line), whereas cellulose dissolved in NapMIM gave a clear fluorescence signal over the whole range of the molecular weight (solid line). The shape of the molecular weight distribution did not change significantly upon reaction with either IL (cf. refractive index (RI) signal).

Indeed, as seen in Figure 2, the cellulose was derivatized by NapMIM as seen by the distinct fluorescence signal of compound (**7**). The cellulose was dissolved in the IL for 8 h, subsequently reprecipitated and redissolved for SEC measurement. Thus, already after such relatively short time in IL solution, the cellulose reacted with the 1-alkyl-3-methyl-imidazolium IL, which caused a derivatization at the reducing end as shown in Scheme 2. The fact that the fluorescence signal follows the molecular weight distribution quite closely in shape moreover demonstrated that this endwise derivatization occurred more or less independent of the chain length. Derivatization proceeded in all molecular weight regions equally well, and no region was suppressed.

In conclusion, it was shown that butylmethylimidazolium ILs react at C-2 with the reducing ends of cellulose and aldopyranose model compounds. Whether a similar reaction occurs in addition at the small number of keto/aldehyde structures along the cellulose chain cannot be answered at present. The resulting modification of the cellulose is rather minor relative to the number of glucopyranose units per cellulose chain, but it demonstrates unambiguously that ILs are not at all inert solvents for cellulose. This is of importance for the processing of cellulosics and cellulose derivatives for use in medical and biological applications where even minor impurities might induce adverse effects. The use of alkylmethylimidazolium ILs in the processing of oxidized cellulosics, such as TEMPO-oxidized or periodate-oxidized cellulose, seems to be rather problematic, as the side reactions with the solvents will become predominant in those cases. By applying 2-alkylsubstituted ILs,[12] the reaction with the reducing end of celluloses can be completely avoided. The reaction can at least be suppressed by the absence of bases (as the common impurities imidazole, methylimidazole and alkyl imidazole in alkylmethylimidazolium ILs, or auxiliary bases used in esterifications) and short reaction or contact times of less than 2 h, if practicable for the respective reaction system.

Acknowledgment

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11. For details of the GPC system used see: Ref. 8c.
12. The protective effect of an alkyl-substitution at C-2 against side reactions of the IL has also been reported for Baylis–Hillman reaction in [bdmim][PF_6] ionic liquid: Hsu, J. C.; Yen, Y. H.; Chu, Y. H. *Tetrahedron Lett.* **2004**, *45*, 4673–4676.