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The First Molecular Level Monitoring of Carbohydrate Conversion to 5-Hydroxymethylfurfural in Ionic Liquids. B₂O₃—An Efficient Dual-Function Metal-Free Promoter for Environmentally Benign Applications

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The mechanistic nature of the conversion of carbohydrates to the sustainable platform chemical 5-hydroxymethylfurfural (5-HMF) was revealed at the molecular level. A detailed study of the key sugar units involved in the biomass conversion process has shown that the simple dissolution of fructose in the ionic liquid 1-butyl-3-methylimidazolium chloride significantly changes the anomeric composition and favors the formation of the open fructoketose form. A special NMR approach was developed for the determination of molecular structures and monitoring of chemical reactions directly in ionic liquids. The transformation of glucose to 5-HMF has been followed in situ through the detection of intermediate species. A new environmentally benign, easily available, metal-free promoter with a dual functionality (B_2O_3) was developed for carbohydrate conversion to 5-HMF.

Introduction

Atmospheric carbon dioxide can be considered as the ultimate carbon source for the sustainable future of the chemical industry and for the elimination of barriers in the production of transportation fuels. The photosynthetic fixation of carbon produces carbohydrates accounting for 75% of the world's renewable biomass (ca. 1.7×10^{11} tonnes).^[1] A central research challenge in the coming century is to develop practical and efficient procedures for converting cellulose into platform chemicals and biofuels. It has been estimated that up to one third of the world's demand for transportation fuels can be obtained from cellulose biomass.^[2]

Continuous efforts have focused on the conversion of various carbohydrates (fructose, glucose, sucrose, cellulose, etc.) into 5-hydroxymethylfurfural (5-HMF)—a single renewable biomass-derived building block.^[3] A variety of relevant target chemicals and petroleum-based industrial applications are accessible through the use of 5-HMF.^[4] A diverse range of chemical and industrial applications take advantage of the nontoxic properties of 5-HMF.^[5] The material safety data sheet for 5-HMF lists it as a low health hazard (Category 1) compound; furthermore, it is present in practically every food that contains carbohydrates,^[6] it is used as a flavor component,^[7] and has been studied as an antitumor agent.^[8]

The one-pot formation of 5-HMF using hexoses derived directly from crude biomass has been achieved in several chemical systems with a high efficiency demonstrated in ionic liquid (IL) media.^[9] Several systems have been developed in recent years involving ILs with Cl⁻ anions to increase the solubility of carbohydrates and various metal-containing promoters, for example, CrCl₂ and CrCl₃,^[10] CoSO₄,^[11] FeCl₂,^[12] GeCl₄,^[13] Ianthanide salts,^[14] Cr/*N*-heterocyclic carbenes,^[15] WCl₆/HCl,^[16] Ta₂O₅/H₂O,^[17]

and others.^[9] An excellent promoter has been discovered recently based on boric acid (B(OH)₃)—a weak, noncorrosive, and nontoxic acid.^[18,19] Zhu and coworkers have shown that B(OH)₃ in combination with an organic ligand and Ru nanoparticles facilitates the conversion of cellulose.^[18] Riisager and coworkers have demonstrated that B(OH)₃ alone is an efficient metal-free reagent for 5-HMF formation.^[19] The combination of a technological advantage (noncorrosive) with biocompatibility (nontoxic and metal-free) and easy availability (low price reagent) makes boric compounds very promising promoters for biomass conversion.

Two pathways—cyclic and acyclic—may be proposed based on the sugar chemistry known for water and common organic solvents (Scheme 1). The cyclic pathway is often discussed for transformations involving ILs, whereas a considerably more complicated picture appears for the acyclic route.^[9,20] A knowledge of the mechanistic pathways of sugar conversion is of principal importance for further development of the field to create efficient procedures, control the selectivity of the reaction, and to avoid side reactions leading to humins.^[9-20] In spite of the tremendous interest in this topic, mechanistic studies in IL systems are rather complicated due to the lack of a powerful nondestructive analytic tool. The optimization of

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Scheme 1. Cyclic and acyclic pathways for fructose conversion to 5-HMF.

the reaction conditions for 5-HMF production in ILs mainly relies on indirect analytical measurements based on extraction. The extraction of 5-HMF from IL systems is a standalone question, and a routinely used procedure involves treatment with water and an organic solvent.^[9] Such treatment destroys the IL system and leads to the production of toxic waste containing IL components and the possible contamination of the environment.^[21] In addition, mechanistic studies and gaining a better insight into the nature of the chemical processes in IL systems are impossible without direct monitoring of the reactions.

The goal of our research was to understand the mechanistic nature of carbohydrate conversion to 5-HMF at the molecular level and to find efficient promoters for environmentally benign applications. A reliable NMR approach was developed for the direct spectral investigation of IL systems and characterization of the intermediate species.

Results and Discussion

Development of an NMR methodology to study IL systems

Our continuous efforts to record NMR spectra of acceptable quality in IL/carbohydrate systems failed in the initial stages

due to very broad spectral lines and the inability to reproduce the chemical shifts of spectral patterns (Figure 1 a). Indeed, the difficulties of obtaining high-resolution NMR spectra in ILs associated with high viscosity, the conductive ionic character of the medium, and absorption of radiofrequencies are well documented.^[22-24] Applying all the known solutions to the issues related to



Figure 1. (a) ¹H NMR spectrum of glucose in [BMIM]CI with conventional sample preparation; (b) the same sample after treatment in our NMR reactor, which is shown in Figure 2. Conditions: 80 °C, 600 MHz. The inserts show the magnified region containing the glucose signals.

NMR spectroscopy in ILs did not improve the quality of the spectra of the studied system.

Surprisingly, a more detailed study has shown that it is the microheterogeneous nature of the sample that causes the challenging problems in the observation of NMR signals in ILs.^[25] High-quality NMR spectra were recorded by using a special reactor that eliminates microheterogeneity below the spectroscopic influence level (Figure 1 b). Stirring the IL sample directly in the NMR tube was the key issue to improve the quality of the NMR spectra. Importantly, stirring in the test tube followed by transfer of the sample into the NMR tube often led to NMR spectra of an unacceptable quality. For better accuracy and reproducibility of the measurements, it was of principal importance to perform stirring directly in the NMR tube prior to recording the spectra.

The NMR setup developed in the present study (Figure 2) can be easily assembled and utilized with standard NMR hardware (verified on NMR spectrometers operating at 300, 500, and 600 MHz for ¹H and 75, 125, and 150 MHz for ¹³C). Not only 1D experiments, but also 2D heteronuclear multiple-bond correlation (HMBC), heteronuclear single-quantum correlation (HSQC), and COSY spectra were successfully recorded and utilized to assign the NMR signals.^[26] When the temperature of the sample was kept constant, the NMR study could be per-

(a)	-	stirrer centered in the tube
stirrer	cap	and the second
(b)		(c)
stirrer		
NMR tube		

Figure 2. (a) Assembled reactor for native-state NMR spectroscopy in ILs. (b) Magnified images of glass stirrer and NMR tube. (c) Example of a sample used to monitor the formation of 5-HMF in an IL by performing NMR spectroscopy.

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formed for a few hours after stirring (sufficient time to record 2D spectra). When the quality of the NMR spectrum decreased over time or after a temperature change, the homogeneity of the sample could be restored by stirring again.

The elimination of microheterogeneity made it possible to record high-resolution NMR spectra for a broad range of IL systems: we have verified the scope for individual solutions of fructose, glucose, sucrose, and 5-HMF as well as reaction mixtures in ILs. Thus, this approach should be very useful for conducting mechanistic studies in native-state IL systems.

α-Glucopyranose (6) IL ΗČ ΟН нό cvclic β -Fructofuranose (2) pathway HC 1 юн IL 5-HMF β-Glucopyranose (7) HO -3 H₂O + HO Humins óн ÓН acyclic IL α -Fructopyranose (3) pathway -3 H₂O ОН 1 HO ́Он ОН HO нон HÔ ÔH ÓН Fructoketose (5) Sucrose (8) OН HO β-Fructopyranose (4) ÓН ٦H

HO

HO

OH

ÔН

OH

ΗÒ

α-Fructofuranose (1)

НÓ

Monitoring of carbohydrate conversion to 5-HMF

Scheme 2. Interconversion of carbohydrates and formation of 5-HMF.

Ó⊢

promoter

Using this NMR approach, we

were able to record high-resolution NMR spectra directly in ILs.^[27] Thus, for the first time, the signals of individual anomers were completely resolved (Scheme 2). Surprisingly, dissolution of fructose in 1-butyl-3-methylimidazolium chloride ([BMIM]Cl) leads to a significant change in the anomeric composition of 1/2/3/4/5=14:24:1:55:6 compared to the known data for a water solution of 8:40:1:50: < 1.^[26] In contrast to fructose, the dissolution of glucose in ILs did not result in a significant change in the ratio between the anomers (cf. Tables S1 and S2 in the Supporting Information).

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An increase in the amount of the open fructoketose 5 is noticeable, as well as the difference in the amounts of 1 and 2. All of the species 1-8 have been characterized, and the data are provided in Tables S1-S9 (Supporting Information). The dehydration of fructose takes place directly in the IL and leads to the formation of 5-HMF (Scheme 2). The conversion of glucose is more difficult and requires a promoter to furnish the transformation into fructose, which is followed by dehydration. Other carbohydrates, such as sucrose, undergo splitting into glucose and fructose in ILs. The changes in the anomeric compositions in ILs give rise to both acyclic and cyclic pathways in the formation of 5-HMF and humins.

This NMR approach was efficient not only for the characterization of molecular systems in ILs, but also for direct monitoring of the chemical transformations. Stirring inside the NMR tube played a dual role-to eliminate microheterogeneity and to ensure continuous mixing of the reaction solution. We recorded high-resolution NMR spectra of the reaction mixtures, which allowed us to monitor the initial reagents, the products, and even to identify a borate/sugar complex (9, Figure 3).

NMR monitoring was successfully performed with the 5-HMF formation reaction using the known promoter B(OH)₃,^[19] which



Figure 3. ¹³C¹H NMR spectrum (150 MHz, 80 °C) of the native reaction mixture: [BMIM]CI (■), glucose (*), 5-HMF (▲), and borate complex 9 (#) shown in Scheme 3.

showed the expected order of relative reactivity: fructose > sucrose > glucose (Table 1, entries 1-3). Interestingly, phenylboronic acid also exhibited moderate activity in this reaction (entries 4 and 5). This suggests that the coordination of $B(OH)_3$ with a single sugar unit is sufficient for the reaction and rules out the assumption that two sugar units are involved.^[28]

Unexpectedly, boron trioxide (B_2O_3) showed excellent activity in 5-HMF formation leading to 98-99% conversion for all of the carbohydrates studied (Table 1, entries 6-8). The reaction was highly anion dependent with Cl⁻ necessary for 5-HMF formation (entries 8–10). The PF₆⁻ anion was found to inhibit the reaction (entry 11), whereas BF_4^- was compatible with Cl^- and resulted in excellent conversion (entry 12). The mixture of [BMIM]Cl and [BMIM][BF₄] has advantages for some practical applications because it is considerably less viscous than pure [BMIM]CI.

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 Table 1. Direct monitoring of carbohydrate conversion to 5-HMF under native-state IL conditions in the NMR reactor.^[a]

Entry	IL	Sugar	Conditions	Conver- sion [%]	
1	[BMIM]CI	fructose	B(OH) ₃ , 100 °C, 2 h	90	
2	[BMIM]CI	sucrose	B(OH) ₃ , 120 °C, 3 h	85	
3	[BMIM]CI	glucose	B(OH) ₃ , 120 °C, 5 h	61	
4	[BMIM]CI	sucrose	PhB(OH) ₂ , 120 °C, 1 h	69	
5	[BMIM]CI	glucose	PhB(OH) ₂ , 120 °C, 1 h	42	
6	[BMIM]CI	fructose	B₂O₃, 100 °C, 1 h	98	
7	[BMIM]CI	sucrose	B₂O₃, 120 °C, 2 h	99	
8	[BMIM]CI	glucose	B₂O₃, 120 °C, 5 h	99	
9	[BMIM][PF ₆]	glucose	B₂O₃, 120 °C, 5 h	0	
10	[BMIM][BF ₄]	glucose	B₂O₃, 120 °C, 5 h	0	
11 ^[b]	[BMIM]CI/[BMIM][PF ₆]	glucose	B₂O₃, 120 °C, 5 h	0	
12 ^[b]	[BMIM]CI/[BMIM][BF ₄]	glucose	B ₂ O ₃ , 120 °C, 5 h	99	
14	[BMIM]CI	sucrose	BF ₃ , 90 °C, 0.5 h	98	
15	[BMIM]CI	glucose	BF ₃ , 90 °C, 0.5 h	93	
[a] The formation of 5-HMF was studied by using NMR spectroscopy, and the conversion of sugars was calculated based on ${}^{13}C{}^{1}H$ spectra. Conditions: $\ U(0,6,\alpha) - U(0,5,\alpha) - U(0$					

tions: IL (0.6 g), sugar (0.56 mmol), and B_2O_3 (0.28 mmol) or $B(OH)_3/$ PhB(OH)_2 (0.56 mmol). For a detailed description of all experimental procedures see the Experimental Section. [b] 1:1 mixture of the ILs.

The complete conversion of carbohydrates as determined by our NMR procedure was independently confirmed by performing chromatography. None of the reagents (fructose, glucose, sucrose) were identified in the separation experiments after full conversion was measured by using NMR spectroscopy. The separation and quantitative recycling of boric reagents was achieved by treatment with water. Good yields of the isolated products were found by using B_2O_3 as the promoter (60%).

Although the optimization of the isolation procedure is out of the scope of this study, we performed a preliminary investigation to understand the issues related to the side reactions and the decrease of the isolated yield of 5-HMF.^[29] After the reactions, we isolated a dark-brown solid consisting of humins, which were insoluble in most organic solvents. Molecular weights of around 2700 Da were measured by using ESI–MS. The formation of humins as byproducts during the conversion of carbohydrates to 5-HMF has been reported and has been shown to decrease the selectivity and yield of 5-HMF production.^[30]

Interesting results were obtained from an ESI-MS study of the isolation procedure, indicating a possible increase of the yield of humins during the isolation step: intense polymer signals were observed after workup, whereas the intensities of the polymer signals were considerably lower in the crude mixtures. These findings show that the isolation procedure itself may affect the composition of the final products.

Another important effect—the slow release of 5-HMF—was observed upon heating/ultrasonic treatment of the isolated brown solid and repeated extraction with organic solvents. This observation may indicate the presence of weak interactions or reversible adsorption involving 5-HMF and humins and/or the slow decomposition of humins resulting in the formation of 5-HMF. This preliminary data deserves further attention as 5-HMF recovery from humins would be a topic of considerable practical importance.

Thus, to develop an efficient IL system and to understand the reaction mechanism it is important to perform an NMR study of the IL systems during the reaction and before the isolation. If native-state NMR spectroscopy is not applied to the characterization of IL systems, the reactions are optimized based on the "indirect" yields determined after workup (this may not always correspond to the real yields after reaction). This again justifies the high importance of our NMR procedure.

In situ study of carbohydrate conversion to 5-HMF

From a mechanistic point of view, the B_2O_3 -promoted conversion of glucose to fructose involves the formation of 1,2-borate derivatives. One such 1,2-borate complex with glucose, **9**, has been detected in situ by performing a ¹³C and ¹H NMR spectroscopy study on an IL (Scheme 3). The difference between B_2O_3 and $B(OH)_3$ is governed by the ability of the former to facilitate dehydration by the trapping of water.

Complex **9** was rather stable and most likely represented a resting state in the studied reaction (Scheme 3). After the complete conversion of glucose and fructose to 5-HMF, there was still a detectable amount of **9**, and the conversion of **9** to 5-HMF was rather slow. Even if the reaction was started with fructose (Table 1, entries 1 and 6), **9** was still detected when performing NMR spectroscopy (due to the equilibrium between fructose and glucose in solution and trapping of the latter as a borate complex). The decomposition of **9** resulted in the elimination of B(OH)₃ as shown by NMR spectroscopy.

In addition to glucose-to-fructose isomerization, B₂O₃ facilitated the dehydration of fructose into 5-HMF by trapping water and shifting the equilibrium. Both the cyclic and acyclic pathway for 5-HMF formation require the elimination of three water molecules for each sugar unit (Scheme 1). As detected by performing ¹¹B NMR spectroscopy, the reaction of B₂O₃ with water furnished the formation of B(OH)₃, which may also act as a promoter. Thus, B₂O₃ was a highly efficient reagent with two functions-a promoter for glucose conversion into fructose and a dehydration agent for 5-HMF formation (Scheme 3). To further test the hypothesis, the process was investigated in the presence of BF₃, which is a more efficient Lewis acid and water-trapping compound and should possess higher activity. In total agreement, the reaction was performed under mild conditions at 90 $^\circ\text{C}$ and resulted in 93–98% conversion in 0.5 h (Table 1, entries 14–15).^[32]

Thus, using our NMR approach, direct monitoring of the reaction with glucose was successfully achieved and resulted in the comprehensive detection of reagent conversion, product formation, interconversion of B_2O_3 and $B(OH)_3$, a borate complex, and the anomeric forms of carbohydrates by using ¹H, ¹¹B, and ¹³C NMR spectroscopy.

Conclusions

A new environmentally benign, easily available, metal-free promoter with dual functionality (B_2O_3) has been found for the conversion of carbohydrates to 5-HMF. We have shown that the complete conversion of the carbohydrate can be achieved



Scheme 3. In situ NMR study of glucose conversion to 5-HMF using our NMR reactor.^[31]

in the IL system studied. The evaluation of the 5-HMF extraction procedure calls for a better understanding of the process of humin formation and more careful consideration of the isolation/purification protocols.

The anomeric compositions of fructose and glucose were determined for the first time in an IL. Quite surprisingly, simple dissolution of fructose in the IL led to the appearance of the open fructoketose form. This is of particular significance for sugar chemistry in ILs beyond the reaction studied here.

We have developed an efficient NMR approach with the ability to characterize molecular transformations in IL systems, to resolve individual species in complex equilibrium, and to detect reaction intermediates. This NMR method can reveal previously inaccessible mechanistic details of native-state IL systems at the molecular level.

Experimental Section

General experimental procedures and methods

The NMR reactor was assembled directly in a standard NMR tube as shown in Figure 2 and Figure S1 (Supporting Information). All NMR measurements were performed on native IL systems without alteration for the purpose of spectral study. All ¹H, ¹³C, and ¹¹B NMR spectra were recorded by using a Bruker Avance II 600 instrument at 303 and 353 K. The NMR spectra and tables of chemical shifts are provided in the Supporting Information. Spectral data for water solutions measured under the same conditions are also provided in the Supporting Information for comparison.

NMR experiments

¹H and ¹³C NMR chemical shifts are given relative to external [D₆]DMSO (capillary insert), $\delta = 2.50$ and 39.5 ppm for ¹H and ¹³C, respectively. ¹¹B NMR chemical shifts are given relative to external 0.1 m H₃BO₃ in a capillary at $\delta = 0.0$ ppm. 90° pulses were recalibrated for the samples in ionic liquids (ILs).

Typical parameters for ¹H NMR spectra were a spectral width of 12 000 Hz and a pulse width of 20 μ s at a power level of 17 W. Typical parameters for ¹³C NMR spectra were a spectral width of 33 kHz and a pulse width of 13.9 μ s at a power level of 63 W and a relaxation delay of 2 s. Inverse gate WALTZ-16^[33] broadband proton decoupling was used for ¹³C NMR spectra, the free induction decays (FIDs) were multiplied by performing an exponential weighting (LB = 2 Hz) before Fourier transformation. Typical parameters for ¹¹B NMR spectra were a spectral width of 7600 Hz and a pulse width of 13.9 μ s at a power level of 58 W. The ¹¹B NMR spectra were recorded without proton decoupling. 1D selective gradient-selected (gs)-NOESY spectra were recorded using 80 ms sinc.1000 180°-shaped pulse with gradient selection.

2D ($^{1}H-^{1}H$) gs-COSY and inverse proton detected heteronuclear spectra ($^{1}H-^{13}C$) gs-heteronuclear single-quantum correlation (HSQC), and gs-heteronuclear multiple-bond correlation (HMBC) were recorded and processed by using standard Bruker NMR software. Parameters for COSY were a spectral width of 3000–4800 Hz, an acquisition data size of 1024 points and eight transients accumulated per increment with 1 s relaxation for a total of 128–256 experiments, data processing by using zero filling in the F1 domain, and shifted sine-bell apodization of factor 0 in both dimensions. Parameters for ($^{1}H-^{13}C$) gs-HSQC and gs-HMBC were a spectral width of 4800–6600 Hz for ^{1}H and 22.0–35 kHz for ^{13}C ,

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1024×256 data sets, four or eight scans (gs-HSQC) and eight or 16 scans (gs-HMBC), and a relaxation delay of 1 s. The ¹H–¹³C coupling value in the HMBC spectrum was set to 8 Hz. The FIDs were processed using zero filling in the F1 domain, and a sine-bell (gs-HMBC) and sine-squared (gs-HSQC) window function in both dimensions was applied prior to Fourier transformation. ¹³C GARP⁽³³⁾ decoupling was used in gs-HSQC experiments.

Electrospray ionization mass-spectrometry

High resolution mass spectra (HR–MS) were measured by using Bruker MicroTOF II and Maxis instruments using electrospray ionization. The measurements were performed in the positive ion mode (interface capillary voltage = 4500 V) and in the negative ion mode (3200 V) for the studied mass range; internal calibration was performed using an electrospray calibrant solution (Fluka). A syringe injection was used for solutions in acetonitrile, methanol, or water (flow rate 3 μ Lmin⁻¹). Nitrogen was applied as a dry gas, and the interface temperature was set at 180 °C. MS was applied to confirm the polymeric nature of the material, but not for the measurements of precise masses as fragmentation/destruction of the polymer may occur.

Carbohydrate conversion to 5-hydroxymethylfurfural

In a typical experiment, a reaction mixture containing glucose (0.56 mmol, 0.1 g), boron promoter (B_2O_3 : 0.28 mmol, 19.5 mg; $B(OH)_3$ 0.56 mmol, 34.6 mg; BF_3 - Et_2O : 0.56 mmol, 79.5 mg) and [BMIM]CI (3.43 mmol, 0.6 g) was transferred under Ar into an NMR tube. The resulting sample was placed in an oil bath at 90–120 °C. The NMR reactor with stirrer was assembled and operated at 90–120 °C with continuous stirring (800 rpm) for the indicated time intervals (Table 1). The NMR tube was taken out of the oil bath, placed into a 200 mL glass beaker containing 100 mL of water at 80 °C and within <3 min transferred into the NMR spectrometer with the probe temperature stabilized at 80 °C. Standing the sample in the NMR tube for a long time after stirring caused deterioration of the spectra quality; thus, microheterogeneity should be eliminated by stirring directly before measurement.

The 5-HMF yield was calculated on the basis of the integrals of the anomeric carbon atoms (C-1) of α -D-glucopyranose, β -D-glucopyranose, α -D-glucopyranose-1,2-borate and C-4 of 5-HMF in $^{13}C{}^{1}H{}$ NMR spectra. The ^{1}H and $^{13}C{}^{1}H{}$ NMR spectra were recorded by applying standard pulse length and shim adjustments. The $^{13}C{}^{1}H{}$ NMR spectra for quantitative analysis and determination of yields were recorded by using an inverse gated pulse sequence. Each experiment (Table 1) was performed three times, and the results were totally reproducible. After complete conversion, the products were separated and isolated in 60% yield by using published procedures (selectivity not determined).^[19,20]

Detection of the borate complex 9

Complex **9** was prepared as follows: 1-butyl-3-methylimidazolium chloride ([BMIM]Cl, 4.01 mmol, 0.70 g), glucose (0.28 mmol, 50.4 mg), and $B(OH)_3$ (0.84 mmol, 51.9 mg) were transferred under Ar into an NMR tube and heated in an oil bath at 100 °C with continuous stirring for 1 h. The sample was transferred into the NMR spectrometer as described above, and the measurements were conducted at 80 °C.

The structure of **9** was established by using 1D selective gs-NOESY and 2D gs-HSQC and COSY spectra.^[26] The signals of protons H-1 and H-2 in the ¹H NMR spectrum were shifted to a lower field in comparison to free glucose in the IL. Due to the strong overlap of IL protons with the H-3, H-4, and H-5 protons of glucose, they were assigned using 1D NOESY spectra, where the following correlations were discovered: H-2 and H-4, H3 and H-5, and H-1 and H-2. The last correlation, as well as a *J* value of 3.8 Hz between H-1 and H-2, indicated the α -anomeric configuration of glucose. The same complex was detected in the reaction involving B₂O₃.

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- a) L. D. Schmidt, P. J. Dauenhauer, *Nature* 2007, 447, 914; b) A. Corma, S. Iborra, A. Velty, *Chem. Rev.* 2007, 107, 2411; c) H. Röper, *Starch/Staerke* 2002, 54, 89.
- [2] M. Chidambaram, A. T. Bell, Green Chem. 2010, 12, 1253.
- [3] Top Value Added Chemicals from Biomass. Vol. I. Results of Screening for Potential Candidates from Sugars and Synthesis Gas (Eds.: T. Werpy, G. Petersen), U.S. Department of Energy, Golden, 2004, http://www.nrel.gov/docs/fy04osti/35523.pdf.
- [4] Selected representative studies: a) J. O. Metzger, Angew. Chem. 2006, 118, 710; Angew. Chem. Int. Ed. 2006, 45, 696; b) T. Thananatthanachon, T. B. Rauchfuss, Angew. Chem. 2010, 122, 6766; Angew. Chem. Int. Ed. 2010, 49, 6616; c) A. A. Rosatella, S. P. Simeonov, R. F. M. Frade, C. A. M. Afonso, Green Chem. 2011, 13, 754; d) M. J. Climent, A. Corma, S. Iborra, Green Chem. 2011, 13, 520; e) J. J. Verendel, T. L. Church, P. G. Andersson, Synthesis 2011, 11, 1649; f) B. Kamm, M. Kamm, M. Schmidt, T. Hirth, M. Schulze in Biorefineries: Industrial Processes and Products, Vol. 2 (Eds.: B. Kamm, P. R. Gruber, M. Kamm), Wiley-VCH, Weinheim, 2006, pp. 97-149; g) F. K. Kazi, A. D. Patel, J. C. Serrano-Ruiz, J. A. Dumesic, R. P. Anex, Chem. Eng. J. 2011, 169, 329; h) A. I. Torres, P. Daoutidis, M. Tsapatsis, Energy Environ. Sci. 2010, 3, 1560; i) X. Tong, Y. Ma, Y. Li, Appl. Catal. A: Gen. 2010, 385, 1; j) T. Buntara, S. Noel, P. H. Phua, I. Melián-Cabrera, J. G. de Vries, H. J. Heeres, Angew. Chem. 2011, 123, 7221: Angew. Chem. Int. Ed. 2011, 50, 7083; k) F. M. A. Geilen, T. vom Stein, B. Engendahl, S. Winterle, M. A. Liauw, J. Klankermayer, W. Leitner, Angew. Chem. 2011, 123, 6963; Angew. Chem. Int. Ed. 2011, 50, 6831.
- [5] The acute toxicity of 5-HMF is rather low, LD₅₀=3.1 gkg⁻¹ body weight in rats: a) R. J. Ulbricht, S. J. Northup, J. A. Thomas, *Fundam. Appl. Toxicol.* **1984**, *4*, 843. For biological and metabolic effects see: b) H. R. Glatt, Y. Sommer in *Acrylamide and Other Health Hazardous Compounds in Heat-Treated Foods* (Eds.: K. Skog, J. Alexander), Woodhead Publishing, Cambridge, **2006**, pp. 328–353.
- [6] For example, up to 0.08 mgg⁻¹ in cookies, 1.9 mgg⁻¹ in roasted coffee, 9.5 mgg⁻¹ in caramel products, etc.: a) M. Murkovic, M.-A. Bornik, *Mol. Nutr. Food Res.* **2007**, *51*, 390; b) L. A. Ameur, G. Trystram, I. Birlouez-Aragon, *Food Chem.* **2006**, *98*, 790; c) M. Murkovic, N. Pichler, *Mol. Nutr. Food Res.* **2006**, *50*, 842; d) S. Bachmann, M. Meier, A. Känzig, *Lebensmittelchemie* **1997**, *51*, 49.
- [7] J. M. de Man, Principles of Food Chemistry, 3rd ed., Springer, Heidelberg, 1999.
- [8] K. Michail, V. Matzi, A. Maier, R. Herwig, J. Greilberger, H. Juan, O. Kunert, R. Wintersteiger, Anal. Bioanal. Chem. 2007, 387, 2801.
- [9] Recent reviews: a) M. E. Zakrzewska, E. Bogel-Łukasik, R. Bogel-Łukasik, Chem. Rev. 2011, 111, 397; b) T. Ståhlberg, W. Fu, J. M. Woodley, A. Riisager, ChemSusChem 2011, 4, 451; c) S. Van de Vyver, J. Geboers, P. A. Jacobs, B. F. Sels, ChemCatChem 2011, 3, 82; d) H. Olivier-Bourbigou, L. Magna, D. Morvan, Appl. Catal. A: Gen. 2010, 373, 1; e) O. A. El Seoud, A.

FULL PAPERS

Koschella, L. C. Fidale, S. Dorn, T. Heinze, *Biomacromolecules* **2007**, *8*, 2629; f) J. Lewkowski, *ARKIVOC* **2001**, *1*, 17; g) H. Wang, G. Gurau, R. D. Rogers, *Chem. Soc. Rev.* **2012**, *41*, 1519.

- [10] a) H. Zhao, J. E. Holladay, H. Brown, Z. C. Zhang, *Science* 2007, *316*, 1597; b) E. A. Pidko, V. Degirmenci, R. A. van Santen, E. J. M. Hensen, *Angew. Chem.* 2010, *122*, 2584; *Angew. Chem. Int. Ed.* 2010, *49*, 2530; c) J.-A. Chun, J.-W. Lee, Y.-B. Yi, S.-S. Hong, C.-H. Chung, *Starch/Staerke* 2010, *62*, 326; d) Y. Zhang, E. A. Pidko, E. J. M. Hensen, *Chem. Eur. J.* 2011, *17*, 5281; e) Z. Zhang, Z. Zhao, *Bioresour. Technol.* 2011, *102*, 3970; f) J.-W. Lee, M.-G. Ha, Y.-B. Yi, C.-H. Chung, *Carbohydr. Res.* 2011, *35*, 1367; h) Q. Cao, X. Guo, S. Yao, J. Guan, X. Wang, X. Mu, D. Zhang, *Carbohydr. Res.* 2011, *346*, 956.
- [11] F. Tao, H. Song, L. Chou, Carbohydr. Res. 2011, 346, 58.
- [12] F. Tao, H. Song, L. Chou, ChemSusChem 2010, 3, 1298.
- [13] Z. Zhang, Q. Wang, H. Xie, W. Liu, Z. K. Zhao, ChemSusChem 2011, 4, 131.
- [14] T. Ståhlberg, M. G. Sørensen, A. Riisager, Green Chem. 2010, 12, 321.
- [15] G. Yong, Y. Zhang, J. Ying, Angew. Chem. 2008, 120, 9485; Angew. Chem. Int. Ed. 2008, 47, 9345.
- [16] L. Lai, Y. Zhang, ChemSusChem 2010, 3, 1257.
- [17] F. Yang, Q. Liu, M. Yue, X. Bai, Y. Du, Chem. Commun. 2011, 47, 4469.
- [18] Y. Zhu, Z. N. Kong, L. P. Stubbs, H. Lin, S. Shen, E. V. Anslyn, J. A. Maguire, *ChemSusChem* **2010**, *3*, 67.
- [19] a) T. Ståhlberg, S. Rodriguez-Rodriguez, P. Fristrup, A. Riisager, *Chem. Eur. J.* 2011, *17*, 1456; b) T. S. Hansen, J. Mielby, A. Riisager, *Green Chem.* 2011, *13*, 109.
- [20] a) J. B. Binder, A. V. Cefali, J. J. Blank, R. T. Raines, *Energy Environ. Sci.* 2010, 3, 765; b) S. J. Dee, A. T. Bell, *ChemSusChem* 2011, 4, 1166; c) R. Karinen, K. Vilonen, M. Niemela, *ChemSusChem* 2011, 4, 1002 and references therein.
- [21] T. Welton, Green Chem. 2011, 13, 225.
- [22] V. P. Ananikov, Chem. Rev. 2011, 111, 418.
- [23] W. R. Carper, Malten Salts in Encyclopedia of Magnetic Resonance, Wiley Online Library, 2011, DOI:10.1002/9780470034590.emrstm0316.pub2.
- [24] R. Giernoth in *lonic Liquids in Chemical Analysis* (Ed.: M. Koel), CRC Press, Boca Raton, 2009, p. 355.

- [25] Possible origins/initiators of heterogeneity in IL (selected examples):
 a) D. Jeong, D. Kim, M. Y. Choi, H. J. Kim, Y. J. Jung, Dynamic Heterogeneity in Room-Temperature Ionic Liquids in Ionic Liquids: Theory, Properties, New Approaches (Ed.: A. Kokorin), InTech, 2011, pp. 167–182; b) Y.-F. Hu, Z.-C. Liu, C.-M. Xu, X.-M. Zhang, Chem. Soc. Rev. 2011, 40, 3802; c) M. F. C. Gomes, J. N. C. Lopes, A. A. H. Padua, Top. Curr. Chem. 2009, 290, 161; d) Z. Hu, C. J. Margulis, Proc. Natl. Acad. Sci. USA 2006, 103, 831; e) Y. T. Wang, G. A. Voth, J. Am. Chem. Soc. 2005, 127, 12192.
- [26] NMR spectra, signal assignment, anomeric composition, and tables of chemical shifts are provided in the Supporting Information.
- [27] It was shown previously that even small amounts of additives used for spectral studies (such as deuterated solvents, internal standards, etc.) can significantly change the properties of ILs (see Ref. [22]). Therefore, the IL systems should be studied in their native state by NMR.
- [28] See Scheme S1 in the Supporting Information for further details.
- [29] In spite of its apparent simplicity, the separation of 5-HMF from ILs is a challenging task with many controversial reports (see Ref. [9] and references therein). Complete and nondestructive separation of 5-HMF leaving the IL intact (rather than destruction by water/organic solvent extraction) is of particular importance.
- [30] a) B. R. Caes, R. T. Raines, *ChemSusChem* 2011, *4*, 353; b) F. S. Asghari, H. Yoshida, *Ind. Eng. Chem. Res.* 2006, *45*, 2163; c) C. Sievers, M. B. Valenzuela-Olarte, T. Marzialetti, D. Musin, P. K. Agrawal, C. W. Jones, *Ind. Eng. Chem. Res.* 2009, *48*, 1277; d) S. K. R. Patil, C. R. F. Lund, *Energy Fuels* 2011, *25*, 4745; e) See also Refs. [2,4k,9,14,20].
- [31] Only two anomers of fructose are shown in the scheme (see Scheme 2), and H^+/H_3O^+ as counterions are omitted for clarity.
- [32] Although BF₃ showed higher activity, further studies are needed to reveal the potential applicability for 5-HMF production as reaction with water may produce toxic and corrosive HF.
- [33] A. J. Shaka, Decoupling Methods in Encyclopedia of Nuclear Magnetic Resonance, Vol. 3 (Eds.: D. M. Grant, R. K. Harris), Wiley, Chichester, 1996, p. 1558.

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