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Conversion of Mono- and Disaccharides to Ethyl Levulinate and Ethyl Pyranoside with Sulfonic Acid-Functionalized Ionic Liquids

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Today most organic chemicals are produced by catalytic transformations of fossil resources such as oil, coal, and natural gas. Within a few decades, the availability of these fossil resources is projected to decrease, which makes the use of alternative carbonaceous resources as feedstock imperative.^[1-3] Carbohydrates are abundant and inexpensive naturally available carbonaceous resources. Because carbohydrates are renewable and carbon-neutral, finding feasible ways to convert them into useful chemicals, such as 5-hydroxymethylfurfural (HMF), lactic acid, levulinic acid, and others, has become increasingly important.^[4-6]

Levulinic acid in particular has been recognized as an important bioderived platform chemical that may provide a starting point for the production of chemicals and fuels.^[7] Levulinic acid is also useful as a solvent, food flavoring agent, plasticizer, resin intermediate and building block for, for example, tetrahydrofuran and succinic acid.^[8] Traditionally, the production of levulinic acid involves treatment of carbohydrates with aqueous mineral acid (H₂SO₄ and HCI) at atmospheric pressure at $100 \,^{\circ}C.^{[9]}$ This method usually yields about 40% of levulinic acid. The yield of levulinic acid may be improved to 60–70% by continuous flow conditions at higher temperatures and pressures using H₂SO₄ as catalyst.^[10] However, a major drawback in this process is tedious work-up during the separation stages.

Acidic ion-exchange resins have also been used as catalysts for the transformation of sucrose to levulinic acid. The major disadvantages of these systems are the moderate yields of levulinic acid (about 25%) and maximum operation temperatures of around 150 °C because of the thermal instability of the resin catalyst.^[11] Y-type zeolites have also been found to give moderate levulinic acid yields of about 40% (and minor amounts of HMF) when investigated as catalysts for the dehydration of glucose and fructose at temperatures between 110 and 160 °C.^[12] In contrast, a Fe-pillared montmorillonite catalyst was found to be very active and able to convert glucose quantitatively, though with low selectivity of 20% to levulinic acid.^[13] Instead a much higher amount of formic acid as well as a significant amount of coke was observed in this study.^[13] To circumvent the drawback of thermal instability and to improve the yield of levulinate, we were inspired to explore the use of ionic liquids as catalysts for these reactions.

lonic liquids (organic salts with melting point below 100 °C) are attractive alternatives to common organic solvents owing to their negligible vapor pressure, relatively high thermal stability, and remarkable catalyst and solvent properties.[14-16] The solubility of mono-/di-/polysaccharides in some ionic liquids is much higher than in common organic solvents.^[17] This has led to their use as solvent/catalyst for producing bioplatform chemicals from carbohydrates. Zhao et al. initially reported that chromium chloride immobilized in imidazolium chloride ionic liquids gave a yield of 70% HMF from glucose.^[6a] Since then, numerous other ionic liquid catalyst systems for transforming monosaccharides into HMF have been investigated.^[18,19] Most of these studies found high yields of HMF but low (or no) yields of levulinic acid, suggesting that the acid strength of the ionic liquids is not sufficient to rehydrate HMF and form levulinic acid.

To enhance the acid strength of ionic liquids, acidic functionalities can be introduced in either the anion or the cation.^[17,18] These "task-specific ionic liquids" have demonstrated their potential to replace traditional mineral acids as catalyst and solvent.^[20,21] Specifically, sulfonic acid-functionalized imidazoliumand phosphonium-based ionic liquids have performed as excellent Brønsted-acidic catalyst systems for Fischer esterification, alcohol dehydrodimerization, and pinacol-benzopinacole rearrangement, being recycled and used in several runs without any significant loss of activity.^[21] Hence, ionic liquids having strong Brønsted acid sites may possibly dehydrate fructose to form HMF followed by the formation of 5-(ethoxymethyl)furan-2-carbaldehyde (HMF-ether) and subsequently rehydrate to form ethyl levulinate. Predominant formation of HMFether from fructose has previously been demonstrated with Amberlite-15 resin catalyst in ethanol at 100 °C.[22]

In the present study, we report the catalytic transformation of the sugars fructose, glucose, and sucrose to ethyl levulinate (Scheme 1) with different sulfonic acid-functionalized ionic liquids (SO₃H-ILs) as catalysts, in the presence of ethanol as reactant and solvent.

Initial experiments were performed with imidazolium-, pyridinium- and ammonium-based SO₃H-ILs containing hydrogensulfate as anion (Table 1). In all these reactions ethyl levulinate was found to be the predominant product and yields of 68, 70 and 74% were obtained with the ionic liquids [BMIm-SO₃H]-[HSO₄], [BPyr-SO₃H][HSO₄], and [NEt₃B-SO₃H][HSO₄], respectively, with full fructose conversion. To evaluate the influence of the ionic liquid anion on the formation of ethyl levulinate, [NTf₂]⁻, [OMs]⁻, and [OTf]⁻ anions were introduced into the sulfonic acid-functionalized imidazolium-based ionic liquids. As shown in Table 1, these ionic liquids gave good yield to ethyl levulinate with practically quantitative conversion of fructose, also. Among the examined ionic liquid catalysts, [BMIm-SO₃H]-

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Scheme 1. A plausible pathway for the formation of ethyl levulinate from sugars.

Table 1. Catalytic transformation of fructose to ethyl levulinate. ^[a]				
Ionic liquid ^(b)	Conversion ^[c] [%]	Yield ^[d] [%]		
[BMIm-SO ₃ H][HSO ₄]	>99	68		
[BPyr-SO₃H][HSO₄]	>99	70		
[NEt ₃ B-SO ₃ H][HSO ₄]	>99	74		
[BMIm-SO ₃ H][NTf ₂]	>99	77		
[BMIm-SO ₃ H][OMs]	>99	67		
[BMIm-SO₃H][OTf]	> 99	69		
[a, b] See Experimental Sect tose. [d] Yield of ethyl levuli	ion for details. [c] Conversion nate.	based on fruc-		

 $[\rm NTf_2]$ gave a higher yield of ethyl levulinate (77%) implying that the formation of ethyl levulinate followed the order of the acid strength of the ionic liquid. $^{[23]}$

The study was further extended to the sugars glucose and sucrose, and the results are presented in Table 2. All of the examined SO_3H -ILs yielded 40 to 43% of ethyl levulinate from su-

crose with 97% conversion. This clearly indicated that only fructose moieties were converted to ethyl levulinate, and no significant isomerization of glucose to fructose occurred which otherwise would have increased the yield of ethyl levulinate. Instead, glucose was found to react readily with ethanol under the applied acidic conditions to form ethyl-D-glucopyranoside (EDGP) (Scheme 1) resulting in EDGP yields of 25 to 32% from sucrose. The preferential transformation of glucose to EDGP instead of isomerization to fructose was confirmed when using glucose as substrate. Here only 6 to 13% yields of ethyl levulinate was obtained with 94% conversion of the substrate, whereas the yields of EDGP were between 50 and 62%. Similarly, the disaccharide cellobiose (consisting of two $\beta(1\rightarrow 4)$ bonded glucose units) gave only 2% of ethyl levulinate with 95% conversion but 63% of EDGP, corresponding to a selectivity of 86%.

Alkyl pyranosides such as EDGP are important nonionic surfactants with good biodegradability and potential applications in cosmetics, food emulsifiers, and pharmaceutical dispersing agents.^[24, 25] In previous reports, alkyl pyranosides were formed from glucose in the presence of alcohol and H-zeolite catalysts.^[5a, 26] H-zeolites contain mostly strong Brønsted acid sites, which are believed to be responsible for the catalytic formation. In this study the presence of strong acid groups, such as SO₃H, was found to be necessary for both the dehydration reaction and the cyclization reaction, since only 13% conversion and essentially no ethyl levulinate or EDGP product were formed when using the less acidic ionic liquid [HNEt₃][HSO₄] as catalyst in the conversion of sucrose.

To understand the reactivity of the intermediates, HMF and levulinic acid were used as substrates in-

lonic liquid ^[b]	Substrate	Conv. ^[c] [%]	Yield ^[d] [%]	Yield ^[e] [%]
[BMIm-SO₃H][HSO₄]	Glucose	94	8	54
	Sucrose	97	41	29
[BPyr-SO ₃ H][HSO ₄]	Glucose	94	13	50
	Sucrose	97	43	27
[NEt ₃ B-SO ₃ H][HSO ₄]	Glucose	94	6	57
	Sucrose	97	41	30
	Cellobiose	95	2	63
[BMIm-SO ₃ H][NTf ₂]	Glucose	94	8	55
	Sucrose	97	43	25
[BMIm-SO₃H][OMs]	Glucose	94	3	62
	Sucrose	97	40	32
[BMIm-SO₃H][OTf]	Glucose	94	8	57
	Sucrose	97	42	28
[HNEt ₃][HSO ₄]	Sucrose	13	0	3

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stead of sugars under identical reaction conditions. After 24 h of reaction with [NEt₃B-SO₃H][HSO₄] as catalyst, 100 % HMF was converted and yields of 85% ethyl levulinate and less than 1% HMF-ether were observed. No other products were found in significant amounts (except insoluble humins and formic acid). With levulinic acid as substrate, the yield of ethyl levulinate was >99% after only 30 min reaction, clearly indicating that levulinic acid was easily converted into ethyl levulinate under these conditions whereas HMF partly transformed into undesired products, that is, humins. Moreover, when water was used as solvent, 40% levulinic acid and 26% HMF were obtained after 24 h with 95% conversion of fructose, indicating that rehydration of HMF was relatively slow in water compared to HMF-ether in ethanol. Consequently, the presence of alcoholic medium was important to enhance the yield of levulinate.

The influence of fructose concentration on the yield of ethyl levulinate was also investigated under similar reaction conditions (Figure 1). When the initial fructose concentration was in-



Figure 1. Influence of fructose concentration on the yield of ethyl levulinate (fructose = 270.2 mg, [NEt₃B-SO₃H][HSO₄] = 0.11 mmol, naphthalene = 30 mg, ethanol = 4.0 g, 140 °C, 24 h).

creased, the yield of ethyl levulinate decreased while the yield of HMF-ether increased. Concomitantly, the conversion of fructose remained more than 99%. Thus, at lower fructose concentration (6.3 wt%) the HMF-ether was completely converted to ethyl levulinate (73%) with more than 99% conversion of fructose, whereas the yield of ethyl levulinate decreased to 65% with significant amount of HMF-ether (8%) also being formed at concentration corresponding to 10 wt%. Hence, the ionic liquid ([NEt₃B-SO₃H][HSO₄]) was able to catalyze the dehydration of fructose and the alkylation of HMF to form HMF-ether but not to rehydrate all HMF-ether to form ethyl levulinate under the examined conditions. Possibly, this difference in reactivity can be related to formation of larger amounts of humins at higher initial fructose concentration. Accordingly, a marked decrease in yield of ethyl levulinate (46, 34, and 28%) was further observed at 15, 20, and 25 wt% fructose, respectively. At the same time, the HMF-ether yield concurrently increased to become the predominant product (32%) at high fructose concentration.

Further investigations showed that the formation of ethyl levulinate increased from a yield of 28 to 49% when the amount of ionic liquid was increased four times in experiments with 25 wt% fructose (6% of HMF-ether formed). In contrast, the yield of ethyl levulinate decreased significantly from 77 to 34% (43% of HMF-ether) when four times less ionic liquid was used in reaction with 6.3 wt% fructose. These experimental results confirm that the number of available SO₃H groups influences the catalyzed rehydration of all HMF-ether to ethyl levulinate: without enough groups undesired products will form.

The ionic liquid [NEt₃B-SO₃H][HSO₄] was further tested for recyclability in three consecutive reaction runs with 6.3 wt% fructose, as shown in Figure 2. In the first run, the yield of



Figure 2. Recycle experiments with 6.3 wt % fructose solution (fructose = 380.2 mg, [NEt₃B-SO₃H][HSO₄] = 0.15 mmol, naphthalene = 43 mg, ethanol = 5.6 g, 140 °C, 24 h).

ethyl levulinate was 72% with more than 99% conversion of fructose. After the first run, the remaining ethanol was evaporated and the reaction mixture treated with a mixture of 5 mL dichloromethane and 5 mL distilled water. The aqueous phase was removed and collected and the organic phase re-extracted with water. This allowed recovery of the ionic liquid after evaporating of the water under reduced pressure. When the recovered ionic liquid was reused a second time a slightly increased ethyl levulinate yield of 74% was obtained, again with more than 99% conversion of fructose. This yield and degree of conversion was also found after testing in a third cycle.

In summary, we have shown that sulfonic acid-functionalized ionic liquids are prominent catalysts for the successive dehydration of fructose to HMF followed by etherification to HMFether and rehydration to form ethyl levulinate. Ionic liquids based on the [NTf₂]⁻ anion gave slightly higher yield of ethyl levulinate (77%) compared to other ionic liquids, thus suggesting that the reaction progression is correlated with the acid strength of the ionic liquid. The disaccharide sucrose was found to yield 36% of ethyl levulinate along with 33% of another useful product, EDGP. Interestingly, glucose was converted into EDGP (63%) with a lower yield of ethyl levulinate. Hence, under strong Brønsted-acidic conditions, fructose preferentially dehydrated to form HMF whereas glucose reacted with ethanol to form ethyl pyranoside. Recycle studies demonstrated that the sulfonic acid derived ionic liquids can be

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reused at least for three cycles without any loss of activity. The facile phase separation, relatively high thermal stability, and ease of recovery makes the introduced ionic liquid systems interesting for industrial feasibility studies, including scale-up synthesis.

Experimental Section

Catalytic tests: The reactions were carried out in 15 mL ace pressure tubes. 270.2 mg of fructose or glucose or 256.7 mg of sucrose, 0.11 mmol of SO₃H-IL, 30 mg of naphthalene and 4 g of ethanol were charged into the ace pressure tube and heated under stirring to 140 $^{\circ}$ C (oil bath temperature).

Recycle study: In the first run, 380.2 mg of fructose, 0.15 mmol of ([NEt₃B-SO₃H][HSO₄]), 43 mg of naphthalene, and 5.6 g of ethanol were charged to an ace pressure tube and heated under stirring to 140 °C for 24 h. After the first run, a second and third run was performed as above by adjusting substrate, naphthalene, and ethanol to the recovered mass of the ionic liquid.

Abbreviations for ionic liquids: 1-methyl-3-(4-sulfobutyl)imidazolium hydrogensulfate ([BMIm-SO₃H][HSO₄]), 1-(4-sulfobutyl)pyridinium hydrogensulfate ([BPyr-SO₃H][HSO₄]), *N*,*N*,*N*-triethyl-4-sulfobutan-ammonium hydrogensulfate ([NEt₃B-SO₃H][HSO4]), 1-methyl-3-(4-sulfobutyl)imidazolium bis((trifluoromethyl)sulfonyl)amide ([BMIm-SO₃H][NTf₂]), 1-methyl-3-(4-sulfobutyl)imidazolium methanesulfonate ([BMIm-SO₃H][OMs]), 1-methyl-3-(4-sulfobutyl)imidazolium trifluoromethanesulfonate ([BMIm-SO₃H][TfO]), triethylammonium hydrogensulfate ([HNEt₃][HSO₄]).

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