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# Metal-Free Dehydration of Glucose to 5-(Hydroxymethyl)furfural in Ionic Liquids with Boric Acid as a Promoter

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**Abstract:** The dehydration of glucose and other hexose carbohydrates to 5-(hydroxymethyl)furfural (HMF) was investigated in imidazolium-based ionic liquids with boric acid as a promoter. A yield of up to 42% from glucose and as much as 66% from sucrose was obtained. The yield of HMF decreased as the concentration of boric acid exceeded one equivalent, most likely as a consequence of stronger fructose–borate chelate complexes being formed. Computational modeling with DFT calculations confirmed that the formation of 1:1 glucose-borate complexes facilitated the conversion pathway from glucose to fructose. Deuterium-labeling studies elucidated that the isomeriza-

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tion proceeded via an ene-diol mechanism, which is different to that of the enzyme-catalyzed isomerization of glucose to fructose. The introduced nonmetal system containing boric acid provides a new direction in the search for catalyst systems allowing efficient HMF formation from biorenewable sources.

# Introduction

The impending exhaustion of fossil resources and climate change has prompted an intensified research for new and better pathways for chemicals and fuels from renewable sources. Particular attention has been set on 5-(hydroxyme-thyl)furfural (HMF), formed by the triple dehydration of hexoses, which is expected to play an important role in a future carbohydrate-based economy (Scheme 1).<sup>[1,2]</sup> HMF is primarily considered to be a starting material for its diacid counterpart (FDA) which is a possible replacement of terephthalic acid as a monomer in plastics.<sup>[3]</sup> Reduction of the furan ring would yield compounds suitable as solvents or fuels (Scheme 1).<sup>[4]</sup>

The formation of HMF from fructose is achieved readily at elevated temperatures in high-boiling molecular solvents

In this work we have focused on finding an alternative to chromium chloride as catalyst for the direct dehydration of glucose to HMF. It is well known that carbohydrates form stable chelate complexes with boric acid<sup>[19–21]</sup> of the form shown in Scheme 2 and catalyze the isomerization of aldohexoses to ketohexoses in aqueous basic environment.<sup>[22,23]</sup>

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or ionic liquids with or without an acid catalyst.<sup>[5-10]</sup> The most important industrial method for fructose production is by the enzymatic isomerization of glucose syrup, a process yielding only about 50% fructose.[11] Direct conversion of the obtained aqueous glucose/fructose mixture would be problematical since the dehydration in water suffers from side reactions by which HMF is rehydrated to leuvulinic acid and formic acid.<sup>[12]</sup> In order to find an economical and environmentally feasible industrial process for the production of HMF, an efficient direct conversion from glucose would therefore be most beneficial. Unlike the dehydration of fructose, however, the dehydration of glucose to HMF demands a special catalyst to attain acceptable yields. This has so far been achieved by lanthanide chlorides,<sup>[13]</sup> stannous chloride<sup>[14]</sup> and chromium chlorides,<sup>[15–18]</sup> with only the latter providing yields that could be adequate for a cost effective process development. The main difficulty in the dehydration is polymerization of the sugars during the reaction. The polymers formed, commonly known as humins, vary in size and are either soluble or insoluble in water depending on chain length.



Scheme 1. Formation of HMF from hexoses and derivatization further to compounds with important applications in a post-petrochemical world, for example, solvents and fuel.

$$\begin{array}{c} OH & HO_{-}OH \\ \stackrel{}{\xrightarrow{}}{}^{s_{1}} & \stackrel{}{\xrightarrow{}}{}^{s_{2}} & + B(OH)_{4}^{-} \longrightarrow O^{B}O + 2H_{2}O \\ OH & OH \end{array}$$

Scheme 2. Formation of boric acid-diol complex.

The ability to form stable complexes with fructose has further been utilized as a method of enriching fructose in the isomerization of glucose to fructose by the enzyme glucose isomerase.<sup>[24]</sup> Boric acid is also known to catalyze several reactions with important synthetic applications such as esterifications,<sup>[25]</sup> cyclization reactions<sup>[26]</sup> and decarboxylations.<sup>[27]</sup> So far no successful dehydrations of glucose to HMF with the aid of boric acid have been reported. With the assumption that the boric acid-sugar interaction also might stabilize intermediates or transition states in the isomerization of glucose to fructose or even the dehydration to HMF, we surmised that boric acid could act as a catalyst for the direct conversion of glucose to HMF in ionic liquids. Compared with the technologies developed up to now, this would be beneficial from both an environmental as well as an economical point of view, since boric acid is a non-toxic, nonmetal and inexpensive compound that exists in great abundance in nature, primarily as sodium borate.

In the work we demonstrate the effect of boric acid in the dehydration with different carbohydrates and bring clarity to the mechanism by the aid of computational modeling and experiments with deuterated glucose.

## **Results and Discussion**

Dehydration of glucose: Based on the results from our previous work,<sup>[13]</sup> we focused on the glucose dehydration using alkylmethylimidazolium chlorides as the reaction media. To demonstrate the effect of the boric acid as a promoter we chose an initial catalyst load of 1.0 equivalent with respect to glucose in order to form a 1:1 sugar/boric acid complex. At a temperature of 120°C the dehydration of glucose (10 wt%) 1-ethyl-3-methylimidazolium in chloride ([EMIm]Cl) and 1-butyl-3-methylimidazolium chloride ([BMIm]Cl) with boric acid showed that up to 40% yield of HMF could be obtained (Figure 1). The yield was higher in [EMIm]Cl than in [BMIm]Cl as is the case with chromium catalysts.<sup>[15]</sup> The yield appeared to reach a maximum in both reactions after 3 h where after it slowly declined as a consequence of degradation or polymerization. In the case of [EMIm]Cl the highest HMF selectivity of approximately 50% was reached after one hour of reaction. Full conversion was not reached until after 21 h. The maximum obtained HMF selectivity in [BMIm]Cl was of around 30% which also coincided with the highest yield of around 20% after 3 h. Close to full conversion in [BMIm]Cl was also reached after 21 h.



Figure 1. Dehydration of glucose in [EMIm]Cl at 120 °C. The reaction contained ionic liquid (1.0 g), glucose (100 mg, 0.56 mmol) and boric acid (34.3 mg, 0.56 mmol);  $\bullet$  = HMF yield;  $\blacktriangle$  HMF selectivity.

A more extensive screening was further made in [EMIm]Cl with a variation of boric acid concentration from 0 to 4.0 equivalents. The HMF yield increased markedly from 0.1 equivalents and reached a maximum between 0.8 and 1.0 equivalents, where after it gradually declined (Figure 2). The observed selectivity drop at high boric acid



Figure 2. Dehydration of glucose in [EMIm]Cl at 120 °C with different concentrations of boric acid (0–2.24 mmol), ionic liquid (1.0 g), and glucose (100 mg, 0.56 mmol);  $\bullet$  = HMF yield;  $\blacktriangle$  HMF selectivity.

content could be a result of formation of more stable sugarboric acid complexes as well as an increase in humin formation. Increasing the temperature above 120°C did not result in a higher HMF yield, indicating that the yield of 42% is the maximum yield obtainable with this procedure.

**Dehydration in various solvents**: To verify the necessity of the chloride anion in HMF formation, a short survey of the dehydration of glucose was performed in different media such as high-boiling molecular solvents and various ionic liquids together with 0.8 equivalents of boric acid. As shown in Table 1, the best HMF yield was obtained in the chloride containing ionic liquids where [EMIm]Cl still proved to be the best (entries 1–5). Unlike with lanthanide catalysts,<sup>[13]</sup> no

Table 1. Dehydration of glucose in various solvents with boric acid as catalyst.  $^{\left[ a\right] }$ 

Entry	Solvent	Yield HMF/%	Selectivity HMF/%
1	[MIm]Cl	19	20
2	[EMIm]Cl	41	43
3	[BMIm]Cl	14	30
4	[HMIm]Cl <sup>[b]</sup>	32	47
5	[OMIm]Cl <sup>[c]</sup>	26	41
6	[EMIm][CH <sub>3</sub> OSO <sub>3</sub> ]	6	57
7	[EMIm][C <sub>2</sub> H <sub>5</sub> OSO <sub>3</sub> ]	6	8
8	[EMIm][AlCl <sub>4</sub> ]	0	0
9	[EMIm][OAc]	0	0
10	$[EMIm][N(CN)_2]$	0	0
11	$[BMIm][N(CN)_2]$	0	0
12	[choline][CH <sub>3</sub> OSO <sub>3</sub> ] <sup>[d]</sup>	6	25
13	DMF <sup>[e]</sup>	7	11
14	NMP <sup>[f]</sup>	2	23
15	DMSO	13	37
16	$\alpha$ -butyrolactone	0	0
17	ethylene glycol	0	0

[a] Reaction conditions: 1.0 g solvent, 100 mg (0.56 mmol) glucose, 27.5 mg (0.44 mmol) boric acid, 120 °C, 3 h. [b] [HMIm]=1-hexyl-3-methylimidazolium. [c] [OMIm]=1-octyl-3-methylimidazolium. [d] [Choline]=N,N,N-trimethylethanolammonium. [e] DMF=dimethylformamide. [f] NMP=N-methyl-2-pyrrolidone. correlation between HMF yield and alkyl chain length on the imidazolium cation of the ionic liquids could be observed. Interestingly, methylimidazolium chloride ([MIm]Cl, entry 1) only exhibited about half the yield of [EMIm]Cl. Since [MIm]Cl is a protic ionic liquid one might have presumed this to inhibit the formation of more stable fructoseborate complexes as is the case with a higher proton concentration in aqueous environments.<sup>[21]</sup> In the examined nonhalide containing ionic liquids, HMF formation was only observed in 1-ethyl-3-methylimidazolium ethylsulfate ([EMIm][C<sub>2</sub>H<sub>5</sub>OSO<sub>3</sub>]), choline methylsulfate ([Choline]-[MeOSO<sub>3</sub>]), 1-ethyl-3-methylimidazolium methylsulfate ([EMIm][CH<sub>3</sub>OSO<sub>3</sub>]), with a yield of 6%, suggesting that the sulfate ion was of some importance (entries 6, 7 and 12). The highest yield for the high-boiling molecular solvents was obtained in DMSO (entry 15) with 13%. All these results substantiate the crucial role of the chloride in the conversion of hexoses to HMF in ionic liquids. The reaction was also performed in ethylene glycol (entry 17) to investigate what effect a competing diol functionality had on the catalytic performance. This resulted in no conversion of glucose to HMF, which was probably caused by stronger binding of the borate to the bulk solvent compared with that of glucose. Dehydration attempts were also made using NaBF4 and sodium tetraborate as boron source in [EMIm]Cl, but resulted in HMF yields below two percent. This suggested that not only was the chloride anion vital, but also the nature of the boron source. The effect of water on the [EMIm]Cl/B(OH)<sub>3</sub> system was also tested. Up to five weight percent of water in the reaction mixture induced no detrimental effect on HMF formation, which is consistent with what previously has been reported.<sup>[10]</sup> Nevertheless, increasing the water concentration further resulted in a significant decrease in HMF yield and above 30% no HMF was formed. The fact that anhydrous or near anhydrous conditions was essential for progression of the reaction suggests that presence of water forms hydrated chloride ions which are unable to take part in the reaction, in accordance with the mechanism described by Binder and Raines.<sup>[16]</sup>

**Dehydration of fructose:** As mentioned above, fructose can be dehydrated directly to HMF in [EMIm]Cl without a catalyst.<sup>[15]</sup> To bring further clarity to whether the boric acid is actually catalyzing the direct conversion to HMF, or merely the isomerization of glucose to fructose, experiments with fructose as starting compound were needed.

In Figure 3 the results from experiments with fructose as starting material together with various boric acid concentrations are depicted (selectivity is excluded from the graph since the conversion was between 98 and 100% in all reactions). At low boric acid concentrations, that is, less than 0.2 equivalents, the obtained HMF yield was high around 80%. Increasing the boric acid content further brought about a gradual decrease in yield, which was even larger than that for glucose. This clearly indicated that boric acid first and foremost promoted the isomerization of glucose to fructose and that a higher concentration inhibited further reaction



Figure 3. Dehydration of fructose in [EMIm]Cl at 120°C with different concentrations of boric acid (0–1.96 mmol), ionic liquid (1.0 g), and fructose (100 mg, 0.56 mmol).

due to strong binding of boric acid to fructose. When the boric acid concentration was increased beyond 2.0 equivalents, the HMF yield was even less than 10%. At boric acid contents higher than what corresponds to two moles of boric acid per mole fructose one would assume the complex with the sugar bound to two borate molecules to predominate. These complexes are likely to be more stable than mono-borate complexes of fructose, something which was also observed in earlier work by Takasaki<sup>[24]</sup> when enriching fructose from glucose with glucose isomerase.

**Dehydration of various carbohydrates**: In the light of the good dehydration results obtained with glucose, we wanted to expand our boric acid–ionic liquid reaction system to the dehydration of other carbohydrates. The direct conversion of polysaccharides such as cellulose and starch is highly desirable for a cost competitive process to make HMF. In Figure 4 our results on the various sugars or polymers of glucose capable of forming HMF are summarized.



Figure 4. Dehydration of various carbohydrates in [EMIm]Cl at 120 °C with 0.5 equivalents of boric acid (1.0 g ionic liquid and 100 mg carbohydrate:  $\bigstar$  maltose,  $\bullet$  sucrose,  $\blacksquare$  starch,  $\checkmark$  cellulose.

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As expected, sucrose, consisting of a linked fructose unit and glucose unit gave the highest HMF yield of 66%. Maltose, a glucose dimer only amounted to 33% which was on the same level as cellulose and starch. Reaction times for obtaining the maximum HMF yield varied from 24 h for starch, to 8 h for cellulose and the disaccharides. For comparison, all samples in Figure 4 were dehydrated using 0.5 equivalents of boric acid. Increasing the boric acid amount to one equivalent actually resulted in a decrease in HMF yield for all carbohydrates, most likely due to the fact that glucose is formed in situ from depolymerization and present in a much lower concentration than in the glucose experiments.

Computational study: The results obtained from the experimental work warranted a supplementary study using molecular modeling to elucidate the reaction mechanism in detail. In particular, we were interested in determining how the presence of boric acid affected the relative energies of the various intermediates along the reaction pathway. From the literature the most feasible mechanisms could be narrowed down to two different pathways<sup>[28-33]</sup> where the rate-determining reaction step consists of either, a) hydride transfer from C2 to C1, or b) the formation of an ene-diol intermediate (also known as Lobryde Bruyn-van Ekenstein isomerization).<sup>[34]</sup> For the enzymatic isomerization by glucose isomerase deuterium labeling at the C2 position of glucose has pinpointed the route to go via a 1,2-hydride shift.<sup>[33]</sup> Recently, a detailed study of the chromium(II) chloride catalyzed reaction was published by Pidko et al.<sup>[35]</sup> In analogy to the enzymatic pathway the authors proposed a dinuclear chromium(II) complex which facilitates the rate-determining hydride shift from C2 to C1. An alternative mechanism involving several protonation and deprotonation steps can also be envisioned, in which a high-energy intermediate ene-diol is formed. The results from the calculations of different complexes and intermediates along the isomerization pathways are illustrated in Figure 5.

**Reaction pathway without boric acid**: Starting from β-glucopyranose (1a) protonation of the anomeric oxygen, followed by ring-opening and depronation gives the corresponding open-chain form of glucose (1b) with a relative energy of 20 kJ mol<sup>-1</sup>. The protonated open-chain glucose is a high-energy intermediate (1c, 141 kJ mol<sup>-1</sup>). An alternative deprotonation route could also be envisioned but when glucose was deprotonated in the 2-position there was a proton shift from O3 during minimization thus resulting in a structure with O3 deprotonated which is no longer en route to the ene-diol (relative energy  $28 \text{ kJmol}^{-1}$ , not shown). From the protonated form of glucose formation of the neutral ene-diol intermediate is very favorable (1d, 54 kJ mol<sup>-1</sup>). We have located the transition state for the direct hydride shift TS<sub>1b-1e</sub> but found the energy to be prohibitively high (183 kJ mol<sup>-1</sup>). From the ene-diol intermediate additional protonation can lead to formation of protonated fructose (154 kJ mol<sup>-1</sup>, not shown) although in this case

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Figure 5. Overview of the two reaction pathways for isomerization of glucose to fructose. The stabilizing effect of boric acid coordination along the reaction pathway is clear.

the deprotonated form of fructose is significantly more favored (**1e**, 82 kJ mol<sup>-1</sup>). Subsequently, the formation of the open-chain form of fructose (**1f**) can take place, which is significantly more stable than the open-chain glucose (relative energy 5 kJ mol<sup>-1</sup>). Finally, a ring-closure yields the final  $\beta$ -fructofuranose (**1g**), and it should be noted that the overall isomerization is energetically unfavored by 10.4 kJ mol<sup>-1</sup>.

**Reaction pathway with boric acid**: For each intermediate we investigated all possible complexes with boron to determine the energetically most favorable coordination site. For glucose we found the complex with boron coordinated in the 4- and 6-position to be most stable. When comparing to the isolated  $\beta$ -glucopyranose the relative energy of the 4,6boroglucopyronose (**2a'**) is -60.5 kJ mol<sup>-1</sup>. Although this comparison involves molecules of different charge the size of the molecules is large enough to allow for reasonable solvation energies. Interestingly, with boric acid present the following ring-opening is now energetically favored resulting in the generation of the open-chain glucose with boron coordinated to the 3- and 4-positions (2b). Since the ring-opening probably is faster than boric acid repositioning we have started the pathway for isomerization with the 3,4-boroglucose (2a). It is clear that the chelating effect of the boric acid results in a stabilization of the open-chain analogue where the O-B-O angles are close to the optimum for a tetrahedral geometry (107.5 and 109.3°, optimum 109.5°) compared with the closed form where they are either too small 3,4-boroglucose (104.4 and 108.8°) or too large 4,6-boroglucose (113.4 and 115.3°). Protonation of O1 is more favorable than in the absence of boric acid (2c,  $-16 \text{ kJ mol}^{-1}$ ), which is probably because it is facilitated by the negatively charged boric acid. Subsequent proton transfers results in the formation of the ene-diol intermediate which also has boron coordinated in the 3- and 4-position (2d,  $-29 \text{ kJ mol}^{-1}$ ). Also in the presence of boric acid we succeeded in locating the transition state for the hydride shift (TS<sub>2b-2f</sub>, 75 kJmol<sup>-1</sup>) but also here the energy is significantly higher than for the route involving successive proton transfers. From the enediol intermediate additional proton transfers can result in the formation of the protonated, open form of 3,4-borofructose (2e) with a relative energy of  $-2 \text{ kJ mol}^{-1}$ . Deprotonation can give a quite stable open form of 3,4-borofructose (2f,  $-53 \text{ kJ mol}^{-1}$ ), from which a final ring-closure furnishes the fructofuranose with boron coordinated in the 3- and 4-position



Scheme 3. Theoretical amount of deuterium incorporated in HMF by the two possible isomerization mechanisms.

(2g) with a relative energy of 0 kJ mol<sup>-1</sup>. Alternatively, a rearrangement of the boric acid moiety to the 2,3-position is very favorable (2g',  $-74 \text{ kJ mol}^{-1}$ ), something which has also been confirmed by NMR studies where 2g' appeared to be the most prevalent monoborate complex of fructofuranose.<sup>[21]</sup> Further on, one could imagine the structure being further stabilized as a very unreactive 2,3,4,6-diborofructose complex (3g,  $-96 \text{ kJ mol}^{-1}$ ). We believe this significant stabilization of the diboron complexes of fructose (both open and closed forms) is responsible for the observed decrease in efficiency when the boric acid/glucose ratio surpasses 1.5 (see Figure 2) and the strong inhibition when converting fructose to HMF (see Figure 3). For the route with monocoordinated boric acid the overall transformation from βglucopyranose to  $\beta$ -fructofuranose is energetically favored by 14 kJ mol<sup>-1</sup> which explains the increased rate of isomerization in the presence of boric acid. It can be seen that the effect of boron is both to lower the energy of the ene-diol intermediate relative to the glucose and also to increase the exothermicity of the overall isomerization from glucose to fructose.

Dehydration of 2-[D]-glucose: In order to finalize an overall mechanism for the entire dehydration of glucose to HMF one of the isomerization mechanisms mentioned above would have to be ruled out. By reacting glucose deuterated at the C2 position a substantially different ratio of isotopelabeled products would be obtained. An ene-diol mechanism would expel all the deuterium into the solvent and form the ketone on the C2 position of fructose. The HMF product would therefore in theory have no deuterium incorporation though some minor exchange with the solvent might be expected. In contrast, the 1,2-hydride shift mechanism would result in a fructose-species containing 100% deuteration at the C1 position. Accordingly, further reaction to HMF would theoretically result in a product mixture in which 50% deuterium would be retained on the aldehyde based on the established mechanism of HMF formation from fructose.<sup>[16,36,37]</sup> The possible reaction scenarios are illustrated in Scheme 3.

We reacted 2-[D]-glucose using the standard dehydration procedure and studied the resulting HMF by NMR and GC/ MS methods. This experiment showed that less than five percent deuterium was incorporated in the final HMF product (see Supporting Information). This result was compatible with an ene–diol mechanism and the small amount of deuterium actually incorporated could be explained by H/D exchange with the bulk. Since the reaction was performed under anhydrous conditions, a limited number of protons are available and consequently some of the deuterium atoms expelled in the first step could be available for incorporation further on during the course of reaction. Interestingly, the experiment showed that the isomerization of glucose to fructose using the borate–ionic liquid system proceeded via a different mechanism than that reported for the enzyme glucose isomerase<sup>[33]</sup> which reacts via a 1,2-hydrideshift mechanism.

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Based on this experiment, the results from the DFT calculations and previous work,<sup>[16,36,37]</sup> we could propose a putative mechanism for the complete reaction of glucose to HMF promoted by boric acid in imidazolium chlorides. As shown in Scheme 4, the glucose-borate complex 2a gives a favorable transition to 2g via the ene-diol intermediate 2d. When 2g loses its borate and forms free fructose it can proceed by two different pathways: either react further to HMF (pathway a) or form the more stable 2,3-borate complex 2g' (pathway b). The energy of 2g is higher than that of 2g' because the boric acid is bound trans to the diol functionality of fructose, whereas it in the latter case is bound cis. Evidently, the first step of fructose dehydration to HMF is made impossible in complex 2g' since the oxygen on C2 is bound to boron and consequently water cannot be eliminated. Once 2g' is formed it can in principle react further with another borate to form the diborate complex 3g, which is even more stable than 2g'. This would explain the lower HMF yield at a boric acid content above 1.0 equivalent mentioned in the previous section. When the reaction is complete the boric acid is bound up as these stable borate esters.

The mechanism of HMF formation from fructose has been debated over the years, where both a pathway with cyclic intermediates<sup>[36-40]</sup> as well as an open-chain mechanism<sup>[41-45]</sup> have been proposed. Through extensive experimental work Antal et al.<sup>[36]</sup> concluded that the cyclic mechanism is the most plausible of the two and the cyclic intermediate **8** was recently identified through an NMR study.<sup>[37]</sup>





Scheme 4. Putative mechanism for the dehydration of glucose to HMF in imidazolium chlorides with boric acid as promoter.

In the mechanism we have depicted the chloride ion acting as a nucleophile, but it could in principal also be acting as a base as proposed by Binder and Raines.<sup>[16]</sup>

#### Conclusion

The boric acid–ionic liquid reaction system presented here is the first metal-free system that catalyzes the conversion of glucose and its polymeric counterparts to HMF. Even though the yields do not surmount what has been achieved so far with chromium catalysts,<sup>[15]</sup> our results introduce a new class of promoter not based on transition metals, which could prove more practical for scaled up applications where utilization of metals might be questionable from an environmental viewpoint.

The main obstacle with the boric acid-ionic liquid system is the formation of stronger fructose-boric acid complexes such as 2g' which in due course stops the isomerization by binding up boric acid and at the same time blocking the elimination of water in the first step of the conversion to HMF. The idea of adding a competitor for fructose as a complexation agent falls on the fact that glucose forms weaker complexes than fructose. Such a complexation agent would be an even stronger competitor to glucose and would most likely have the consequence of inhibiting the isomerization of glucose to fructose, something which was evident when performing the reaction in ethylene glycol where no HMF was formed. The challenge for the future development of this system is therefore to find a catalyst for the dehydration of fructose in [EMIm]Cl which does not have a detrimental impact on the boric acid promoted isomerization of glucose to fructose. This could be achieved by screening the reaction together with different catalysts known for catalyzing the dehydration of fructose in ionic liquids. The additional catalyst must naturally meet the criteria of being green and sustainable to obtain a system that would be advantageous to the previous transition metal systems. An alternative to this approach could imply boric acid derivatives which possibly display a different behavior towards isomerization.

Another vital aspect of the introduced reaction system is the ionic liquid. The structure of the cation has evidently a momentous impact on the

HMF yield. As mentioned in the previous section, there is no clear reactivity pattern regarding the chain length of the alkyl group on the alkylmethylimidazolium ion. Extended screening of other cations might therefore result in the discovery of a cation that would enhance the HMF yield even more or give a rational explanation for the superior performance of the 1-ethyl-3-methylimidazolium ion.

We believe that with extensive experimental work and modeling on different boric acid based catalytic systems the yields of HMF could be enhanced and be a strong competitor to other catalysts in a future biopetrochemical industry.

#### **Experimental Section**

Materials and equipment: All chemicals were used as received. p-glucose (99.5%), 2-[D]-D-glucose (98 atom % D), dimethyl sulfoxide (98%), cellulose (powder, ca 20 micron), dimethylformamide (99%), α-butyrolactone (98%) and *N*-methyl-2-pyrrolidone (99%) were purchased from Aldrich. Boric acid (puriss), starch (p.a.) and D-fructose (puriss) were purchased from Riedel-de Haën. Ethylene glycol (normapur) and D-maltose (p.a.) were purchased from Prolabo. Sucrose (99%) was purchased from Alfa Aesar. [EMIm][N(CN)<sub>2</sub>] (98%), [choline][CH<sub>3</sub>OSO<sub>3</sub>] (98%) and [EMIm][C<sub>2</sub>H<sub>3</sub>OSO<sub>3</sub>] (98%) were purchased from BASF (>95%). The dehydration experiments were performed under nitrogen atmosphere using a Radley Carousel 12 Plus Basic System with temperature control (+/ -1°C). All samples were analyzed by HPLC (Agilent 1200 series, Bio-Rad Aminex HPX-87 H, 300 mm × 7.8 mm pre-packed column, 0.005 M H<sub>2</sub>SO<sub>4</sub> mobile phase, 60°C, 0.6 mLmin<sup>-1</sup>). The HMF yields and selectivi-

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ties were based on conversion of glucose and confirmed by calibration of standard solutions of the products and reactants involved.

**General dehydration procedure:** A 40 mL reaction tube was charged with ionic liquid (1 g) and boric acid (34.6 mg, 0.56 mmol) and heated at 100 °C for 1 h. Glucose (100 mg, 0.56 mmol) or different carbohydrate (0.56 mmol) was then added and the solution stirred for 3 h at 120 °C. After reaction the reaction tube was cooled in an ice bath and water (5 mL) added. The solids were filtered off and the filtrate analyzed by HPLC. Alternatively filtrate was extracted with ethyl acetate ( $3 \times 30$  mL) and the solvent then removed in vacuo.

Computational method: Density functional theory (DFT) in combination with the B3LYP functional<sup>[46-48]</sup> as incorporated in Jaguar version 7.6 from Schrodinger Inc.<sup>[49]</sup> was used for the calculations. In the current study we employed the LACVP\* basis set in Jaguar which uses the Hay-Wadt small-core ECP and basis set for boron<sup>[50]</sup> and the 6-31G\* basis set for the remaining elements. Solvation energies were obtained using the PB-SCRF solvation model<sup>[51,52]</sup> employing parameters suitable for dichloromethane (dielectric constant 9.08 and probe radius 2.33237 Å). In this model the solvent is described as a continuum, where the molecule is put into a reaction field consisting of surface charges on a solvent accessible surface constructed using a hypothetical spherical solvent probe molecule with the indicated radius.<sup>[53]</sup> The wavefunction and the reaction field charges are solved iteratively until self-consistency is reached. Physical data on ionic liquids in the literature are still scarce, for example it was not possible to find a dielectric constant for [EMIm]Cl. Thus, we have in the current study used parameters suitable for dichloromethane since its dielectric constant ( $\epsilon = 7.26$ ) was close to the ones reported of several 1-ethyl-3-methylimidazolium based ionic liquids.[54,55]

In previous projects<sup>[56,57]</sup> we have found that energies calculated with the continuum solvent model gives a fair correspondence with experimental ratios, but for a quantitative agreement we frequently also need to account for the vibrational component of the free energy. The free energy adjustment was then added to the corresponding energy determined in solvent, to arrive at a composite free energy that is our best estimate of the free energy in solvent.

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