Direct conversion of glucose to 5-(hydroxymethyl)furfural in ionic liquids with lanthanide catalysts

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The direct conversion of glucose to 5-(hydroxymethyl)furfural (HMF) in ionic liquids with lanthanide catalysts was examined in search of a possibly more environmentally feasible process not involving chromium. The highest HMF yield was obtained with ytterbium chloride or triflate together with alkylimidazolium chlorides. Notably, a higher reactivity was observed when the hydrophobicity of the imidazolium cation was increased, in contrast to analogous chromium catalyst systems. This indicates a different reaction mechanism for the lanthanides than for the chromium catalyst systems.

Introduction

In recent years, the search for alternatives to today's platform chemicals derived from fossil sources has intensified. One molecule under particular scrutiny has been 5-(hydroxymethyl)furfural (HMF), which is expected to become an important precursor to fuels, solvents and polymers in the chemical infrastructure.¹⁻³

HMF is formed by dehydration of hexoses under elevated temperature (Scheme 1, exemplified for glucose). The mechanism of the dehydration of hexoses has been subject of some debate, and proposals include both a mechanism consisting of only cyclic intermediates⁴⁻⁸ as well as an open-chain mechanism.⁹⁻¹³



Scheme 1 Dehydration of glucose to HMF.

The dehydration of fructose is quite facile – even in the absence of catalyst – in high-boiling solvents such as DMSO, DMF and DMA,^{14,15} whereas glucose requires a special catalyst for the formation of HMF.¹⁶⁻¹⁹ However, fructose is derived from glucose in a process that only yields about 50% of fructose and involves a chromatographic step in order to be purified.²⁰ Consequently, in order to find an economical and environmentally feasible industrial process for the production of HMF, an efficient direct conversion from glucose would be most beneficial.

In the last five years or so, interesting results have been presented on the dehydration of hexoses by the use of ionic liquids. As in the case of high-boiling organic solvents, ionic liquids have proven to be efficient media for converting fructose to HMF.²¹⁻²⁵ More importantly, very good results have been shown for the direct conversion of glucose to HMF (up to 70% yield) in 1-ethyl-3-methylimidazolium chloride ([EMIm]Cl) with a catalytic amount of chromium(II) chloride.¹⁶ In the proposed mechanism, a complex between ionic liquid and CrCl₂ interacts with the open chain of glucose, leading both to isomerization to fructose and direct conversion to HMF (Scheme 2).

An even higher yield of HMF was obtained when using chromium(II) or chromium(III) chloride complexed with sterically hindered carbenes.¹⁷ Comparable yields were also shown using a large surplus of metal halides in DMA together with chromium(II/III) chloride.¹⁸ Here a detailed mechanism of the actual role of the halide in the dehydration was also proposed. In this mechanism, fructose initially loses one water molecule, and the nucleophilic halide is then added to the anomeric carbon. The intermediate formed is then deprotonated to an enolic species, which is subsequently dehydrated twice to form HMF. Alternatively, the halide acts as a base in the second step and generates the enolic intermediate by deprotonation (Scheme 3).

Apart from chromium chloride, there are no reports of equally efficient catalysts for the direct conversion of glucose to HMF. A very recent publication showed, however, that a dual-function catalyst composed of sulfated zirconia on alumina support could convert glucose directly to HMF with a moderate yield, presumably *via* glucose isomerization to fructose followed by dehydration.¹⁹ Furthermore, lanthanide chlorides have been shown to have a catalytic effect on glucose dehydration in supercritical water.²⁶ Notably, no leuvulinic acid or formic acid was observed here, as is normally the case when exposing HMF to aqueous acidic conditions.²⁷ In the study, kinetic and spectroscopic experiments suggested weak interaction between lanthanide and saccharide, resulting in higher reaction rates for smaller, less hydrated and heavier lanthanide ions.^{28,29}

Our objective in this work was to combine in particular the heavier lanthanide catalysts with ionic liquids and to investigate its catalytic effect on the direct conversion of glucose to HMF. Thus, imidazolium-based ionic liquids were used as solvents together with various lanthanide chloride catalysts in

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Scheme 2 Possible mechanism for the chromium-catalyzed dehydration of glucose to HMF in ionic liquids.¹⁶



Scheme 3 Proposed mechanism for the dehydration of fructose to HMF with halides.¹⁸

Table 1 HMF degradation in ionic liquids4

Ionic liquid	Conversion of HMF (%)		
[MIm]Cl	9		
[EMIm]Cl	3		
[BMIm]Cl	29		
[HMIm]Cl	9		
[OMIm]Cl	11		
[EMIm]OAc	> 99		
[BMIm]OAc	> 99		
[Choline][dmp] ^b	6		
[MIm][HSO4]	69		
$[EMIm][N(CN)_2]$	59		
[EMIm][C ₂ H ₃ OSO ₃]	9		
[EMIm][AlCl ₄]	77		

^a Reaction conditions: 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose, 100 °C, 8 h. *^b* dmp = dimethyl phosphate.

the temperature range 120–200 °C. Additionally, the investigation was expanded to include even stronger Lewis acids such as ytterbium triflate.

Results and discussion

We initially screened the stability of HMF in several ionic liquids at elevated temperature to make sure that the ionic liquid used was not detrimental to the desired product. As seen from the data in Table 1, all ionic liquids induced some degradation of HMF during the stability tests. The acidic and basic ionic liquids proved to promote highest degree of degradation, whereas the imidazolium chlorides, [EMIm][$C_2H_5OSO_3$] and [Choline][dmp] were the most benign.

On the basis of the initial experiments, we further discovered that there was no HMF formed from glucose in ionic liquids that did not have chloride or other halides as anion. This is in agreement with the mechanism proposed by Binder and Raines,¹⁸ where the chloride acts as a nucleophile and promotes the dehydration of the furanose fructose. Consequently, our study focused on the alkylimidazolium chlorides as solvents. [BMIm]Cl or [EMIm]Cl converted only fructose to HMF without additives (as also reported by Zhao *et al.*¹⁶) and not glucose. The addition of lanthanide chlorides, on the other hand, revealed a catalytic effect on glucose conversion (but not on fructose conversion), even though temperatures above 140 °C were required to avoid slow reactions and negligible yields. Furthermore, methylimidazolium chloride, which previously has given an excellent conversion of fructose to HMF,²³ gave less than one percent HMF from glucose with any lanthanide.

In the experiments with lanthanides (Table 2), cerium had very little catalytic effect in both [BMIm]Cl and [EMIm]Cl, whereas the other lanthanides showed quite different behaviours depending on the liquid. In the case of [EMIm]Cl, the reactivity for the lanthanide chlorides was the highest for promethium and then decreased almost linearly through the heavy lanthanides to YbCl₃. Moreover, when using the more Lewis-acidic ytterbium

Table 2 Lanthanide-catalyzed dehydration of glucose in [EMIm]Cl and [BMIm]Cl $^{\alpha}$

	[EMIm]Cl		[BMIm]Cl	
Catalyst	Yield (%)	Selectivity (%)	Yield (%)	Selectivity (%)
CeCl ₃	3	3	3	4
PrCl ₃	13	27	7	22
NdCl ₃	12	24	8	23
DyCl ₃	10	19	10	23
YbCl ₃	5	7	12	15
Yb(OTf) ₃	10	16	24	37

^a Reaction conditions: 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose, 0.056 mmol catalyst, 140 °C, 6 h. triflate, a comparable yield to that of dysprosium chloride was obtained.

In [BMIm]Cl a completely different pattern was observed. Here the yield increased gradually from CeCl₃ to YbCl₃. This is consistent with the earlier relative catalytic effect found in supercritical water.^{26,28,29} Furthermore, ytterbium chloride and ytterbium triflate gave significantly higher yields in [BMIm]Cl than in [EMIm]Cl. This is the opposite of what has been shown earlier using chromium catalysts, where the yields were markedly better in [EMIm]Cl,¹⁶ thus clearly suggesting different catalyst– ionic liquid interaction in the systems.

Increasing the catalyst concentration of $YbCl_3$ in [EMIm]Cl, up to as much as 30 mol%, did not reveal any improvement in HMF yield. In contrast, the amount of catalyst had a significant effect on the HMF yield in [BMIm]Cl, thus further signifying differences between the catalytic systems (Fig. 1).



Fig. 1 Dehydration of glucose in [EMIm]Cl and [BMIm]Cl at $140 \,^{\circ}$ C for 6 h with different amount of YbCl₃ catalyst. The reaction contained 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose and 16 mg (0.056 mmol), 32 mg (0.112 mmol) and 48 mg (0.168 mmol) YbCl₃, respectively.

During dehydration in [BMIm]Cl, the selectivity towards HMF reached a maximum already after 10 min and a maximum yield after 30 min. The HMF was then slowly degraded due to the high temperature (Fig. 2). At an even higher temperature of 200 °C the yield was slightly increased, but at the expense of an even faster degradation of the product. In this case maximum yield was obtained after five minutes, and HMF was completely degraded after two hours (Fig. 3). All reactions formed substantial amounts of humins, but no other by-products were detected, as the essential anhydrous conditions (small amount of water is formed upon dehydration) prevented rehydration of HMF into leuvulinic acid and formic acid.

When it comes to finding an explanation why a longer alkyl chain on the imidazolium ring gave higher reaction rates for YbCl₃ and Yb(OTf)₃ catalysts, a possible reason could be related to ion pairing in the solvent. Cations with more hydrophobic character would be expected to have a weaker association with the chloride ion, which in turn would become more reactive. Earlier work has already shown that rates of reactions in ionic liquids involving halides are highly dependent on the nature of the cation.³⁰ This was also one of the rationales in the work of



Fig. 2 Dehydration of glucose in [BMIm]Cl catalyzed by YbCl₃ at 160 $^{\circ}$ C as a function of the reaction time. The reaction contained 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose and 16 mg (0.056 mmol) YbCl₃.



Fig. 3 Dehydration of glucose in [BMIm]Cl catalyzed by YbCl₃ at 160 $^{\circ}$ C and 200 $^{\circ}$ C as a function of time. Both reactions contained 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose and 16 mg (0.056 mmol) YbCl₃.

Binder and Raines,¹⁸ who combined LiCl with DMA in order to produce weakly ion-paired chloride ions for sugar dehydration. In order to examine the effect of ion-pairing more closely, additional experiments with even longer alkyl chains, such as 1-hexyl-3-methylimidazolium chloride ([HMIm]Cl) and 1-octyl-3-methylimidazolium chloride ([OMIm]Cl), were performed. In these experiments, a faster conversion and a small increase in yield could actually be seen when using [HMIm]Cl or [OMIm]Cl as solvents (Fig. 4), even though it was less pronounced than the difference between [EMIm]Cl and [BMIm]Cl. The decrease in selectivity for [HMIm]Cl and [OMIm]Cl compared to [BMIm]Cl could be a result of the faster formation of humins.

Conclusions

We have shown that lanthanides catalyze the conversion of glucose to HMF in dialkylimidazolium chlorides. The strongest Lewis acids, YbCl₃ and Yb(OTf)₃, gave the highest yields, even



Fig. 4 Dehydration of glucose in [EMIm]Cl, [BMIm]Cl, [HMIm]Cl and [OMIm]Cl at 160 $^{\circ}$ C for 1 h. All reactions contained 1.0 g ionic liquid, 100 mg (0.56 mmol) glucose and 16 mg (0.056 mmol) YbCl₃.

though these were moderate (24%) compared to $CrCl_2$ (70%).¹⁶ Our results also suggest that the mechanism of the reaction might be different to that of chromium-catalyzed dehydration of glucose.

In the chromium system, highest yields are obtained with [EMIm]Cl, whereas the yield decreases with more hydrophobic imidazolium cations.¹⁶ In this reaction, chromium(II) chloride is believed to form a complex with the ionic liquid and then associate with the open chain form of glucose.¹⁶ Ytterbium showed a different reaction pattern, whereby the yield increased as the hydrophobic character of the imidazolium ring increased. We believe that the increase in reaction rates are due to weaker ion pairing between the chloride and imidazolium cation, making this more reactive in the dehydration mechanism. Furthermore, ytterbium could be less prone to form complexes with the imidazolium chlorides, which would explain the difference in reactivity compared to chromium.

Further studies on the actual complexation between lanthanide chlorides and imidazolium chlorides are needed to clarify the exact reaction pattern with glucose. Modeling of the various structures and intermediates together with the metals could also give new insights into the mechanism. Combined, this information could provide valuable directions on how to improve the lanthanide–ionic liquid systems to become competitive with present chromium systems.

Experimental

Materials and apparatus

Glucose (99.5%), 1-hexyl-3-methylimidazolium chloride (98%), 1-octyl-3-methylimidazolium chloride (98%) and ytterbium triflate (99%) were purchased from Aldrich. [EMIm][N(CN)₂] (98%), [Choline][dmp] (98%) and [EMIm][C₂H₅OSO₃] (98%) were purchased from Solvent Innovation. All other ionic liquids were obtained from BASF (>95%). Lanthanide chlorides (p.a.) were purchased from Rare Earth Ltd. All experiments were performed under nitrogen atmosphere using a Radley Carousel 12 Plus Basic System.

Dehydration reactions

A 40 mL reaction tube was charged with ionic liquid (1 g) and lanthanide(III) chloride (0.056 mmol) and heated at 100 °C for 1 h. Glucose (100 mg, 0.56 mmol) was then added and the solution stirred for 3 h at 140 °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 (Agilent 1200 series, Bio-Rad Aminex HPX-87H, 300 mm × 7.8 mm pre-packed column, 0.005 M H₂SO₄ mobile phase, 60 °C, 0.6 mL min⁻¹).

Definitions of yield and selectivity

The yields and selectivities were based on conversion of glucose and confirmed by calibration of standard solutions of the products and reactants involved. With a known molar amount of all components, the conversion, yield and selectivity were calculated from the equations below:

Glucose conversion =
$$\left(1 - \frac{\text{Amount of glucose}}{\text{Starting amount of glucose}}\right) \times 100\%$$
(1)

Yield of HMF =
$$\frac{\text{Amount of HMF}}{\text{Starting amount of glucose}} \times 100\%$$
 (2)

Selectivity of HMF =
$$\frac{\text{Yield of HMF}}{\text{Glucose conversion}} \times 100\%$$
 (3)

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