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Highly Selective and Near-Quantitative Conversion of Fructose to 5-Hydroxymethylfurfural Using Mildly Acidic Ionic Liquids

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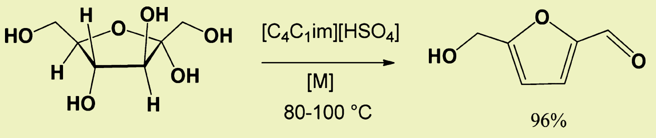
S *Supporting Information*



ABSTRACT: The room-temperature ionic liquid, $[C_4C_1im][HSO_4]$, provides a multi-faceted medium in which to convert fructose to the versatile chemical building block, 5-hydroxymethylfurfural (HMF). A range of metal salts have been investigated in order to establish some of the properties required for the optimization of this process. This has led to almost quantitative conversion of fructose to 5-HMF in a system that is both selective for the desired product, less energy intensive, and more environmentally benign than the commercial process.

KEYWORDS: *Biorenewables, Platform chemicals, Catalysis, Biorefinery, Lignocelluloses, Cellulose*

INTRODUCTION

Conversion of biomass to useful platform chemicals is a vital aspect in the replacement of petroleum-based feedstocks with sustainable alternatives.[1,2] It is likely that lignocellulosic biomass will be heavily used as a feedstock for future large-scale biorefineries as lignocellulose is distributed widely and can be grown on a billion ton scale. This offers opportunities for reducing the carbon footprint and diversifying fuel and material supplies. A major driving force behind this is the fact that the fuels and materials derived from such biomass are potentially "carbon neutral"; however, the current production of lignocellulosic biomass requires extensive, costly, and environmentally harmful pretreatment.[3] Ionic liquids have provided a far more benign method of separating cellulose, and this process is critical in the development of the functionalization of the resultant biopolymer.[4−9]

In 2004, the U.S. Department of Energy identified 5-hydroxymethylfurfural (HMF) as a key platform chemical that can be the precursor to both chemical feedstocks and potential fuels, such as 2,5-dimethylfuran (40% higher energy density than ethanol).[10] The versatility of this synthetic building block is now widely recognized, leading to an increase in transformations using HMF being reported.[11,12]

In 2007, pioneering work by Zhao illustrated that an ionic liquid (IL), $[C_4C_1im]Cl$, could be used in combination with various metal salts to break down fructose to HMF in 70% yield at 120 °C over the course of 3 h.[13] Chromium salts were found to provide the highest conversions, and this has been confirmed by subsequent work in closely related studies.[14−17] While the "green" credentials of ILs can be overstated,[19] they have environmental benefits such as their reusability and negligible vapor pressure. More importantly, they offer a vast improvement over the currently used process, which employs highly acidic aqueous solutions with all the attendant safety, environmental, and containment issues.[3]

Over the last five years, a plethora of reports have appeared in which ILs have been employed to dissolve and breakdown sugars (fructose, sucrose, cellulose, etc.) derived from biomass.[14−18] The majority of these have followed the original research in using imidazolium chloride ionic liquids, such as $[C_4C_1im]Cl$ and $[C_2C_1im]Cl$ (Figure 1). However, an overview of the catalytic literature using ILs illustrates that the presence of chloride (an excellent ligand) as part of the solvent system (and hence in huge concentration) in many cases inhibits the ability of transition metals to generate a vacant site in order to perform catalytically.[20]

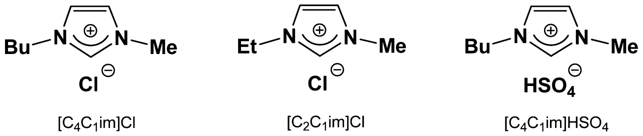


Figure 1. Ionic liquids used in the dissolution and breakdown of biomass.

One of the many strengths of ionic liquids is the ability to tune their physical and chemical properties to provide the best medium for a specific transformation. The breakdown of fructose is known to be favored by acidic conditions so the IL, $[C_4C_1im][HSO_4]$, was chosen as a suitable candidate for this transformation due to the mildly acidic proton located on the anion. Dilute acids have been reported to accelerate fructose conversion to HMF in both water[21] and ILs.[16] In addition, the absence of a chloride counterion and the presence of only a weakly coordinating hydrogensulfate anion were also important factors in the choice of this solvent.

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The coordinating ability of the IL anion was demonstrated to be a significant factor by Hu et al. when they reported the conversion of glucose to HMF using a Lewis acid ($SnCl_4$) in ILs with a range of anionic species, while the cation used in all cases was $[C_4C_1im]^+$.[14] The best results were obtained when the anion was $[BF_4]^-$, while lower yields were obtained with the anions of ILs Cl^-, Tf_2N^-, TFA^-, $Trif^-$, and $Sacc^-$, all of which have the ability to coordinate (Figure 2).[14] The coordinating anions would have stronger interactions with the metal center, which would compete with the interaction between sugar and catalyst and thus inhibit the formation of HMF.[14]

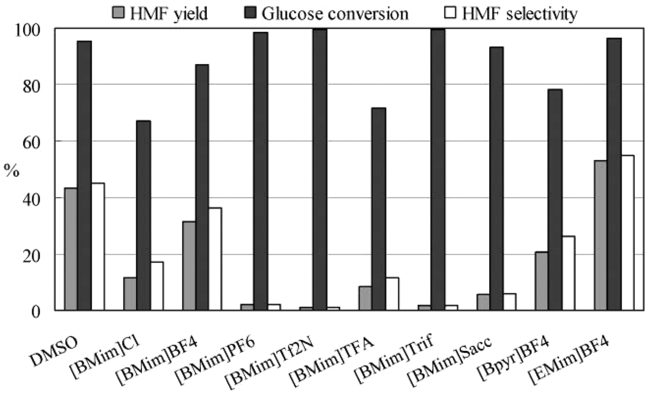


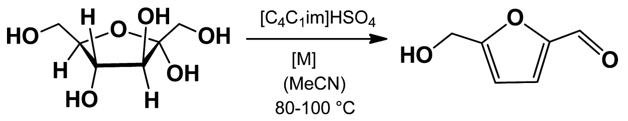
Figure 2. HMF yields in various ILs and DMSO. Reprinted with permission from ref 14.

It was proposed that a suitable medium should have strong solvent power for sugar dissolution but low coordination ability to a metal center.

CATALYTIC STUDIES

In order to ascertain the conversion of fructose to HMF without any additives, the sugar was heated at 80 °C in $[C_4C_1im][HSO_4]$ in air (Scheme 1), and the reaction was monitored by removing aliquots after 0.5, 1, 3, and 24 h. The conversion was determined by ^1H NMR analysis (methodology confirmed by HPLC comparison). This conversion is performed industrially in acidic aqueous media, so it was not a surprise to see some HMF being formed after 0.5 h (11%), rising to 38% conversion after 24 h.

Scheme 1. Fructose Conversion to 5-Hydroxymethylfurfural (HMF)



Chromium salts have been shown to be particularly active in catalyzing this transformation, and so 7 mol % chromium(III) chloride hexahydrate was introduced, maintaining the same conditions as before. This resulted in substantial conversion after only 0.5 h (54%), rising to 80% after 3 h, which was also the final conversion after 24 h (Table 1, entry 2). This represented an improvement on the results obtained using $[C_4C_1im]Cl$ under the same conditions.[13] Using the hydrated salt, $CrCl_3{\cdot}6H_2O$, introduced a small amount of water into the system, so anhydrous $CrCl_3$ was investigated and found to result in a much slower reaction (Table 1, entry 4). However, when 15% water (v/v with the IL) was used, a higher overall conversion (at 80 °C) of 85% was observed (Table 1, entry 1). The addition of 50% water slowed the conversion substantially, although the addition of other cosolvents, such as acetonitrile, did not lead to the same observed sluggishness. Anhydrous chromium(II) chloride was also found to be a reasonable catalyst for the formation of HMF, resulting in 74% conversion after 24 h. This is higher than anhydrous chromium(III) chloride, which performed very poorly in our system (only 6% conversion in the first 0.5 h, although increasing to 65% after 24 h). The anhydrous chromium(III) chloride salt did not dissolve in the anhydrous IL; only after approximately 1 h did the catalyst fully dissolve. We believe that the water yielded by the dehydration reaction was necessary to hydrate the chromium(III) chloride enough for it to become soluble, and the catalyst performance therefore suffered until this condition was met.

While other group 6 transition metal (Mo, W) salts led to acceptable conversions after 24 h, none tested here matched the chromium salts. This has been remarked upon in many reports and has been the subject of a combined experimental and computational study.[15] Metal salts from later in the transition series fared even worse. This led us to ponder whether the activity observed was an effect of Lewis acidity[14] and the general 'hard' nature of the metal compounds, as salts of higher oxidation state metals generally performed better against comparable related species. However, the strongly Lewis acidic lanthanide triflate ions showed unremarkable activity under the conditions tested (Table 1).

Once variation of the duration of the reaction and the nature of the catalyst had been investigated, the effect of raising the temperature to 100 °C was analyzed. Maintaining the other variables constant, this change led not only to the highest conversions observed in this study (96% after 3 h) but also to over 87% after only 1 h (Table 2, entry 20). At higher temperatures, high conversions were observed after only 0.5 h (87%, Table 2, entry 21). However, under these conditions, the formation of humins becomes an issue, leading to darkening of the ionic liquid and a lower conversion after 3 h than at 100 °C. The addition of acetonitrile has previously been shown to limit this process.[22] Conducting the reaction at 80 °C with 15% acetonitrile (v/v with the IL) leads to equally high yields (Table 2, entry 6). There are several possible explanations for this result. As these ILs are highly viscous, acetonitrile may simply be acting as a diluent, reducing the viscosity of the solution, thereby enabling faster mass transport. Acetonitrile also has a fairly high dielectric constant (about 36), which could affect the dissociation ability of the acidic IL solvent. In order to test this effect, we measured Hammett acidity values using the technique described by Fărcaşiu[23] for the IL with and without added acetonitrile. As Hammett acidity is intended as an extended pH scale, lower values indicate a more strongly acidic medium. Our measured value for pure $[C_4C_1im][HSO_4]$ (H_0 = 1.96) was noticeably lowered by the addition of 15% acetonitrile (H_0 = 1.12). This suggests that adding acetonitrile to the IL enhances the ability of the $[HSO_4]$ anion to protonate the substrate, increasing the acidity of the solvent medium. It should be noted that the Cr(II) chloride system also benefitted from higher temperature (conversion to 5-HMF increased from 70% at 80 °C to 87% at 100 °C after 3 h), though the effect of acetonitrile on this system was negligible.

Adding 50% water (v/v) to the chromium(III) chloride system was found to decrease the final conversion after 24 h

Table 1. Fructose Conversion to HMF[a]

entry	metal salt	conversion to HMF (%) 0.5 h	1 h	3 h	24 h
1	$CrCl_3 \cdot 6H_2O$ + 15% H_2O	11	30	65	85
2	$CrCl_3 \cdot 6H_2O$	54	60	80	80
3	$CrCl_2$ (anhydrous)	48	54	70	74
4	$CrCl_3$ (anhydrous)	6	11	32	65
5	$CrCl_3 \cdot 6H_2O$ + 50% H_2O	5	5	15	65
6	$CrCl_3 \cdot 6H_2O$ + 15% MeCN	54	60	80	65
7	WCl_4	49	54	60	65
8	$MoCl_3$	33	49	54	60
9	$Y(OTf)_3$	27	38	49	60
10	$LaCl_3$	11	22	38	60
11	$RuCl_3$	27	37	48	59
12	K_2PtCl_4	22	32	42	58
13	$NiCl_2$	22	37	41	54
14	$RhCl_3$	16	26	42	53
15	$La(OTf)_3$	22	33	49	49
16	$Sc(OTf)_3$	27	38	43	49
17	no catalyst + 15% water	5	5	11	44
18	$ZnCl_2$	16	21	32	38
19	no catalyst	11	21	27	38

[a]7 mol % catalyst loading, 80 °C. Table ordered in terms of conversion after 24 h. Entries numbered sequentially across both tables.

Table 2. Fructose Conversion to HMF[a]

entry	metal salt	temp. (°C)	conversion to HMF (%) 0.5 h	1 h	3 h	24 h
20	$CrCl_3 \cdot 6H_2O$	100	69	87	96	–
21	$CrCl_3 \cdot 6H_2O$	120	87	87	89	–
22	no catalyst	100	51	69	69	–
23	no catalyst	120	71	71	78	–
24	$CrCl_2$ (anhydrous)	100	69	80	87	–
25	$CrCl_2$ (anhydrous) + 15% MeCN	100	64	73	80	–
3	$CrCl_2$ (anhydrous)	80	48	54	70	74
2	$CrCl_3 \cdot 6H_2O$	80	54	60	80	80
6	$CrCl_3 \cdot 6H_2O$ + 15% MeCN	80	54	60	80	65
1	$CrCl_3 \cdot 6H_2O$ + 15% H_2O	80	11	30	65	85
5	$CrCl_3 \cdot 6H_2O$ + 50% H_2O	80	5	5	15	65

[a]7 mol % catalyst loading. Table ordered in terms of conversion after 3 h. Entries numbered sequentially across both tables.

substantially (Table 1, entries 1 and 5). Adding such a large amount of water is likely to dissociate any metal–substrate complexes and will also solvate the sugar substrates, likely retarding catalytic effects. Water will also stabilize the Cr(III) complex ions in solution, possibly reducing impetus for substrate binding. This same principle would lead to the formation of dehydrated intermediates being less favorable. As water is eliminated during this reaction, the water byproduct (or water from a "wet" IL) is not likely to result in ligation to the Cr due to the solvation of the IL anion taking precedence (it is present in much higher concentration, although it is a poorer reaction partner).[19]

There are several possible reasons for the high performance of the IL, $[C_4C_1im][HSO_4]$, as a solvent for HMF formation. The mildly acidic $[HSO_4]$ proton (pK_a = 1.7) is likely to be acting as a co-catalyst for this reaction as well as acting as the solvent (and thus present in large excess). However, most strong acids promote over-dehydration of sugars to levulinic acid and formic acid, in both water[21] and ILs,[16] even in catalytic amounts. A large excess of a weaker acid appears to be a compromise between acid strength and concentration that optimizes the formation of the dehydration intermediate HMF without promoting either levulinic acid or humin formation (as observed on adding concentrated H_2SO_4 to this system). The $[HSO_4]$ anion itself is also a mild hydrogen bond acceptor, compared to the much more basic chloride anion.[24] It is also less likely to compete with the substrate for the coordination sites at the metal catalyst, being a weakly coordinating anion. This result is in stark contrast to that found by Qi et al.,[25] where a sulfonated zirconia catalyst was much more selective in $[C_4C_1im]Cl$ (89% HMF) than $[C_4C_1im][HSO_4]$ (43%), likely due to the overacidity of the combined catalyst and solvent in the latter system.

CONCLUSIONS

In conclusion, a room-temperature ionic liquid (IL) has been selected on the basis of the combination of the properties it provides as a medium for almost quantitative conversion of fructose to 5-hydroxymethylfurfural (HMF) in the presence of a low loading of chromium(III) chloride. Previous to this report, the transformation of sugars to HMF in ILs had been carried out predominantly in dialkylimidazolium chloride salts.

However, careful tailoring of the IL properties beyond the standard chloride salts improves the performance of the system substantially. The best condition that we report is a 96% yield of 5-HMF in 3 h at 100 °C. The selectivity of this process is indicated by the fact that no trace of levulinic acid or formic acid was encountered after conversion of fructose. This combination of the well-established advantages of ILs (negligible vapor pressure, recyclability) with a weakly acidic and weakly coordinating medium provides an excellent environment for selective catalysis by a low toxicity metal species in only a few hours. Because HMF has recently become the starting point for scaled up production of "green" beverage packaging,[26] the optimization of high yielding routes to this platform chemical has never been more important or timely.

ASSOCIATED CONTENT

Supporting Information

Synthesis and preparation of ionic liquids and catalytic procedure for HMF formation. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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