Direct Catalytic Conversion of Cellulose to 5-Hydroxymethylfurfural Using Ionic Liquids

Sanan Eminov [1,2], Paraskevi Filippousi [2], Agnieszka Brandt [2], James D. E. T. Wilton-Ely [1,*] and Jason P. Hallett [2,*]

[1] Department of Chemistry, Imperial College London, London SW7 2AZ, UK; sanan.eminov10@imperial.ac.uk
[2] Department of Chemical Engineering, Imperial College London, London SW7 2AZ, UK;
    p.filippousi12@imperial.ac.uk (P.F.); a.brandt07@imperial.ac.uk (A.B.)
* Correspondences: j.wilton-ely@imperial.ac.uk (J.D.E.T.W.-E.); j.hallett@imperial.ac.uk (J.P.H.)

Abstract: Cellulose is the single largest component of lignocellulosic biomass and is an attractive feedstock for a wide variety of renewable platform chemicals and biofuels, providing an alternative to petrochemicals and petrofuels. This potential is currently limited by the existing methods of transforming this poorly soluble polymer into useful chemical building blocks, such as 5-hydroxymethylfurfural (HMF). Ionic liquids have been used successfully to separate cellulose from the other components of lignocellulosic biomass and so the use of the same medium for the challenging transformation of cellulose into HMF would be highly attractive for the development of the biorefinery concept. In this report, ionic liquids based on 1-butyl-3-methylimidazolium cations $[C_4C_1im]^+$ with Lewis basic ($X = Cl^-$) and Brønsted acidic ($X = HSO_4^-$) anions were used to investigate the direct catalytic transformation of cellulose to HMF. Variables probed included the composition of the ionic liquid medium, the metal catalyst, and the reaction conditions (temperature, substrate concentration). Lowering the cellulose loading and optimising the temperature achieved a 58% HMF yield after only one hour at 150 °C using a 7 mol % loading of the $CrCl_3$ catalyst. This compares favourably with current literature procedures requiring much longer reactions times or approaches that are difficult to scale such as microwave irradiation.

**Keywords:** biorenewables; platform chemicals; catalysis; biorefinery; lignocellulose

1. Introduction

The biorefinery concept requires routes that are efficient in terms of both materials and energy for the conversion of biomass to useful platform chemicals [1,2]. Lignocellulosic biomass represents a promising renewable feedstock for commercial large-scale biorefining, as it is diverse, widely distributed, and can be grown on a billion ton scale [1]. Agricultural byproducts (e.g., wheat straw, sugarcane bagasse, corn stover) or bioenergy crops, which do not rely on the use of arable land (e.g., *Miscanthus*, switchgrass, tree wood), avoid competition with food production (the food vs. fuel debate) and result in a higher reduction of net CO_2 emissions. Unfortunately, the processing of lignocellulosics requires energetically demanding pretreatment routes to separate lignin from cellulose [3], and subsequent cellulosic sugar and biofuel production relies on slow biocatalytic transformations (enzymatic saccharification and microbial fermentation) [4].

Cellulose and hemicellulose make up the largest part of lignocellulosic biomass and account for 50%–80% of the total mass [5]. Many recent papers have reviewed the use of ionic liquids for accessing the cellulose in lignocellulosic biomass; however, these articles focus mainly on the advantages of ionic liquids in the isolation of cellulose compared with traditional methods [6–12]. For example, it has been shown that ionic liquids can decrystallise the cellulose portion of biomass and disrupt linkages

to the hemicellulose and lignin portion [6], while George et al. studied the possibility of removing lignin from the other biomass constituents using ionic liquids and selectively extracting the lignin and hemicellulose fractions [13]. These two aspects could combine with the present research to enable the direct synthesis of platform chemicals, such as 5-hydroxymethylfurfural (HMF), from biomass.

The hydrolysis of cellulose and hemicellulose produces different sugar monomers, from which a wide range of important chemicals could be produced. Several papers have been published on the chemical transformation of low-molecular weight carbohydrates to chemicals with useful industrial application profiles [14–23]. For example, Dumesic and co-workers studied the catalytic transformation of biomass-derived oxygenated feedstocks into useful fuels and chemicals. These processes included hydrolysis, dehydration, isomerisation, aldol condensation, reforming, hydrogenation, and oxidation [24]. A summary of the alternative methods used to catalytically transform lignocellulose biomass is shown in Figure 1 [25].
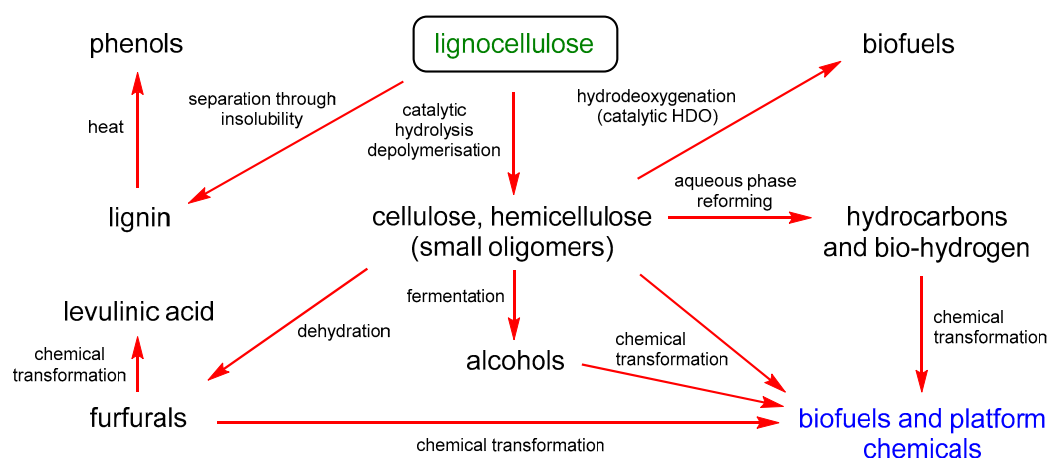
Figure 1. Lignocellulosic pathways. A scheme for a chemo-catalytic biorefinery [25].

Various review articles have provided an overview of key areas, such as the synthesis and use of sugar derivatives from hemicellulose and cellulose [26] and the methods used for conversion of biomass waste into useful platform chemicals [22,27]. Among the important bio-derived building blocks, 5-hydroxymethylfurfural (HMF) has been reported as one of the most promising [28,29], after the U.S. Department of Energy identified it as a major platform chemical that could be derived from lignocellulosic biomass on a large scale [30]. HMF is a versatile intermediate between biomass-based carbohydrate chemistry and the petroleum-based industrial chemistry, with widespread potential use in a variety of chemical manufacturing applications and industrial products [31,32]. Most prominent among these is 2,5-furandicarboxylic acid (FDCA) [33], which can be used to make renewable polymers [34] and liquid transport fuels, such as 2,5-dimethylfuran [35]. The potential of HMF as a synthetic building block is now widely recognised, which has led to a surge in the amount of research utilising HMF as a feedstock [36]. While HMF is an attractive renewable building block, several byproducts from degradation reactions occur during or after HMF transformation, leading to the formation of levulinic acid, formic acid, and humins [37,38], and reducing the overall HMF yield; this is particularly prevalent under acidic aqueous conditions, where the HMF product combines with unreacted sugars to produce water-insoluble humins [39]. However, HMF can be produced with sufficient selectivity and yield from food-grade fructose for it to become a nascent industrial process [40]. Production from more prevalent, lower cost sugars (such as glucose) requires a two-step catalytic mechanism involving isomerisation and dehydration, under Lewis basic and Brønsted acidic conditions (Figure 2) [41]. The solubility of HMF can also be an issue at high sugar loadings in aqueous systems, leading to byproducts formed from sugars with the HMF. This has led some researchers to explore removing HMF from the aqueous phase (which contains the sugars) using immiscible organic solvents, thereby reducing humin formation [42].
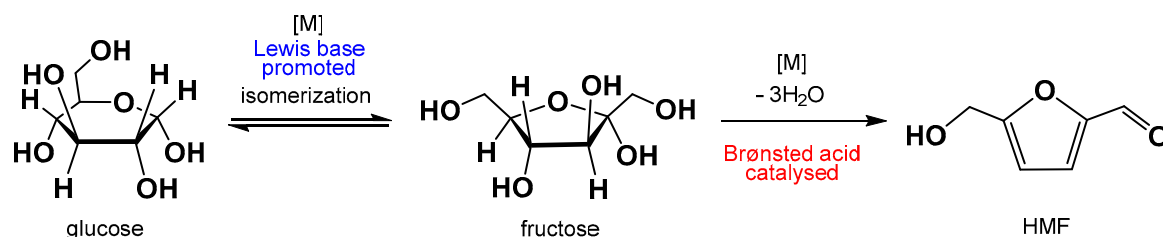
Figure 2. Transformation of glucose to 5-hydroxymethylfurfural (HMF) via fructose.

While HMF production from sugar monomers is largely straightforward, the most desirable and challenging route to produce HMF involves widely available renewable sources such as cellulose [43]. However, a high-yield, low-cost, energy-efficient, and direct conversion of cellulose into HMF is still a challenge and the subject of substantial research. Many different routes and methods have been proposed but the routes published to date are low-yielding, complex, and hence high in cost or energy inefficient.

The proposed synthetic route from cellulose to HMF is a multistep approach consisting of the production of glucose from cellulose, followed by glucose isomerisation to fructose, and finally HMF formation from the dehydration of fructose [44]. Interestingly (in the context of this work), the conversion of cellulose to HMF has also been shown to occur in the absence of a catalyst using ionic liquids, albeit in low yields [33].

The key step in the conversion of cellulose to HMF (Figure 3) is the hydrolysis of cellulose to sugar molecules, which is hampered by the poor solubility of polymeric cellulose in most solvents. Acid-catalysed hydrolysis of cellulose is one method that has been studied widely, in which the hydroxonium cations interact with the cellulose network, leading to breakdown of the polymer.

The most common acids used in cellulose hydrolysis are mineral acids (H_2SO_4, HCl) and organic acids, such as *p*-toluenesulfonic or carboxylic acids. Sulfuric acid has been used most frequently (at elevated temperatures), which is unsurprising due to its low cost. While higher temperatures and longer reaction times are required with dilute acid [45], the treatment of cellulose with concentrated acid accelerates the hydrolysis markedly, such that the polymer molecules depolymerise to monomers and this substantially increases dehydration of the monomeric sugars to HMF [46]. However, due to low selectivity and corrosion concerns, dilute acid is preferable for the controlled hydrolysis of cellulose. Heterogeneous solid acid catalysts have also been used for the depolymerisation of cellulose [47,48], though the catalytic activity and selectivity of solid acids are very low for the poorly soluble cellulose and so longer reaction times are required for these systems compared with liquid acid catalysts. Overall, while offering advantages for removal of the catalyst from the medium, the catalytic activity and selectivity of such solid acids are very low and so longer reaction times are required for these systems compared with liquid acid catalysts.

Besides the acid catalysed depolymerisation of cellulose, there exist other methods to achieve this effect, such as solvolysis [49] and catalytic hydrothermal liquefaction [50]. However, none of these methods has provided to be an effective and selective direct ("one-pot") chemical transformation of cellulose to useful chemicals such as HMF and, as a result, they are either uneconomical or environmentally unfriendly (or both). For this reason, the challenge remains to find a potentially economically viable method for cellulose conversion to useful products without significant environmental impact.
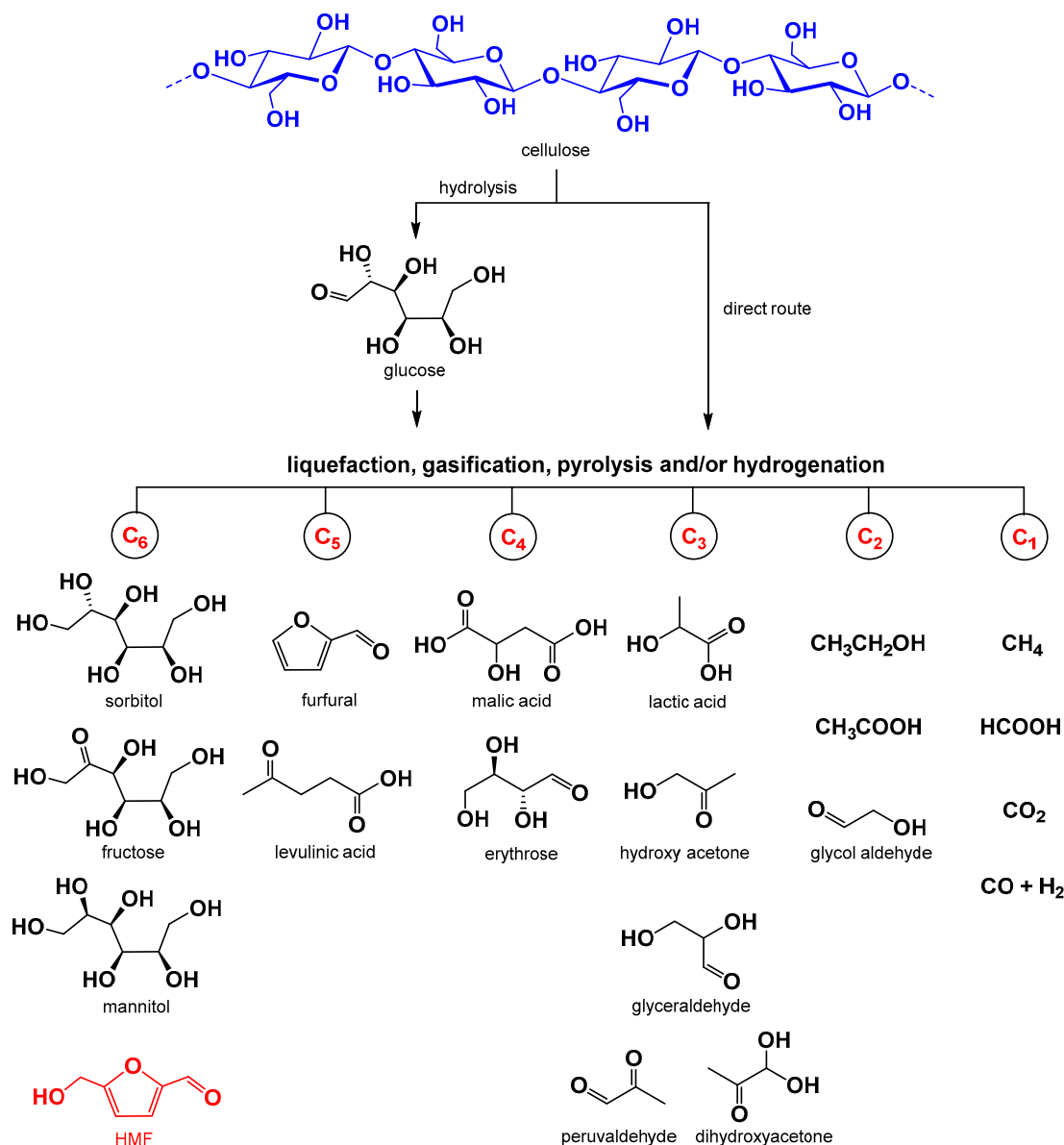
Figure 3. Pathway to HMF from cellulose.

Ionic liquids (ILs) [51] are being developed as alternative, potentially more commercially attractive and low-emission media for separating cellulose from lignin due to their unique chemical and solvent characteristics [6–12,52–57]. The research reported here combines ionic liquids as effective low impact solvents (relatively easily handled, negligible vapour pressure, recyclable) with low-toxicity metal catalysts for the direct conversion of cellulose to value-added chemicals. For this purpose, two ionic liquids (Figure 4) have been systematically studied under different conditions in order to arrive at an effective system for cellulose dissolution. The potential for selectively making HMF from fructose or glucose using ionic liquids (ILs) as solvents was first demonstrated by Zhao et al. [57], who used catalytic amounts of metal salts to convert sugars to HMF in [C_4C_1im]Cl, with $CrCl_2$ providing 70% HMF yield at 100 °C in 3 h. The yields were higher than those achievable in most aqueous systems, due to the suppression of HMF hydrolysis to levulinic and formic acids. Chromium salts were subsequently verified by other groups as the preferred catalyst [52–56]. However, the perceived toxicity of chromium is a key issue for commercial application, although this is largely based on Cr(VI) compounds, whereas the Cr(III) used here is an essential trace metal required for the formation of

glucose tolerance factor and for insulin metabolism, and is therefore widely used as a nutritional supplement for humans and animals [58]. Additionally, the risk of exposure to metal salts dissolved in ionic liquids is lowered as they are retained in the solvent medium during extraction or separation of the product.
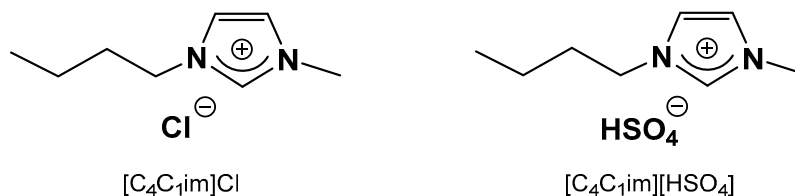
Figure 4. Ionic liquids used for the dissolution and breakdown of biomass in this work.

Since ILs can be tuned or designed to suit a certain application, and Brønsted acids have proven effective catalysts for fructose dehydration [55,59], the mildly acidic ionic liquid 1-butyl-3-methylimidazolium hydrogen sulphate, $[C_4C_1im][HSO_4]$ (Figure 4), was chosen as a solvent system for the conversion of fructose to HMF [52] with a low loading of chromium(III) chloride. An excellent HMF yield of 96% was reported using this system after 3 h at 100 °C without any detectable trace of the common byproducts, levulinic acid, formic acid, or humins (water-insoluble polymers formed from the reaction of HMF with the monosaccharide or a reactive intermediate). This imidazolium-based ionic liquid shares the same anion ($[HSO_4]^-$) with a family of ionic liquids that have recently been identified as true low-cost options ($[HNEt_3][HSO_4]$ and $[C_1Him][HSO_4]$), with a similar cost to traditional organic solvents such as acetone [60]. However, when using cellulose as the feedstock for HMF formation, it appears that the key step is the dissolution and depolymerisation of cellulose to glucose monomers rather than the glucose to fructose isomerisation and subsequent fructose dehydration. Ionic liquids appear to overcome these problems as they can play the role of both solvent and catalyst. Therefore, our attention turned principally to Lewis basic ILs, such as those with halide anions. This approach is similar to the interplay between acidity and basicity during glucose to HMF transformation in all solvent systems, including ILs, with the coordinating ability of the IL anion used to promote glucose isomerisation. For example, the Lewis acidic metal catalyst $SnCl_4$ has been used in ILs with a $[C_4C_1im]^+$ cation and a range of anions [53] where the non-coordinating BF_4^- anion gave the highest yield from glucose. This is in contrast to the acid-catalysed mechanism for HMF production from fructose reported previously. It was therefore decided that the solvent system best suited to direct cellulose conversion to HMF would draw inspiration from those used to achieve high yields from glucose and capable of some cellulose dissolution, such as chloride-based systems.

2. Results and Discussion

2.1. Catalyst and Ionic Liquid Selection

Our previous study on monosaccharides achieved a yield of 96% HMF from fructose and 90% from glucose by employing sulphate-based and chloride-based ILs, respectively [52,61]. The next goal was to find suitable conditions and ILs for the conversion of cellulose, which is the most important target of renewable chemicals due to its high abundance [1]. The conversion of cellulose is more challenging as it requires suitable conditions to be dissolved and hydrolysed to monosaccharides before it can be converted to HMF (Figure 5).

The experiments were carried out in ionic liquids with a low water content; however, rigorous exclusion of moisture during the reactions was employed. Many of the catalysts used were added in their hydrated form.
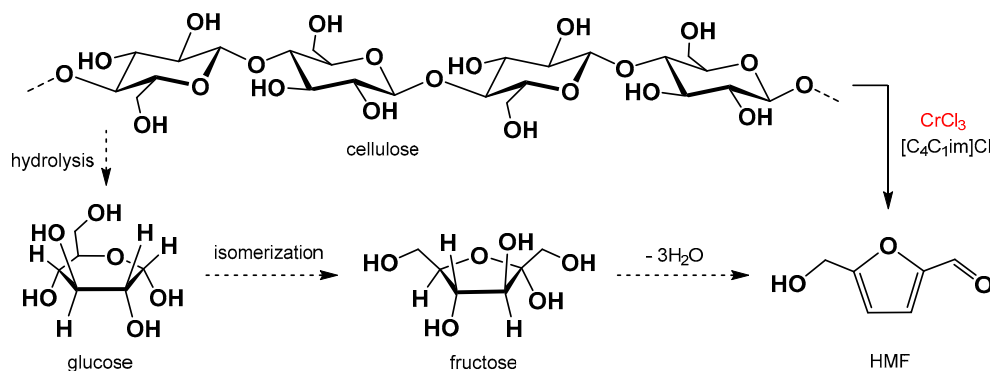
Figure 5. Transformation of cellulose to HMF via glucose and fructose.

Initially, the conditions and IL used were kept exactly the same as in our previous studies on monosaccharides and applied to cellulose as a substrate in order to directly compare HMF yields from cellulose to those from monosaccharides. Two ionic liquids $[C_4C_1im][HSO_4]$ and $[C_4C_1im]Cl$ were examined with the use of chromium, zinc, and copper salts, which have been reported as good catalysts for the dehydration of sugars to HMF [52], and aliquots were collected after 1.5 and 3 h. The samples were not collected before 1 h because the dissolution of cellulose was slower than expected at these conditions. After 1.5 and 3 h, HMF yields were very poor with the use of chromium catalysts and other catalyst mixtures in the $[C_4C_1im][HSO_4]$ ionic liquid (Table 1). Only a 5% HMF yield was observed using $CrCl_3 \cdot 6H_2O$ and $CrCl_3 \cdot 6H_2O$–$CuCl_2$ catalysts after 3 h at 120 °C (Table 1, Entries 1 and 2). In the presence of this IL without any catalyst, no HMF formation was detected after 3 h (Table 1, Entry 3). Unlike the sulphate-based ionic liquid, the yields were higher in the $[C_4C_1im]Cl$ ionic liquid, with 54% and 11% HMF yields with the use of $CrCl_3 \cdot 6H_2O$ and $CrCl_3 \cdot 6H_2O$–$CuCl_2$ catalysts, respectively (Table 1, Entries 4 and 5). Only 3% yield was observed in the presence of $[C_4C_1im]Cl$ without any catalyst (Table 1, Entry 6). After the selection of the IL, $ZnCl_2$ and $CrCl_3 \cdot 6H_2O$–$ZnCl_2$ were also examined as potential catalysts for the conversion of cellulose to HMF. The maximum yields of 3% and 30% were obtained using $ZnCl_2$ and $CrCl_3 \cdot 6H_2O$–$ZnCl_2$ catalysts (Table 1, Entries 8 and 9).

Table 1. Conversion of cellulose to HMF (% yield) in ionic liquids at 120 °C.

Entry	Ionic Liquid	Catalyst	1.5 h	3 h
1	$[C_4C_1im][HSO_4]$	$CrCl_3 \cdot 6H_2O$	<5	<5
2	$[C_4C_1im][HSO_4]$	$CrCl_3 \cdot 6H_2O$ + $CuCl_2$ (1:1)	<5	<5
3	$[C_4C_1im][HSO_4]$	No catalyst	0	0
4	$[C_4C_1im]Cl$	$CrCl_3 \cdot 6H_2O$	36	54
5	$[C_4C_1im]Cl$	$CrCl_3 \cdot 6H_2O$ + $CuCl_2$ (1:1)	11	11
6	$[C_4C_1im]Cl$	No catalyst	<3	<3
7	$[C_4C_1im]Cl$ + $[C_4C_1im][HSO_4]$ (1:1)	$CrCl_3 \cdot 6H_2O$	<3	<5
8	$[C_4C_1im]Cl$	$ZnCl_2$	0	3
9	$[C_4C_1im]Cl$	$CrCl_3 \cdot 6H_2O$ + $ZnCl_2$ (1:1)	8	30

0.1 g cellulose in 0.7 g ionic liquid; 7 mol % catalyst, 120 °C; HMF yields shown were determined in the IL by ^{1}H-NMR spectroscopy.

Based on our previous research on glucose and fructose, it was found that $[C_4C_1im]Cl$ enhances the isomerisation of glucose to fructose through the improved coordinating ability of the metal centre when Lewis basic Cl^- anions (acting as additional ligands) are present, while $[C_4C_1im][HSO_4]$ accelerates the conversion of fructose to HMF [61]. It was also assumed that the acidity of $[C_4C_1im][HSO_4]$ will promote the hydrolysis of cellulose to monomers. In order to probe this, mixtures of ionic liquids were tested for the conversion of cellulose to HMF but very poor (5%) HMF yields were detected (Table 1, Entry 7). These results suggested that the presence of $[C_4C_1im][HSO_4]$ actually

lowers the conversion of cellulose to HMF, and strongly suggests that the $[HSO_4]^-$ anion actually inhibits the glucose–fructose interconversion, as was already verified in our previous research on glucose to HMF [61]. These results indicate that, while the chromium catalyst is a good choice for cellulose conversion to HMF, the $[C_4C_1im][HSO_4]$ ionic liquid inhibits HMF formation, and the $ZnCl_2$, $CrCl_3 \cdot 6H_2O–ZnCl_2$, and $CrCl_3 \cdot 6H_2O–CuCl_2$ catalyst systems do not provide a viable reaction system at 120 °C in the presence of $[C_4C_1im][HSO_4]$.

2.2. Cellulose Concentration

The cellulose (substrate) concentration is an important factor in this conversion pathway, as it has been shown that reducing glucose concentration improves the HMF yield by reducing humin formation [61] due to a lower concentration of sugarsreacting with 5-HMF to form humins (insoluble carbohydrate degradation products). As a result, improving the reaction kinetics for the conversion of glucose and fructose into 5-HMF can have a significant effect on supressing humins formation. To explore this hypothesis, the amount of cellulose present in the reaction medium was reduced. The results for this series of experiments are illustrated in Figure 6.
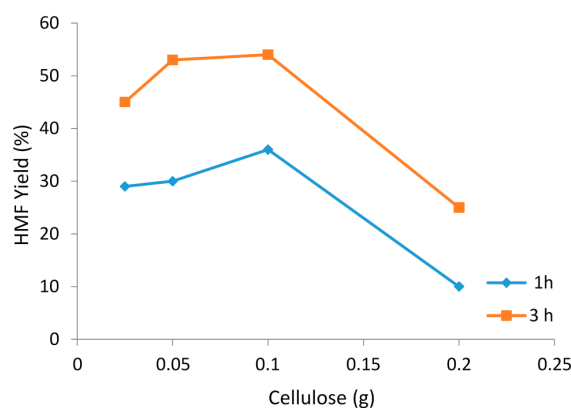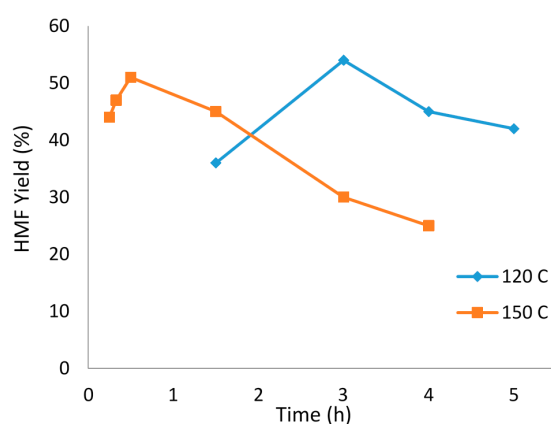

Figure 6. HMF yield from cellulose at 120 °C in $[C_4C_1im]Cl$; 0.7 g ionic liquid; 7 mol % $CrCl_3 \cdot 6H_2O$ catalyst. HMF yields shown were determined in the IL by ^{1}H-NMR spectroscopy.

A maximum yield of 54% was obtained after 3 h using a 0.1 g cellulose loading (120 °C). Lowering the amount of cellulose from 0.1 to 0.05 g and then to 0.02 g led to yields of HMF of 53% and 45%, respectively, whilst increasing the cellulose concentration from 0.1 to 0.2 g led to an HMF yield of 25% after 3 h. This could be explained by the limited solubility of cellulose in the IL creating a multiphasic reaction system. To overcome the solubility issue, the amount of IL was tripled (0.7 to 2.1 g), while keeping the cellulose amount at 0.2 g and maintaining the catalyst loading at 7 mol %. The HMF yield after 3 h consequently improved from 25% to 39%. These results suggest that decreasing the cellulose loading (from the standard conditions of 0.1 g cellulose in 0.7 g IL) has only a minor effect on the HMF yield. This is likely to indicate that a multiphasic system run above the cellulose solubility limit will perform adequately with a steady state (solubility limited) concentration of cellulose substrate dissolved in the IL. However, it is worth noting that it was ensured that all cellulose had dissolved by the time the first samples of the media were taken for analysis.

Based on glucose-HMF conversions in $[C_4C_1im]Cl$, our previous hypothesis was that the isomerisation of glucose to fructose was the limiting step, rather than the conversion of fructose to HMF [61]. It was found that decreasing the glucose concentration left less sugar to react with HMF at 120 °C, and thus successfully preventing humin formation. However, in the system described here, it appears that the limiting step is dissolution and hydrolysis of cellulose to glucose monomers rather than the isomerisation of glucose to fructose. This will influence both reaction engineering approaches and reactor design considerations in the future.

2.3. Reaction Time

Figure 7 shows the effect of time on the yield of HMF from cellulose at 120 and 150 °C at the same catalyst (CrCl$_3$·6H$_2$O) and cellulose loadings in [C$_4$C$_1$im]Cl. Prolonging the reaction time initially improves the HMF yield, but after reaching a maximum, the HMF yield at 120 °C declined by 9% between 3 and 4 h and by 6% between 0.5 and 1.5 h at 150 °C. Measurements were not taken before 1 h at 120 °C because cellulose dissolution was not yet complete. The reaction was very fast at 150 °C, and the maximum yield was obtained after only 0.5 h (51%). Prolonging the reaction from the maximum yield point led to a decrease in the HMF yield, indicating that decomposition of HMF and the formation of humins (observed as a precipitate) was occurring at these high temperatures. Not only was an HMF yield of 51% obtained after 30 min at 150 °C, but after only 15 min at this temperature, an HMF yield of 44% was obtained. These are exceptionally high HMF yields from cellulose, achieved over a very short reaction time.

Figure 7. Yield of HMF from cellulose at 120 °C and 150 °C in [C$_4$C$_1$im]Cl; 0.1 g cellulose, 0.7 g ionic liquid; 7 mol % CrCl$_3$·6H$_2$O catalyst. HMF yields shown were determined in the IL by ^{1}H-NMR spectroscopy.

2.4. Water and Catalyst Loading

Due to its involvement in all stages of the process, the presence of water is a significant factor in the conversion of cellulose to HMF (Table 2). In order to explore this further, different amounts of water were added to the reaction mixture at 150 °C. However, increasing the water content above adventitious levels resulted in no clear benefit (Table 2, Entries 1 and 2). This could be attributed to a dramatic decrease in the solubility of cellulose in [C$_4$C$_1$im]Cl–water mixtures as a result of the reorganisation of the hydrogen bonding network. The hydrogen bonds between [C$_4$C$_1$im]Cl and the hydroxyl group of cellulose are orientated to favour breakage of the β-1,4-glycosidic bonds [62]. When substantial amounts of water are present (Table 2, Entry 1), the water molecules preferentially hydrogen bond with cellulose, reducing the interaction between this substrate and [C$_4$C$_1$im]Cl, resulting in the lower solubility observed for cellulose in [C$_4$C$_1$im]Cl [63]. However, the presence of small amounts of water (Table 2, Entry 2) appears to slow the formation of HMF yet still results in 51% yield after an hour. Overall, it is clear that the presence of a small amount of water is beneficial and is needed for hydrolysis. Indeed, rigorous exclusion of moisture has a detrimental effect on the yield (see Supplementary Materials).

The catalyst loading was also tested in order to confirm that there was sufficient catalyst to perform the conversion of cellulose to HMF and that catalyst poisoning was not a significant factor in the reaction medium. The catalyst loading was increased threefold (to 21%) and the yield was observed to decrease slightly (Table 2, Entry 4). This is surprising but could be due to the additional catalyst present promoting side reactions, which lower the HMF yield.

Table 2. Effect of addition of water and catalyst loading on HMF formation (%) at 150 °C.

Entry	Ionic Liquid	Catalyst (mol %)	0.5 h	1 h	3 h
1	$[C_4C_1im]Cl + H_2O$ (1:1)	7	-	22	28
2	$[C_4C_1im]Cl + H_2O$ (3:1)	7	-	51	44
3	$[C_4C_1im]Cl$	7	51	45	30
4	$[C_4C_1im]Cl$	21	44	37	22

0.1 g cellulose in 0.7 g ionic liquid; $CrCl_3 \cdot 6H_2O$ catalyst, 150 °C. HMF yields shown were determined in the IL by ^{1}H-NMR spectroscopy. Ratios are by weight.

2.5. Reaction Temperature

The reaction temperature is an important factor in the conversion of cellulose to HMF that directly affects the yield and reaction rate, as both increase as temperature increases. After reaching the maximum yield, humins start to form at elevated temperatures, and lower the yield considerably (Figure 8). The reaction is very fast at high temperatures, with an HMF yield of 44% observed after only 15 min at 150 °C (and after 10 min at 170 °C). An increase in temperature of 50 °C (from 100 to 150 °C) led to a 15-fold higher HMF yield at the 30 min time point. At the three-hour time point, seven times more HMF was being produced at 120 °C compared to at 100 °C. Although the reaction rate increases with temperature, the HMF yield dropped after 30 min at the highest temperatures (150 or 170 °C), which can be attributed to the formation of humins. The maximum HMF yield of 54% was obtained after 3 h at 120 °C but the restriction on yield at this temperature was due to the reaction rate, which was slow due to the low solubility (and slow dissolution) and breakdown of the cellulose polysaccharide in the ionic liquid. The presence of humins was also detected after 3 h at 120 °C and their formation led to the subsequent observed decrease in HMF yield after this point.
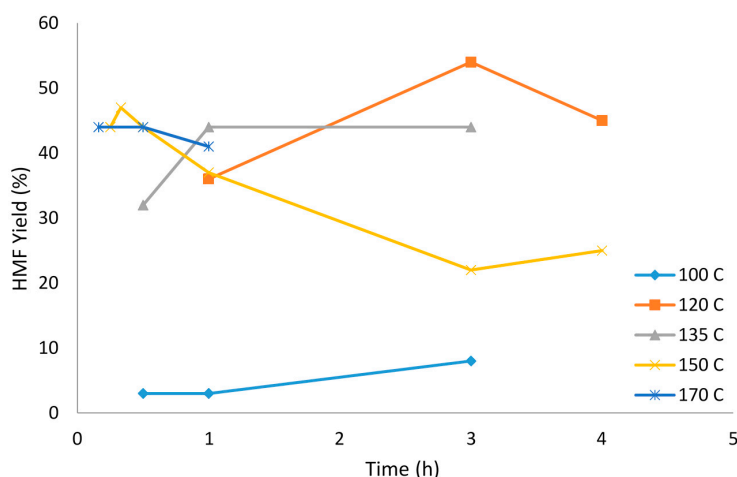
Figure 8. Yield of HMF from cellulose at temperatures from 100 to 170 °C as a function of time; 0.1 g cellulose in 0.7 g ionic liquid; 7 mol % $CrCl_3 \cdot 6H_2O$ catalyst. HMF yields shown were determined in the IL by ^{1}H-NMR spectroscopy.

At temperatures above 120 °C, the reaction rate increased and moderate yields were obtained after only 10 min. This could be due to the reduced viscosity of the reaction medium, which accelerates the mass transfer for cellulose dissolution and breakdown. Moreover, an HMF yield of 44% was obtained from the conversion of cellulose after only 10 min at 170 °C, which is one of the highest reported yields of HMF directly from cellulose. However, when the reaction temperature was very high the formation of humins was unavoidable and the yield dropped significantly after only a short period of time (Figure 8), creating a narrow operating window in time. In order to overcome this problem, low cellulose concentrations were tested to limit the formation of humins at high temperatures. This built on the runs conducted at 120 °C (Figure 6), which suggested that changing the standard

0.1 g cellulose in 0.7 g IL had a detrimental effect on HMF yield. It was hypothesised that, as the reaction rate above 150 °C is very fast, lowering the free sugar concentration in solution will limit the formation of humins. This follows from the fact that there would be less sugar remaining under these conditions to react with the HMF formed (to form humins). As an additional benefit, it was considered that the higher temperatures would also make cellulose dissolution more rapid. Different cellulose concentrations at elevated temperatures were investigated in order to test this hypothesis (Table 3).

Table 3. Effect of cellulose concentration on HMF yield (%) at elevated temperatures.

Entry	Ionic Liquid	Cellulose (g)	Temp. (°C)	10 min	0.5 h	1 h	3 h
1	[C$_4$C$_1$im]Cl	0.025	150	40	52	58	58
2	[C$_4$C$_1$im]Cl	0.015	150	25	45	57	51
3	[C$_4$C$_1$im]Cl	0.1	170	44	44	41	-
4	[C$_4$C$_1$im]Cl	0.015	170	31	50	50	-

0.7 g ionic liquid; 7 mol % CrCl$_3$·6H$_2$O catalyst. HMF yields shown were determined in the IL.

In contrast to the results at 120 °C, reducing the cellulose concentration improved the yield at elevated temperatures. With the cellulose loading decreased to 0.025 g (Table 3, Entry 1), the reaction was very fast (40% HMF yield after only 10 min) and produced a maximum HMF yield of 58% after only 1 h. This represents the optimum conditions in our research on direct HMF production from cellulose in ionic liquids. Decreasing the cellulose concentration further to 0.015 g (Table 3, Entry 2) did not have any positive effect on the yield, probably because the solution became too dilute. Raising the temperature still further to 170 °C increased the reaction rate and gave 6% more HMF yield after 10 min (Table 3, Entries 2 and 4) using a 0.015 g loading. However, the overall yield dropped by 7% after 3 h due to a higher rate of humin formation.

In this work, all conversions to HMF are reported as non-isolated yields that were obtained by ^{1}H-NMR spectroscopy using [C$_4$C$_1$im]Cl as the internal standard. The isolation of 5-hydroxymethylfurfural from the ionic liquid reaction medium is a significant challenge [33,36] due to the high boiling point (291 °C at atmospheric pressure) of HMF and its instability on removal from the system (it is significantly stabilised in the ionic liquid). There have been a number of reports addressing this [53,64–66], including the use of methyl isobutyl ketone (MIBK) [64] or ethyl acetate [65] to extract from similar ionic liquid/metal salt systems. These typically employ multiple extractions (between 3 and 10) to isolate 90%–95% of the HMF present in the ionic liquid media, and introduce a volatile organic solvent into the system. An alternative approach using an entrainer-intensified vacuum distillation process has also been employed for the separation of HMF from metal salt–ionic liquid mixtures, though at a high energy penalty [66]. This isolation issue is common to all ionic liquid based systems and can either be addressed through improved extraction procedures or, alternatively, converting the HMF generated into further products without isolation [67].

3. Materials and Methods

3.1. General Comments

All experiments were carried out under aerobic conditions using dried ionic liquids; however, moisture was not rigorously excluded during the reactions. The ionic liquids used, [C$_4$C$_1$im]Cl and [C$_4$C$_1$im]HSO$_4$ were prepared using procedures slightly modified from those detailed in an earlier report [52]. The metal salts were obtained from Sigma-Aldrich (St. Louis, MO, USA), as were the cellulose and HMF (to provide data for a pure sample). NMR spectroscopy was performed at 25 °C using a Bruker DRX-400 (400 MHz) spectrometer (Bruker, Billerica, MA, USA). All couplings are reported in Hertz. A Shimadzu Prominence HPLC instrument (Shimadzu, Kyoto, Japan) with refractive index (RI) and ultraviolet (UV) detectors equipped with an Aminex HPX-87H column was used. A comparison of the yield determination using ^{1}H-NMR spectroscopy and HPLC is reported in the Supplementary Materials.

3.2. Catalytic Formation of 5-Hydroxymethylfurfural (HMF) from Cellulose

In a typical run, cellulose (100 mg, 0.62 mmol) was added to a round-bottomed flask containing $[C_4C_1im][Cl]$ (700 mg, 4.01 mmol). The catalyst (0.043 mmol, 7 mol %) under study (CrCl$_3$·6H$_2$O, CuCl$_2$, ZnCl$_2$) was added to the flask. The flask was equipped with a reflux condenser and the reaction mixture was stirred at the desired temperature (80, 100, 120, 140, 150 or 170 °C) for 24 h. Samples were collected after various reaction times (0.5, 1, 3, or 24 h) and analysed by ^{1}H-NMR spectroscopy. HMF yields were calculated from the integration of HMF peaks against the ionic liquid $[C_4C_1im][Cl]$ itself. The ionic liquid was considered to be an internal standard, as it has negligible vapour pressure. The distinct HMF resonance at 9.55 ppm in the ^{1}H-NMR spectrum was chosen for calculation of the yields and measured against resonances for the $[C_4C_1im]^+$ cation, which can be considered completely non-volatile under the conditions employed. Experiments were performed three times and an average was taken. A discussion of the accuracy of the ^{1}H-NMR spectroscopy method compared to HPLC can be found in the Supplementary Materials. The following NMR spectroscopic data were recorded for HMF: ^{1}H-NMR (400 MHz, DMSO) δ 9.55 (s, 1H, CHO), 7.50 (d, 1H, furan-CH, $^3J_{HH}$ = 3.5 Hz), 6.61 (d, 1H, furan-CH, $^3J_{HH}$ = 3.5 Hz), 5.57 (t, 1H, OH, $^3J_{HH}$ = 6.0 Hz), 4.51 (d, 2H, CH$_2$O, $^3J_{HH}$ = 6.0 Hz) ppm. All HMF yields reported are therefore non-isolated yields.

4. Conclusions

The conversion of cellulose to HMF was probed using a range of different variables, including the nature of the ionic liquid medium, the catalyst selection, and modification of the reaction conditions. The conversion of cellulose to HMF is clearly much more challenging than the generation of HMF from sugar monomers due to the polymeric nature of cellulose and its resulting low solubility in the majority of solvent systems. At elevated temperatures (above 150 °C), lowering the cellulose concentration led to an increase in the yield of HMF but only to a certain level, beyond which the yield decreased. This suggests that there is a balance to be struck between successful dissolution of cellulose and sufficiency of material to make the process effective. As has been noted previously [68,69], the presence of moisture is necessary (see also Supplementary Materials), though a high water content displays no benefit and slows the formation of HMF (Table 2). More work is needed to probe this aspect further. Prolonged reaction time led to a decrease in HMF yield due to the formation of humins. The reaction temperature is one of the most important factors in the conversion of cellulose to HMF, as it directly affects the yield and reaction rate. At 150 °C, 47% yield of HMF was obtained after only 30 min in contrast to the maximum 54% HMF yield observed at 120 °C, which required 3 h, indicating that longer reaction times are needed at this lower temperature. Both prolonged reaction times at lower temperature and shorter reaction times at higher temperatures led to the formation of humins. A compromise was found to achieve a 58% HMF yield after one hour at 150 °C using a relatively low cellulose concentration. This result needs to be viewed in the context of leading HMF yields (as opposed to cellulose conversion) in the literature, which fall in the range of 50%–60% over longer reaction times (e.g., 5 h [70]) or non-scalable approaches, such as microwave heating [71].

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