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Selectivity enhancement in the aqueous acid-catalyzed conversion of glucose to 5-hydroxymethylfurfural induced by choline chloride†

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In this work we wish to show that choline chloride (ChCl), a cheap and safe quaternary ammonium salt industrially produced at a few thousand tons per year through a 100% atom economy process, is capable of enhancing the selectivity of metal chlorides such as $AlCl_3$, $FeCl_3$ and $CuCl_2$ in the aqueous tandem isomerization/dehydration of glucose to HMF. Under optimized conditions, 70% yield of HMF was obtained in a water/methylisobutylketone (MIBK) biphasic system which is a competitive yield to those traditionally obtained in imidazolium-based ionic liquids in the presence of hazardous chromium salts. By means of counter experiments, we show that the selectivity enhancement is optimal for a ChCl content of 50 wt% in water. At higher loading of ChCl, strong molecular interaction occurs between ChCl and HMF making the extraction of HMF from the aqueous phase difficult with MIBK, thus enhancing side reactions of HMF with water and hexoses to unwanted products. Interestingly, this process can be transposed to the direct conversion of cellulose to HMF which is an even more challenging reaction. In this case, we show that combination of $FeCl_3$ with $AlCl_3$ allowed cellulose to be converted to HMF with 49% yield in a one pot reaction. From the viewpoint of sustainable chemistry, this work shows noticeable advantages such as the use of (1) water as a solvent, (2) ChCl as a cheap and safe additive, (3) cheap and naturally abundant metals (Al, Fe, and Cu) and (4) renewable raw materials.

Introduction

The development of Chemistry Safety Rules, the proposition of the twelve principles of green chemistry in 1998 by P. Anastas and J. Warner as well as the price and scarcity of oils are now key elements in establishing sustainable reactions/processes.[1] Within this framework, the use of renewably-sourced raw materials for the production of innovative products has become a top priority in the chemical industry. In this context, much attention has been paid to the synthesis of 5-hydroxymethylfurfural (HMF) as a chemical platform from which solvents, monomers, fuel additives, among others, can be then produced.[2] HMF is produced by an acid-catalyzed triple dehydration of hexoses. Although a plethora of studies have been dedicated to the acid-catalyzed dehydration of fructose to HMF, the direct use of glucose (directly available from lignocellulosic biomass) is much less widespread, mainly because it requires tackling the isomerization of glucose to fructose prior to the dehydration step to HMF. Isomerization of glucose to fructose can be catalyzed by Lewis acids such as for instance tin-containing zeolites but yields of fructose remained rather low.[3] Basic catalysts were also proposed but hexoses are relatively unstable under alkaline conditions affording fructose in low yield.[4] Currently, industrial processes involve enzymes which are capable of producing up to 50% yield of fructose from glucose although this process has clearly some drawbacks (enzyme deactivation, a large quantity of enzymes and low activity of enzymes).[5] Note that enzymatically produced fructose can then be dehydrated to HMF in a sequential process (fermentation followed by acid catalysis).[6] In 2007, Zhang and co-workers reported that chromium chloride can

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efficiently catalyze the tandem isomerization/dehydration of glucose to HMF with an unprecedented yield of 70% in ionic liquids.[7] Recently, variants of this process have been proposed, especially from cellulose and lignocellulosic biomass. Although from an environmental point of view the sustainability of such processes is debatable, this work presents a benchtop methodology that allows a better understanding of the different elementary steps involved in the catalytic isomerization of glucose to fructose.

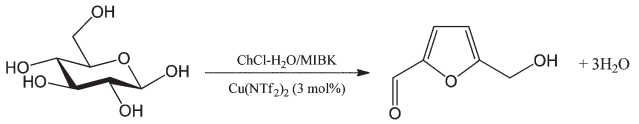
Choline chloride (ChCl), a cheap, biodegradable and safe quaternary ammonium salt industrially produced at a few thousand tons per year through a 100% atom economy process, is known to be capable of producing a deep eutectic solvent (DES) when mixed with metal chlorides or hexoses such as glucose or fructose.[8] This particular property of ChCl suggests that this moiety has the unique ability to stabilize or destabilize not only hydrogen bond donors such as hexoses or HMF but also metal-derived catalytic species. In this context, this work aims at identifying fundamental issues on the way in which ChCl may impact the catalytic cycles involved in the tandem isomerisation/dehydration of glucose to HMF (*i.e.* role as a ligand, stabilization of HMF, *etc.*). By comparing data from the current literature with our experimental results, we wish to show here that the use of ChCl as an additive in water is a great tool for assisting Lewis acid catalysts in the direct conversion of glucose to HMF. Under the optimized conditions, HMF was produced with up to 70% yield in water which is a very competitive yield to those obtained from traditional imidazolium-based ionic liquids with chromium-based catalysts. Besides the clear economic and environmental advantages stemming from the use of ChCl (<2€ per kg, biocompatible) and water, we wish to demonstrate here that the assistance of ChCl also allows using safe metal chlorides such as $AlCl_3$, $FeCl_3$ or $CuCl_2$.

Results and discussion

Catalytic experiments

In a first set of experiments, glucose was mixed with ChCl (glucose–ChCl weight ratio = 1/1, 2/1, 1/5). As described earlier, when the solution was heated at 100 °C a transparent and viscous liquid DES was formed. Next, 3 mol% of $Cu(NTf_2)_2$ were added to the solution and heated first at 180 °C under microwaves (250 W). The choice of this Lewis acid was motivated by our recent results obtained with metal triflates in the catalytic etherification of glycerol.[9] Note that catalyst screening is described later in the manuscript. Unfortunately, under these conditions, HMF was only produced as a trace, presumably due to the low reactivity of glucose when engaged in the formation of a DES as similarly observed in the current literature by Kazlauskas and co-workers in a ChCl–glycerol eutectic mixture (Table 1, entry 1).[10] With the aim of lowering the interaction between glucose and ChCl, water was progressively added to the reaction medium. In all experiments, the glucose content was kept constant at 10 wt%. As water was added, we were pleased to see that formation of HMF occurred and the yield of HMF reached 31% at a ChCl–H_2O weight ratio of 1 (*i.e.* 7.1 M) which corresponds to an HMF selectivity of 42% (Table 1, entry 3). Upon prolonged reaction time, the yield of HMF slightly dropped due to its side degradation and condensation. Note that, under these conditions, levulinic acid was not detected but formation of soluble black materials called humins was observed. When the amount of water was further increased (ChCl–H_2O weight ratio of 1/2), the yield of HMF also decreased suggesting that an optimal ChCl–H_2O ratio needs to be respected (Table 1, entry 4). More information about the role of the ChCl–water ratio is provided later in the manuscript.

Table 1 Acid-catalyzed conversion of glucose to HMF in the presence of $Cu(NTf_2)_2$



Entry	ChCl–H_2O/MIBK weight ratio	T (°C)	Time (min)	Conv. glucose (%)	HMF yield[a] (%)	Selectivity (%)
1	—	180	60	—	<5%	—
2	5–2/0	180	3	82	18	22
3	2–2/0	180	20	74	31	42
4	1–2/0	180	20	90	20	23
5	2–2/2	180	15	72	46	64
6	2–2/2	180	30	85	33[b]	39
7	2–2/2	165	30	70	30	43
8	2–2/2	200	7	89	29	33
9	2–2/2[c]	180	7	83	38	46

[a] Molar yield. [b] Along with 9% yield of levulinic acid. [c] From a glucose content of 20 wt%.

Next, in an attempt to increase the yield of HMF, methylisobutylketone (MIBK) was added to the system in order to "continuously" extract HMF from the catalytic phase and to limit its acid-catalyzed side reaction with water or hexoses to unwanted products. As expected, when 10 wt% of glucose was heated at 180 °C in a ChCl–H_2O/MIBK (ratio of 1–1/1) biphasic system for 15 min, the selectivity to HMF was improved and HMF was produced with 46% yield (Table 1, entry 5). Note that upon prolonged reaction time, the yield of HMF started to decrease and, in this case, we clearly observed the formation of levulinic acid (9% yield after 30 min, Table 1, entry 6). A decrease of the reaction temperature from 180 °C to 165 °C obviously lowered the reaction rate but unfortunately had a negative impact on the reaction selectivity. At 165 °C, the maximum yield of HMF was 30% which corresponds to an HMF selectivity of 43% *vs.* 64% at 180 °C (Table 1, entry 7). Similarly, an increase of the reaction temperature from 180 °C to 200 °C (Table 1, entry 8) also lowered the HMF selectivity (from 64% to 33%) mainly due to the dominant formation of soluble and insoluble black materials as well as other side products. Hence, one may conclude that 180 °C is the optimal temperature when working with $Cu(NTf_2)_2$ as a catalyst. In a

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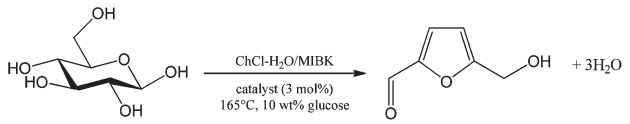
similar manner to a previous work,[2] an increase of the glucose content from 10 wt% to 20 wt% also lowered the selectivity of the reaction and HMF was produced with 38% yield (*vs.* 46% at a glucose content of 10 wt%, Table 1, entries 5, 9).

Although promising yields of HMF have been obtained in the ChCl–H_2O/MIBK system in the presence of $Cu(NTf_2)_2$, we then screened other Lewis acid catalysts in order to select the most active ones. Unless otherwise noted, all the conditions employed for catalytic experiments are 10 wt% of glucose, a ChCl–H_2O/MIBK (ratio of 1–1/1) biphasic system and 3 mol% of catalyst. The reaction temperature was fixed at 165 °C (*vs.* 180 °C with $Cu(NTf_2)_2$) in order to reduce the reaction rate and to better select the most active catalysts. To compare the activity of all catalysts, the reaction time was first fixed at 15 min in all cases. Results are summarized in Table 2.

Among the tested metal triflates and metal triflimidates, Al is the most active one affording a glucose conversion of 99% followed by Fe and Cu (Table 2, entries 1–7). In the case of metal chlorides, large differences in activity were observed. As previously described in imidazolium-based ionic liquids[7] or in a water–NaCl mixture,[11] $AlCl_3$, $CrCl_2$ and $CrCl_3$ were the most active ones (Table 2, entries 8, 10, 11). It is noteworthy that safe metal chlorides such as $FeCl_3$ and $CuCl_2$ also exhibited an acceptable activity leading to a glucose conversion of 58% and 56%, respectively (Table 2, entries 12, 13). Activity of metal chlorides can be classified as follows: $AlCl_3$, $CrCl_2$, $CrCl_3$ > $FeCl_3$, $CuCl_2$ > $MgCl_2$, $FeCl_2$ > $MnCl_2$, $BiCl_3$ > $ZnCl_2$. The great catalytic activity of $AlCl_3$, $FeCl_3$ and $CuCl_2$ in an aqueous solution of ChCl is attractive mainly because of their low price and natural abundance. Hence, we selected these metal chlorides and we tried to optimize the yield of HMF. As the yield of HMF passes through a maximum during the catalytic process, we first monitored the HMF yield *versus* time. At 165 °C, kinetic studies confirmed the high activity of $AlCl_3$ and we found that HMF was produced with a maximum yield of 67% after only 3 min of reaction which corresponds to a glucose conversion of 89% and an HMF selectivity of 75% (Table 2, entry 8). $AlCl_3$ is so active that we were able to decrease the temperature to 150 °C (entry 9). At this temperature, a slight increase of the HMF yield to 70% was observed. Note that this yield value is similar to that previously reported by Zhang in the presence of 6 mol% of $CrCl_2$ in 1-butyl-3-methylimidazolium chloride (the reference work in this field of chemistry),[7] thus showing the potential of such a catalytic system for the sustainable production of HMF. In the case of $FeCl_3$, a maximum yield of HMF of 43% (entry 12) was obtained after 25 min of reaction, which is quite close to the yields of HMF collected with chromium-based catalysts under our conditions (49% and 57% yield in the presence of $CrCl_2$ and $CrCl_3$, respectively, entries 10–11). Remarkably, whereas Bronsted acid usually provides very low yields of HMF from glucose (also observed here in the absence of ChCl), we were pleased to see here that, in the presence of ChCl, HMF was produced with 34% and 22% yield with BHC (betaine hydrochloride) and HCl, respectively (Table 2, entries 19–20), reinforcing the key role played by ChCl in the conversion of glucose to HMF.

Table 2 Catalytic conversion of glucose to HMF over various Lewis acids



Entry	Catalyst	Conv. glucose (%) after 15 min	Optimized conditions to get the maximum molar yield of HMF[a] Time (min)	Conv. (%)	HMF yield (%)
1	$Al(NTf_2)_3$	99	3	87	56
2	$Fe(NTf_2)_3$	63	15	63	34
3	$Cu(NTf)_2$	23	15	72	46
4	$Al(OTf)_3$	99	3	93	54
5	$Cu(OTf)_2$	47	20	54	23
6	$Fe(OTf)_3$[b]	44	15	66	24
7	$Bi(OTf)_3$	22	nd	nd	nd
8	$AlCl_3$	99	3	89	67
9	$AlCl_3$[c]	—	15	90	70
10	$CrCl_2$	99	15	99	49
11	$CrCl_3$	99	3	93	57
12	$FeCl_3$	58	25	72	43
13	$CuCl_2$	56	30	69	37
14	$MgCl_2$	26	nd	nd	nd
15	$FeCl_2$	23	nd	nd	nd
16	$MnCl_2$	15	nd	nd	nd
17	$BiCl_3$	12	nd	nd	nd
18	$ZnCl_2$	5	nd	nd	nd
19	BHC[d]	—	10	74	34
20	HCl[d]	—	5	50	22

[a] nd, not determined. [b] Result collected at 180 °C. [c] Result collected at 150 °C. [d] BHC = betaine hydrochloride, pH = 1.

Next, we tried to rationalize the greater selectivity of $AlCl_3$ as compared to that of $FeCl_3$ under our conditions. Interestingly, we found that yields of HMF were comparable between $FeCl_3$ and $AlCl_3$ (43%) for up to 70% conversion of glucose (see ESI, Fig. S1, S2 and S3†). However, upon prolonged reaction time significant differences were observed between both metal chlorides. In the presence of $AlCl_3$ the yield of HMF gradually increased to 70% (at 90% conversion). Conversely, in the presence of $FeCl_3$, the yield of HMF dramatically dropped at conversion higher than 70%. This surprising difference in behaviour between both metal chlorides prompted us to more deeply investigate the stability of catalytically active species in our system.

Recent works have shown that, in the presence of water, metal chlorides such as $CrCl_2$ and $AlCl_3$ are in equilibrium with metal hydroxide species $M(OH)_x(H_2O)_y$ and HCl.[12] Metal hydroxide is suspected to be the catalytically active species in the isomerization of glucose to fructose while released HCl would catalyze the dehydration of fructose to HMF. Assuming that metal hydroxide species are suspected to be the catalytically active sites in the isomerization of glucose to fructose, we first heated $FeCl_3$ and $AlCl_3$ in neat water (30 min at 165 °C under microwaves) prior to adding ChCl and glucose. The pH of the solution was measured before and after heating of the corresponding metal chloride in neat water (Table 3). As

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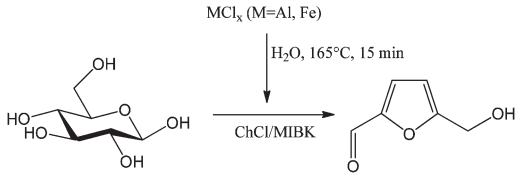
Table 3 Stability of catalytic species[a]



	Without pre-heating			With pre-heating		
Catalyst	pH[b]	Conv. glucose (%)	HMF molar yield[a] (%)	pH[c]	Conv. glucose (%)	HMF molar yield[a] (%)
$AlCl_3$	3.54	73	44	1.86	77	42
$FeCl_3$	2.10	72	43	1.18	72	22

[a] 3 mol% of catalyst, 150 °C, the reaction time was adjusted to compare data at the same conversion. [b] Initial pH of the solution after addition of the catalyst. [c] Initial pH of the solution after pre-heating metal chlorides in water for 30 min at 165 °C.

expected, in both cases, an important drop in the pH was observed after heating in water which is in accordance with a partial hydrolysis of metal chlorides accompanied by the release of HCl in the medium. Note that the measured pHs were in the same range between $AlCl_3$ and $FeCl_3$ suggesting that the higher activity of $AlCl_3$ cannot be ascribed to a greater acidity. However, noticeable visual differences were observed between pre-heated aqueous solutions of $AlCl_3$ and $FeCl_3$. Whereas the solution remained homogeneous in the case of $AlCl_3$, we clearly observed the formation of a rust-coloured precipitate in the case of $FeCl_3$ which was attributed to the formation of hydrated iron oxide as supported by Raman and XRD analyses (see ESI, Fig. S4 and S5†) (Fig. 1). Hence, we suspected here that the lower efficiency of $FeCl_3$ might be ascribed to the precipitation of iron oxide species during the reaction resulting in a dramatic decrease of the glucose/fructose isomerization rate to the benefit of side reactions catalyzed by released HCl. To further support this hypothesis, ChCl and glucose were added to the pre-heated aqueous solution of $AlCl_3$ and $FeCl_3$. Whereas a similar yield of HMF was recovered using a pre-heated aqueous solution of $AlCl_3$, the selectivity to HMF was dramatically decreased in the case of $FeCl_3$ further demonstrating that precipitation of iron oxide species has a detrimental effect on the catalyst activity and selectivity. Note that when ChCl was added during the pre-heating step of metal chlorides in water, a rust-coloured precipitate was also observed from $FeCl_3$ while all species remained soluble with $AlCl_3$ suggesting that ChCl did not prevent the deactivation of $FeCl_3$.

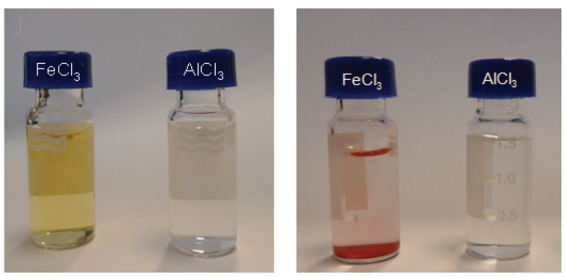
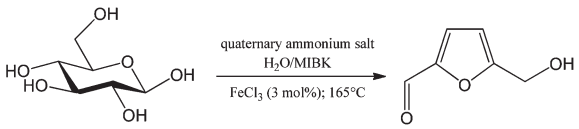


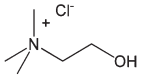
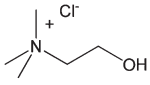
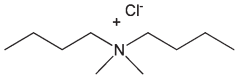
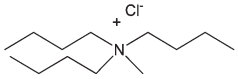
Fig. 1 Pictures of the solution of $FeCl_3$ and $AlCl_3$ (a) before and (b) after heating in water at 165 °C.

Role of ChCl

To collect more information on the synergistic role of ChCl and water in our system, the reaction was carried out without ChCl either in neat 1-butyl-3-imidazolium chloride or in neat water. All reactions were performed at 165 °C (250 W under microwaves) with a glucose loading of 10 wt% and a H_2O/MIBK ratio of 2/2. Although $AlCl_3$ is more stable than $FeCl_3$ in our conditions, $FeCl_3$ has been selected in the following experiments mainly because this metal chloride is generally considered as a poorly active catalyst in such reactions. Hence, $FeCl_3$ appears as a good candidate to clearly highlight the promoting effect of ChCl on the catalyst selectivity. In the absence of ChCl, HMF was produced with a very low yield of 9% and 1% in [BMIM]Cl and in neat water, respectively, and an important formation of black materials was observed (Table 4, entries 2, 3). Similarly, when the catalytic reaction was conducted without water in a ChCl–DMSO mixture, HMF was produced with only 1% yield (Table 4, entry 4) suggesting that combination of ChCl with H_2O is one of the key factors explaining the selectivity improvement observed with $FeCl_3$. ChCl was also replaced by other water soluble quaternary ammonium salts to confirm its effect on the reaction selectivity. In this case, the amount of salt was adjusted to keep constant the mol% of salt introduced into water. Reactions were

Table 4 Effect of various salts on the acid-catalyzed dehydration of glucose to HMF[a]



Entry	Salt	Reaction media	Conv. glucose (%)	HMF molar yield (%)
1		H_2O	58[b]	33
2	—	[BMIM]Cl	87[b]	9
3	—	H_2O	15[b]	1
4		DMSO	45[b]	1
5		H_2O	57[b]	18
6		H_2O	50[c]	12
7	NaCl	H_2O	56[b]	15

[a] $FeCl_3$, 3 mol%, 165 °C, 10 wt% of glucose; [b] 15 min; [c] 30 min.

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all stopped and compared at a conversion range of 50–60% to evaluate the role of choline on the HMF selectivity. When ChCl was replaced by dimethyldibutylammonium chloride, methyltributylammonium chloride or NaCl, the yield of HMF dramatically dropped to 18%, 12% and 15%, respectively (*vs.* 33% with ChCl, Table 4, entry 1). Additionally, when ChCl was replaced by ethanol, the selectivity of the reaction was shifted towards the formation of fructose (18% yield at 63% conversion) in agreement with the recent work of Riisager.[13] From these results, one may also conclude that both the –OH and ammonium groups of ChCl play a crucial role in the reaction mechanism.

To get more insight into the role of ChCl in such a catalytic reaction, we carried out additional experiments. ChCl is capable of producing eutectic mixtures with hydrogen bond donors such glucose or fructose.[14] In a first approximation, one may suspect that, in water, ChCl interacts stronger with fructose than with glucose thus facilitating the isomerization of glucose to fructose. By means of calculations (see ESI†), we found that the total energy of the solutions, including terms due to the solutes (sugars), the solvent (ChCl–H_2O) and also solute–solvent interactions, was similar between the glucose/ChCl–H_2O and fructose/ChCl–H_2O systems. Additionally, decomposition of the energy into different terms, either by nature (electrostatic, van der Waals, intramolecular) or by component (solute, solvent), gave very close values for the two systems. Hence, from these results, one may conclude that the two systems have a similar energy and thus rule out the possible "assisting role" of ChCl in the glucose/fructose isomerization step.

Considering that the yield of HMF is optimal at a ChCl–H_2O ratio of 1/1, we next focused our attention on the partition coefficient of HMF in these biphasic systems. Dumesic and coworkers have previously shown that a "continuous" extraction of HMF from the aqueous phase allowed its side reactions with water or hexoses (*i.e.* rehydration to levulinic and formic acids, condensation to humins, *etc.*) to be limited.[15] To this end, we reproduced the composition of the reaction media obtained at the end of the reaction (see composition entry 9 of Table 2). In a typical experiment, HMF (a quantity equivalent to 70% yield) was heated in a biphasic water/MIBK system (each phase = 10 mL) at 100 °C for 10 min. The MIBK and aqueous phase were then separated and analyzed by HPLC. The partition coefficient was defined as the mass ratio between the amount of HMF detected in the MIBK and water phases, respectively. Then, the same experiments were reproduced by progressively substituting water by ChCl. The result of this study is presented in Fig. 2.

Interestingly, up to a ChCl content of nearly 50 wt%, the partition coefficient did not significantly vary and remained around 1.2 (*i.e.* about 53 wt% of HMF was extracted with MIBK). Conversely, at a higher ChCl content, the partition coefficient significantly and continuously decreased up to 0.6 (*i.e.* about 38 wt% of HMF in the MIBK phase) at a ChCl content of 80 wt%. This result suggests that, at a ChCl content higher than 50 wt%, HMF is strongly retained in the aqueous

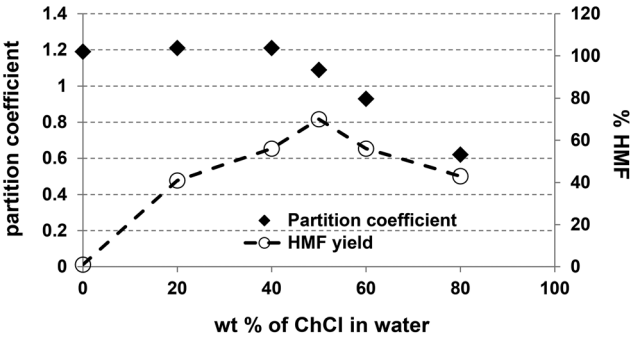

Fig. 2 Partition coefficient of HMF in biphasic ChCl–H_2O/MIBK systems and HMF yield (see the conditions in Table 2, entry 9) as a function of the ChCl concentration.

phase, presumably through hydrogen bond interaction. As a consequence, in this scenario, side reactions of HMF with water (and hexoses) should be more favourable and should result in a drop in the reaction selectivity which is consistent with our experimental observation.

Although consideration of the partition coefficients allowed explaining the behaviour of our system at high loading of ChCl, it does not explain why the selectivity to HMF was increased when the ChCl content was concomitantly raised from 0 to 50 wt% (in this range of concentration, the partition coefficients are similar, Fig. 2). Recently, K. Binnemans and R. Van Deun have investigated the speciation of copper chlorides in ChCl–water mixtures.[16] This work clearly showed by EXAFS, electrochemical measurements and crystallography that the environment of the cupric ion is modified according to the amount of ChCl in water. At a water concentration of 39 wt% in ChCl, ChCl is coordinated on copper while at a concentration higher than 95%, the cupric ion is fully hydrated. At an intermediate water/ChCl composition, mixed chloro–aquo complexes are dominant species. Inspired by data from the current literature and by our experimental results, we propose here a plausible explanation for rationalizing our results. At a ChCl content lower than 50 wt%, metal hydroxide species are produced in water which is accompanied by the release of HCl. The coordination sphere of these metal hydroxide species may be modified by increasing the amount of ChCl in the reaction medium as previously shown by K. Binnemans and R. Van Deun. Note that the possible role of ChCl as a ligand is consistent with our above-described experiments summarized in Table 4. In particular, by increasing the concentration of ChCl in water, the nature and concentration of catalytic species in the reaction medium might change which would be consistent with a change in the selectivity to HMF. Concomitantly, the possible extraction of HMF from the aqueous phase with MIBK allowed limiting side reactions of HMF with water and hexoses. In this context, the best selectivity to HMF was obtained in a biphasic aqueous solution of ChCl (50 wt%)/MIBK. At a ChCl content higher than 50 wt%, strong molecular interaction between ChCl and produced HMF became dominant and HMF was more strongly retained in the

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aqueous phase. As a consequence, HMF is subjected to side reactions with water or hexoses leading to a drop in the reaction selectivity. Note that this hypothesis is supported by our recent findings that suggested the formation of a possible DES between HMF and ChCl.[17] Hence, one may conclude that 50 wt% of ChCl in water is an acceptable compromise between the catalyst activity/selectivity and the extraction of HMF from the aqueous phase.

One should comment that when all the above-described reactions were performed in conventional heating, HMF was produced with a much lower selectivity (in this case insoluble black materials were produced in a higher amount) whatever the reaction conditions (temperature, time, fructose and catalyst loading, *etc.*). In conventional heating, it has been previously demonstrated that the isomerization rate of glucose to fructose was nearly 4 times lower than the dehydration rate of fructose to HMF.[18] Because of the relative instability of HMF under aqueous acidic conditions, it is clear that the production of HMF is in competition with its own degradation, rehydration or condensation. Although we are fully convinced that microwaves also contributed to better control of the reaction selectivity, all attempts to identify which elementary step was affected by microwaves to a greater extent unfortunately failed, mainly due to the complexity of the system. Note that during the course of our investigations, a similar observation has been reported by Rinaldi, Dumesic and co-workers.[19]

Recyclability of the system

Having all these results in hand, we then evaluated the recyclability of the ChCl–H_2O phase containing the acid catalyst. Recycling experiments were performed at 150 °C for 15 min in the presence of 3 mol% of $AlCl_3$. In all cases, MIBK was added to continuously extract HMF from the reaction media (ChCl–H_2O/MIBK ratio = 2–2/2). After the first catalytic run, the reaction medium was cooled down to room temperature and decanted. The MIBK phase was separated and the aqueous phase containing ChCl and $AlCl_3$ was washed again with MIBK to ensure the complete removal of HMF from the catalytic phase. Then, glucose was directly added to the catalytic phase and heated for another 15 min at 150 °C. One can see from Fig. 3 that the yield of HMF remained constant during at least three consecutive recyclings. After the third recycling, the yield of HMF however continuously dropped, mainly due to the accumulation of impurities in the catalytic phase. After the fifth run, we attempted to recover ChCl to reuse it. To this end, the reaction medium was diluted with 20 mL of water, resulting in the precipitation of black materials which were filtered off. Water was then evaporated and the recovered residue was dried overnight at 150 °C prior to being extracted with ethanol. After removal of ethanol under reduced pressure, ChCl was recovered (>90 wt%) with sufficient purity to be reused (see Fig. S6† for copies of NMR spectra). Indeed, after extraction and reuse of ChCl, a yield of HMF of 60% was recovered demonstrating the relative stability of ChCl under our working conditions.

Transposition to cellulose

Encouraged by all these results, we then attempted the direct conversion of cellulose to HMF which is an even more challenging reaction. This cascade reaction requires first a hydrolysis of cellulose to glucose followed by the isomerization/dehydration of glucose to HMF (Fig. 4). Reactions were first performed at 200 °C (under microwave irradiation) in the presence of 4 wt% of $FeCl_3$ or $AlCl_3$ for 5 min. Microcrystalline cellulose (PH AVICEL 101) was used in all experiments. Interestingly, in the absence of ChCl, cellulose was selectively converted to glucose (41% yield) in the presence of $FeCl_3$ whereas $AlCl_3$ afforded glucose, HMF and levulinic acid in 2%, 8% and 3% yield respectively (along with many other side products) (Table 5, entries 1, 2). This difference in selectivity between $FeCl_3$ and $AlCl_3$ is consistent with our previous observations. During the reaction with $FeCl_3$, iron hydroxide precipitated (in the form of hydrated iron oxides) from the reaction media leading to an important release of HCl in the solution, a Bronsted acid known to efficiently catalyze the depolymerization of cellulose to glucose. Conversely, from $AlCl_3$, all species (HCl and aluminium hydroxides) remained soluble and, without ChCl, the reaction suffered from an important lack of selectivity.

Next, ChCl was added to a solution containing $FeCl_3$ and cellulose. In this case, the selectivity of the reaction was changed and glucose was produced with 26% yield along with

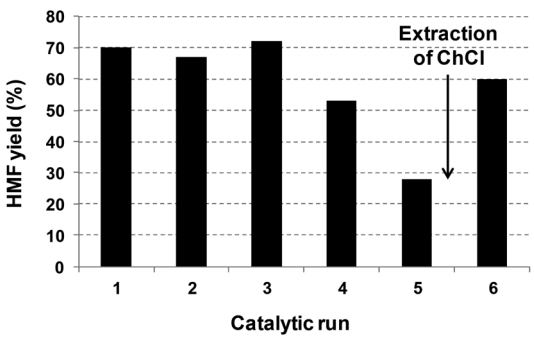

Fig. 3 Recycling experiments (150 °C, 15 min, 3 mol% of $AlCl_3$, ChCl–H_2O/MIBK ratio = 2–2/2).

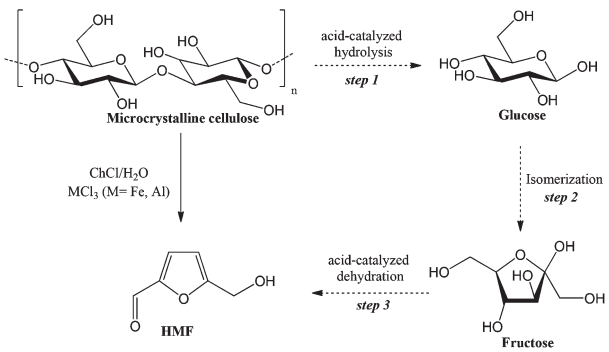

Fig. 4 Catalytic conversion of cellulose to HMF in an aqueous solution of ChCl containing $FeCl_3$ and $AlCl_3$.

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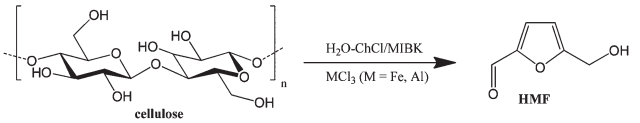
Table 5 Catalytic conversion of cellulose to HMF in an aqueous solution of ChCl



Entry	Cellulose crystallinity	Catalyst	ChCl	Glucose molar yield (%)	HMF molar yield (%)
1	High[a]	$FeCl_3$	No	41	6
2	High[a]	$AlCl_3$	No	—	8[b]
3	High[a]	$FeCl_3$	Yes	26	17
4	High[a]	$AlCl_3$	Yes	—	14[c]
5	High[a]	$FeCl_3/AlCl_3$[d]	Yes	—	27
6	Low[e]	$FeCl_3$	No	70	7
7	Low[e]	$FeCl_3/AlCl_3$[d]	Yes	—	49

[a] Microcrystalline cellulose PH AVICEL 101. [b] Along with 2% of glucose and 3% of levulinic acid. [c] Similar yields were obtained with $CrCl_2$ (17% yield). [d] Reaction was performed in two steps. First, 200 °C for 5 min in neat water containing 4 wt% (*vs.* cellulose) of $FeCl_3$ followed by the addition of 3 mol% of $AlCl_3$ (*vs. in situ* produced glucose) and 50 wt% of ChCl (heating at 135 °C for 90 min). [e] Cellulose with low crystallinity index was obtained by a ball-milling or a dissolution/regeneration from 1-butyl-3-imidazolium chloride. Note that similar results were obtained whatever the pre-treatment.

17% yield of HMF, further demonstrating the beneficial effect of ChCl for the production of HMF (Table 5, entry 3). Note that the reaction selectivity was more difficult to control from cellulose than from glucose. Under such conditions, HMF was indeed also readily converted to levulinic and formic acids. A similar trend was also observed using $AlCl_3$ and $CrCl_2$ (14% and 17% yield of HMF, respectively, entry 4).

To increase the selectivity to HMF, cellulose was first heated in the presence of $FeCl_3$ (hydrolysis of cellulose to glucose) prior to adding $AlCl_3$ (conversion of glucose to HMF). As observed above, glucose was produced with 40% yield in the presence of $FeCl_3$ only. Then $AlCl_3$ was directly added to the solution (without intermediate purification) and the resulting mixture was heated at 135 °C for 90 min. Interestingly, in this case, the *in situ* produced glucose was converted to HMF with a similar selectivity (68%) as that described above from glucose leading to HMF with a yield of 27% (Table 5, entry 5). Please note that combination of HCl and $AlCl_3$ did not provide similar results suggesting that $FeCl_3$ still participates to some extent in the conversion of glucose to HMF. To further increase the yield of HMF, microcrystalline cellulose was subjected to a pre-treatment process prior to its catalytic conversion to HMF. To this end the crystallinity index of microcrystalline cellulose was decreased either by dissolution/regeneration in 1-butyl-3-methylimidazolium chloride ([BMIM]Cl) or by ball-milling. As expected, after these two pre-treatments, cellulose was found to be much less recalcitrant. During the first step in the presence of $FeCl_3$, cellulose was deconstructed to glucose with a yield of 70% *versus* 40% without pre-treatment (Table 5, entry 6). Then, after addition of $AlCl_3$, *in situ* produced glucose was readily converted to HMF with 49% yield (*i.e.* 70% selectivity) (Table 5, entry 7). Although the large energy input required by the pre-treatment of cellulose by ball-milling or by dissolution in ionic liquids nowadays represents a major drawback, coupling of our methodology with a recent work reported by F. Schüth[20] in the field of mechanocatalytic deconstruction of cellulose to water soluble cello-oligomers may open a more eco-efficient route for the production of HMF from cellulose.

Conclusion

We report here that ChCl can be considered as a safe and cheap additive capable of assisting the catalytic conversion of glucose to HMF in water. Under the optimized conditions, HMF was produced with 70% yield which is a competitive yield to those traditionally obtained in imidazolium-based ionic liquids in the presence of hazardous chromium salts. Screening of various Lewis acids revealed that ChCl has the ability to improve the selectivity of various safe and abundant metal chlorides such as $AlCl_3$, $FeCl_3$ and $CuCl_2$, thus increasing the sustainability of this process. It should be noted that the promoting effect of ChCl on HMF selectivity is however closely dependent on the ChCl content. Although the exact the reaction mechanism involved in the presence of ChCl is difficult to determine with accuracy at this stage, we suggest that at a ChCl content lower than 50 wt% in water, the selectivity is governed by (1) the coordinating ability of ChCl that presumably modifies the nature and the concentration of catalytic species in water, and (2) the extraction of HMF from the aqueous phase, thus limiting side reactions of HMF with water or hexoses. At a ChCl content higher than 50 wt%, strong molecular interaction between HMF and ChCl became dominant making extraction of HMF from the aqueous phase more difficult which resulted in a decrease of the reaction selectivity.

The scientific strategy of this work can be transposed to the direct production of HMF from cellulose which is a much more challenging reaction. In this case, combination of $FeCl_3$ and $AlCl_3$ allowed cellulose to be converted to HMF with 49% yield in a one pot process.

From the viewpoint of sustainable chemistry, this work shows noticeable advantages such as the use of (1) water as a solvent, (2) ChCl as a cheap and safe additive, (3) cheap and naturally abundant metals (Al, Fe, and Cu), and (4) renewable raw materials. We do believe that this work, together with the recent progress reported in the field of process intensification (including biphasic catalysis), will definitely contribute to increasing again the eco-efficiency and sustainability of this route.

Experimental section

Chemicals

Fructose, glucose, choline chloride and methylisobutylketone (MIBK) were purchased from Sigma Aldrich as well as

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anhydrous and hydrated Lewis acids. All chemicals were used as received without further purification. Microcrystalline cellulose PH AVICEL 105 was purchased from FMC BioPolymer (degree of polymerization about 250, glucose content >99%, water content = 5 wt%, particle size <40 μm). Distilled water was used as in all catalytic reactions.

Catalytic experiments

All reactions were performed using an automated multimode microwave oven MicroSynth from Milestone s.r.l. (Italy). This oven operates at 2.45 GHz and is temperature controlled using a fiberoptic sensor. Temperature was monitored by inserting the calibrated fiberoptic sensor into the reaction mixture while stirring properly. The maximum power input could be adjusted between 0 and 1000 W. Under microwave heating, the internal temperature of the reaction vessel reached the reaction set-points in 20 min, and was maintained at ±5 °C using a power compensation feedback control.

Catalytic conversion of glucose to HMF

In a typical experiment, 0.4 g of glucose was dissolved in 2 g of water containing 2 g of ChCl and 3 mol% of a Lewis acid. Then 2 g of MIBK were added and the biphasic solution was heated under microwaves (250 W) at the desired temperature for 1–60 min (see the tables for conditions).

Recycling procedure

At the end of the reaction (conditions: 10 wt% of glucose, 3 mol% of $AlCl_3$, T = 150 °C, 15 min, 6 g of ChCl–H_2O/MIBK (ratio 2–2/2)), the reaction was cooled down to room temperature and the MIBK phase containing the HMF was separated by decantation. Next, the catalytic phase was washed two times with 2.5 mL of MIBK to remove the residual HMF. Then, glucose was added to the catalytic phase and the reaction was heated again at 150 °C for 15 min.

Catalytic conversion of cellulose to HMF

200 mg of cellulose was first suspended in 2 mL of water containing 18 mg of $FeCl_3$. The solution was then heated under microwaves (250 W) for 5 min at 200 °C. Then the reaction was cooled down and 16 mg of $AlCl_3$, 2 g of ChCl and 2 mL of MIBK were directly added to the solution. The mixture was then heated for 30–180 min at 120–135 °C under microwaves (250 W).

Analytical

The conversion of glucose was calculated by external calibration using a Shimadu Prominence LC equipped with a degasser DGU-20A3, a pump system (5LC-20AQ), a thermostated autosampler SIL-20AC and an oven CTO-20AC maintained at 40 °C. Glucose was separated on a Shodex KS-802 column using water as an eluent and quantified by an RID. Yields of HMF were determined by external calibration at 25 °C using an HPLC equipped with a Nucleosil 100–5C18 column (250 × 4.6 mm), a Shimadzu LC-20AT pump, a Shimadzu RID-10A detector, and an acetonitrile–water (10 : 90) mixture in mobile phase (0.8 mL min^{-1}).

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Notes and references

1 P. T. Anastas and J. C. Warner, in *Green Chemistry-Theory and Practice*, Oxford University Press, New York, 1998.
2 (*a*) M. E. Zakrzewska, E. Bogel-Lukasik and R. Bogel-Lukasik, *Chem. Rev.*, 2001, **111**(2), 397–417; (*b*) J. Lewkowski, *ARKIVOC*, 2001, **2**, 17–54; (*c*) T. Ståhlberg, W. Fu, J. M. Woodley and A. Riisager, *ChemSusChem*, 2011, **4**(4), 451–458; (*d*) A. A. Rosatella, S. P. Simeonov, R. F. M. Frade and C. A. M. Afonso, *Green Chem.*, 2011, **13**, 754–793.
3 For representative selected works see: M. Molinier, Y. Roman-Leshkov and M. E. Davis, *Proc. Natl. Acad. Sci. U. S. A.*, 2010, **107**(14), 6164–6168.
4 For selected works see: (*a*) R. O. L. Souza, P. D. Fabiano, C. Feche, F. Rataboul, D. Cardoso and N. Essayem, *Catal. Today*, 2012, **195**(1), 114–119J; (*b*) S. Yu, E. Kim, S. Park, I. K. Song and J. C. Jung, *Catal. Commun.*, 2012, **29**, 63–67; (*c*) B. Y. Yang and R. Mongomery, *Carbohydr. Res.*, 1996, **280**(1), 27–45.
5 For an example see: (*a*) S. Bhosale, M. Rao and V. Deshpande, *Microbiol. Rev.*, 1996, **60**(2), 280–300; (*b*) H. Yu, Y. Guo, D. Wu, W. Zhan and G. Lu, *J. Mol. Catal. B: Enzym.*, 2011, **72**(1–2), 73–76; (*c*) A. M. Dehkordi, M. S. Tehrany and I. Safari, *Ind. Eng. Chem. Res.*, 2009, **48**(7), 3271–3278.
6 For a recent work see: P. M. Grande, C. Bergs and P. Dominguez de Maria, *ChemSusChem*, 2012, **5**(7), 1203–1206; and references cited therein.
7 H. Zhao, J. E. Holladay, H. Brown and Z. C. Zhang, *Science*, 2006, **316**, 1597–1599.
8 (*a*) Q. Zhang, K. De Oliveira Vigier, S. Royer and F. Jérôme, *Chem. Soc. Rev.*, 2012, **41**, 7108–7146; (*b*) A. P. Abbott, J. C. Barron, K. S. Ryder and D. Wilson, *Chem.–Eur. J.*, 2007, **13**, 6495–6501; (*c*) D. Carriazo, M. C. Serrano, M. C. Gutierrez, M. L. Ferrer and F. del Monte, *Chem. Soc. Rev.*, 2012, **1**(14), 4996–5014; (*d*) P. D. de Maria and Z. Maugeri, *Curr. Opin. Chem. Biol.*, 2011, **15**(2), 220–225.
9 F. Liu, K. De Oliveira Vigier, M. Pera-Titus, Y. Pouilloux, J.-M. Clacens, F. Decampo and F. Jérôme, *Green Chem.*, 2013, **15**, 901–909.
10 J. T. Gorke, F. Srienc and R. J. Kazlauskas, *Chem. Commun.*, 2008, 1235–1237.
11 Y. J. Pagán-Torres, T. Wang, J. M. R. Gallo, B. H. Shanks and J. A. Dumesic, *ACS Catal.*, 2012, **2**, 930–934.

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12 For a very recent work see: V. Choudhary, S. H. Mushrif, C. Ho, A. Anderko, V. Nikolakis, N. S. Marinkovic, A. I. Frenkel, S. I. Sandler and D. G. Vlachos, *J. Am. Chem. Soc.*, 2013, **135**, 3997–4006 and references cited therein.
13 S. Saravanamurugan, M. Paniagua, J. A. Melero and A. Riisager, *J. Am. Chem. Soc.*, 2013, **135**(14), 5246–5249.
14 F. Ilgen, D. Ott, D. Kralish, C. Reil, A. Palmberger and B. König, *Green Chem.*, 2009, **11**, 1948–1954.
15 For a selected comprehensive review from the authors see: S. G. Wettstein, D. Martin Alonso, E. I. Gürbüz and J. A. Dumesic, *Curr. Opin. Chem. Eng.*, 2012, **1**, 218–224 and references cited therein.
16 P. De Vresse, N. R. Brooks, K. Van Hecke, L. Van Meervelt, E. Matthijs, K. Binnemans and R. Van Deun, *Inorg. Chem.*, 2012, **51**, 4972–4981.
17 F. Liu, J. Barrault, K. De Oliveira Vigier and F. Jérôme, *ChemSusChem*, 2012, **5**(7), 1223–1226.
18 (*a*) Y. Yang, C.-W. Hu and M. M. Abu-Omar, *ChemSusChem*, 2012, **5**, 405; (*b*) Y. Yang, C.-W. Hu and M. M. Abu-Omar, *Green Chem.*, 2012, **14**, 509.
19 R. Carrasquillo-Flores, M. Käldstöm, F. Schüth, J. A. Dumesic and R. Rinaldi, *ACS Catal.*, 2013, **3**, 993–997.
20 N. Meine, R. Rinaldi and F. Schüth, *ChemSusChem*, 2012, **5**, 1449–1454.