The Activity of a Heterogeneous Catalyst in Deep Eutectic Solvents: the Case of Carbohydrate Conversion into 5-Hydroxymethylfurfural

*Salvatore Marullo, Carla Rizzo and Francesca D'Anna**

Università degli Studi di Palermo, Dipartimento di Scienze Biologiche, Chimiche e Farmaceutiche,
Viale delle Scienze, Ed. 17, 90128 Palermo, Italia

*Corresponding author: Prof. F. D'Anna. E-mail: francesca.danna@unipa.it

Abstract

Obtaining industrially relevant products from renewable resources and developing processes under the light of sustainable chemistry, is a prominent endeavor of present-day chemical research. In this context, herein we investigated the dehydration of fructose and sucrose in deep eutectic solvents, promoted by the ion exchange resin Amberlyst 15 as heterogeneous catalyst. We optimized the reaction conditions in terms of temperature, catalyst loading and initial amount of substrate. Then, we looked at the effect of structural variations in the solvent components, on the reaction outcome. Under the best experimental conditions, we obtained very good yields of 78 % at 60 °C and 69 % at 80 °C for fructose and sucrose, respectively. Our catalytic system could also be reused for at least five cycles without loss in yield. Finally, this study evidenced what structural features in the solvent components lead to the highest yields.

Keywords: Deep Eutectic Solvents, Amberyst 15, Carbohydrates, 5-HMF, Catalyst Recycling.

Introduction

Contemporary society is currently facing pressing environmental challenges, like the depletion of fossil fuels and their environmental impact. Replacing fossil fuels with renewable and low impacting energy sources, has geared research towards the conversion of vegetable biomass into industrially relevant products.[1-4] Biomass is indeed abundant, cheap, safe and readily available since it derives also from the waste of agricultural industry.[5] A relevant fraction of vegetable biomass is composed by cellulose and carbohydrate-rich materials. Hence, the conversion of carbohydrates into value added products, also known as chemical platforms, provides a viable route to tackle this problem.[6] One of the most important biomass-derived chemical platforms is 5-hydroxymethylfurfural (5-HMF). This latter is indeed a quite versatile compound which, owing to the presence of both a hydroxyl and aldehydic group, can give synthetic access to a range of industrially relevant products via reduction, oxidation, etherification and polymerization processes.[7] For this reason, considerable effort is currently being put on the efficient transformation of mono- and polysaccharides into 5-HMF. Among these processes, the most studied, and generally the easiest, is the obtainment of 5-HMF from fructose. Although from a stoichiometric point of view the reaction looks quite simple, *i.e.* the formal elimination of three water molecules from fructose, the mechanism is actually quite articulated and can involve acyclic or cyclic intermediates.[8,9] The conversion of glucose and polysaccharides is even more complicated, since for glucose a first isomerization step to fructose is required, while polysaccharides must first be hydrolyzed into their monosaccharide units. Furthermore, the reaction is promoted by acidic catalysts. Conventional methods require quite harsh conditions, with high temperatures coupled with strong mineral acids or Lewis acidic metal salts as catalysts.[10] This entails the use of potentially corrosive reaction media.

A common drawback of these methods is that such conditions can also promote the degradation of 5-HMF into decomposition products like formic or levulinic acids, as well as the formation of dark colored, polymeric species called humins.[11] These considerations highlight the necessity to find milder reaction conditions, ensuring proper consideration of the process sustainability.

Among the crucial factors to achieve this goal, the solvent and the catalyst are of paramount importance. In particular, the exploration of catalysts effective under relatively mild conditions has brought out heterogeneous catalysts like nanoporous zeolites[12] and acidic ionic exchange resins,[13] which allow obtaining high selectivities in 5-HMF, thus minimizing the occurrence of side reactions. Another important advantage of heterogeneous catalysts is their easy separation from the reaction mixture and often recyclability.

Regarding the solvent, one of the most commonly used is DMSO or its biphasic systems.[10] However, a large body of work has shown that non-conventional solvents like ionic liquids (ILs), enable the obtainment of high yields and selectivity in 5-HMF.[14,15] Owing to their negligible vapor pressure and low flammability, ILs are often safer and more environmentally friendly than common organic solvents.[16,17] In the context of biomass conversion and processing, a distinct advantage of ILs over conventional solvents is their high solubilizing power toward cellulose and polysaccharides, largely due to their ability to disrupt intra- and intermolecular hydrogen bonds.[18] Furthermore, due to the wide possibility of tuning their properties by changing the nature and charge of ions,[19,20] by functionalization with reactive moieties[21,22] or by mixing,[23-27] ILs prove fit to this task.[28]

The most recent development in the field of non-conventional solvents is represented by Deep Eutectic Solvents (DES).[29-31] These are mixtures which, at a particular composition, display a definite melting point, lower than those of each individual component. This behavior occurs as a consequence of the establishment of a network of hydrogen bonds between a hydrogen bonding accepting component (HBA) and a hydrogen bonding donating one (HBD). Oftentimes, they are also liquid at room temperature and generally share many physico-chemical properties with ILs, such as low volatility and flammability.

Notably, their preparation requires only the mixing of components, without any synthetic or purification steps. Furthermore, their components are often cheap, readily available, with low or negligible toxicity, although recent reports suggest that the toxicological behavior of DES might be different from that of individual components.[32] Following this criterion, DES featuring all components of natural origin are labelled as NADES.[33-35] Hence, DES make suitable candidates to be used as sustainable solvents for the processing and valorisation of lignocellulosic biomass.[36] In particular, after the seminal paper by König,[37] most works have focused on the conversion of monosaccharides in choline chloride-based DES,[38,39] using catalysts like HCl,[40] organic acids,[41,42] or heteropolyacids.[43] In other cases, DES have proven suitable for the obtainment of 5-HMF from biomass hydrolisate[44] and sunflower stalk.[45] In this context, we have previously obtained high yields in 5-HMF from carbohydrates in IL mixtures under heterogeneous and homogeneous conditions employing relatively low temperatures and the resin Amberlyst 15[46] as well as zeolites[47] or functionalized ILs as catalysts.[47]

Bearing all this in mind, we herein report a study of the dehydration of fructose and sucrose in eight DES. In particular, three of them differ for the HBA, namely tetrabutylammonium chloride:ethylene glycol 1:2 (Bu_4NCl:EG), tetrabutylphosphonium chloride:ethylene glycol 1:2 (Bu_4PCl:EG) and choline chloride:ethylene glycol 1:2 (ChCl:EG). The remaining five are ChCl-based DES at 1:1 or 1:2 composition, bearing different HBD comprising polyalcohols, like glycerol (Gly; 1:2) or mono- and dicarboxylic acids, namely lactic acid (LA; 1:2), malic acid (MA; 1:1) and glutaric acid (GA; 1:1, Chart 1) Furthermore, we also considered a phenol-based DES, ChCl:PhOH, 1:3 to study the effect of a DES with an aromatic HBD (Chart 1). The acidic ion exchange resin Amberlyst 15 was used as heterogeneous catalyst. In ionic media, Amberlyst 15 acts as an acidic catalyst by exchanging cations with protons, which are thus released in solution.[48]

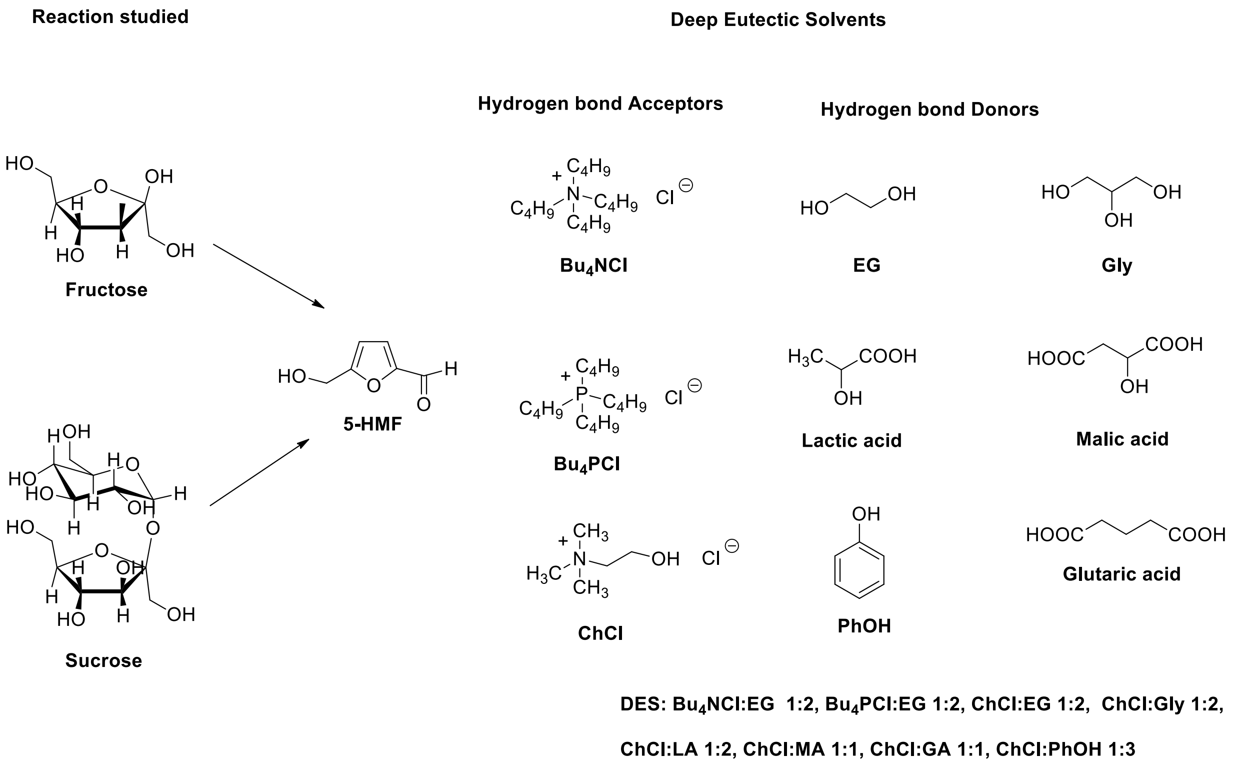


Chart 1. Reaction studied and DES used.

We investigated the effect of operational parameters like catalyst loading, nature of the solvent and initial concentration of substrate, to find the optimal reaction conditions. We obtained very good yields in 5-HMF at relatively low temperatures, such as 78 % at 60 °C and 69 % at 80 °C for the dehydration of fructose and sucrose, respectively. Notably, these results are competitive or superior compared with those of other related systems reported in the literature for the same reactions. Finally, our catalytic system could be recycled at least five times without significant loss in yield. For the sake of simplicity, we will discuss the transformation of the two substrates separately.

Experimental section

Materials

Commercially available fructose, sucrose, choline chloride, tetrabutylammonium chloride, tetrabutylphosphonium chloride, ethylene glycol, glycerol, phenol, (±) malic acid, (±) lactic acid, glutaric acid and methyl orange were used without further purification. Amberlyst 15 (hydrogen form) was purchased and kept in a glass oven at 100 °C overnight under reduced pressure before usage.

General procedure for the preparation of DES

The suitable amount of each DES component was weighed in a round bottom flask. The resulting mixture was heated for 1h at 80 °C under stirring until formation of a limpid liquid phase.[49] The liquid obtained was dried under reduced pressure at 60 °C for 1 hour and kept in a dessiccator over calcium chloride.

Characterization of DES

^{1}H and ^{13}C NMR spectra of DES were recorded on a Bruker 300 MHz NMR spectrometer, in D_2O. FTIR spectra of DES were recorded on a Agilent Cary 630 FTIR instrument, on liquid films. FTIR spectra were processed with Spectragryph Software.[50] All FTIR and NMR spectra of DES are reported in Figures S1-S2.

General procedure for the carbohydrate dehydration in DES

For a typical reaction, 50 mg of fructose or 25 mg of sucrose, were added in a screw-capped vial to 1 g of the relevant DES and stirred at 80 °C for 30 minutes to achieve complete dissolution. The solution was then allowed to cool down at room temperature and the suitable amount of Amberlyst 15 was added. The resulting mixture was heated at the opportune temperature and kept under stirring. To analyze the reaction mixture composition, aliquots (~10 mg) were withdrawn at suitable times, weighed and diluted with 1 ml of methanol/water 75/25 mixture. This solution was further diluted with methanol to reach a formal concentration of 5-HMF ranging from $7\cdot10^{-6}$ M up to $7\cdot10^{-5}$ M. Then, the resulting solution was transferred in a quartz cuvette to record its UV-vis spectrum to determine the amount of 5-HMF formed. The concentration of 5-HMF was determined from the absorbance at 277 nm in the basis of a calibration curve previously determined.

To determine the amount of unreacted carbohydrates, an aliquot of the reaction mixture was dissolved in acetonitrile/water 80/20 v:v and injected in a HPLC system equipped with a LC-NH_2 column, using acetonitrile/water 80/20 as eluting mixture, with a flow of 0.8 mL/min. However, in all chromatograms the peaks of carbohydrates were not distinguishable from those of the DES components and their amounts could not be determined. Similar results were obtained also using a SUPELCOSIL-C18 column (methanol/water 80/20, 0.6 mL/min). Conversely, 5-HMF was eluted using a SUPELCOSIL-C18 column (methanol/water 80/20, 0.6 mL/min), after a retention time t_R = 5.0 min. Yields in 5-HMF determined by HPLC were in agreement with those measured by UV-vis spectroscopy within ± 3%.

Recycle of the DES

The reaction mixture was extracted with ethyl acetate (7 x 2 mL), then the residual extraction solvent was removed by evaporation under reduced pressure. To the resulting DES a fresh batch of carbohydrate was then added, and the reaction was carried out as described above. The amount of 5-HMF extracted was determined spectrophotometrically as described above.

UV-vis spectra of methyl orange in DES

Samples were prepared by employing a reported procedure.[51] A suitably concentrated solution of methyl orange was added in a vial and the solvent was removed by reduced pressure evaporation, and the appropriate amount of DES was added. To ensure complete dissolution the mixture was sonicated for 5 minutes. The concentration of methyl orange in each solution was $2 \cdot 10^{-4}$ M. The resulting solution was then transferred in a quartz cuvette (light path 0.2 cm) and thermostated at 25 °C before recording the UV-vis spectrum.

In situ ^1H *NMR analysis*

^{1}H NMR spectra were recorded on a 300 MHz spectrometer at 60 °C. Samples were prepared by mixing in a NMR tube, a solution containing 25 mg of fructose in 500 mg of ChCl:EG in the presence of 12.5 mg of Amberlyst 15. The sample was rapidly transferred into the chamber of the spectrometer and spectra recorded at selected times. A coaxial capillary tube loaded with d_6-DMSO was used for the external lock of the NMR magnetic field/frequency, and its signal at δ=2.56 ppm was used as the ^{1}H NMR external reference.

Results and Discussion

Dehydration of fructose in DES

Firstly, we performed preliminary catalytic tests to find the optimal reaction temperature. To this aim, we carried out the dehydration reactions in Bu_4NCl:EG, for 2 hours, using a substrate:catalyst mass ratio of 2:1 at 25 °C, 40 °C and 60 °C. From these experiments, we observed no detectable formation in 5-HMF at 25 °C. Furthermore, at 40 °C only a very low yield of 15% was obtained, whereas conducting the reaction at 60 °C afforded a much more satisfying yield, 58%. Based on these results, we employed a temperature of 60 °C to carry out the dehydration of fructose in DES.

Then, we set out to find the optimal catalyst loading. To this aim, we carried out the reaction in the presence of increasing amounts of Amberlyst 15, in Bu_4NCl:EG, at 60 °C, following the reaction until no significant increase in yield was detected. The results obtained are reported in Figure 1a and Table S1.

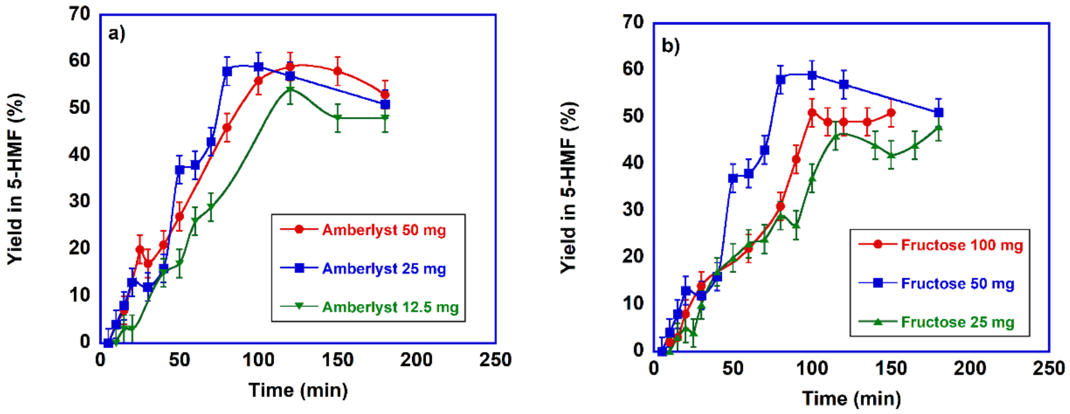


Figure 1. Yields in 5-HMF, as a function of time, obtained from fructose in Bu_4NCl:EG at 60 °C a) in the presence of increasing amounts of Amberlyst 15, using 50 mg of fructose, b) in the presence of 25 mg Amberlyst 15, using increasing initial amounts of fructose. Yields are reproducible within ± 3%. Lines are drawn as mere visual aid.

Inspection of Figure 1a, points out that going from 12.5 mg to 25 mg of Amberlyst 15, induced an appreciable increase in yield and dehydration rate. Conversely, further raising the catalyst loading to 50 mg, barely affects the yields. For these reasons, we chose 25 mg as the amount of Amberlyst 15 for the other reactions. Subsequently, we investigated the effect of the initial concentration of fructose. To this aim, we conducted the reaction varying the mass of the substrate and maintaining the same catalyst:substrate mass ratio (1:2). We performed these reactions in Bu_4NCl:EG, using 50 mg and 100 mg of fructose. Yields obtained as a function of time, are reported in Figure 1b and Table S2.

Inspection of the plots reported in Figure 1b, reveals that the best results were obtained using an initial amount of fructose of 50 mg, in which case we found a yield of 60% after 100 minutes. In the two other cases, the yield observed barely exceeded 50%. Accordingly, we used this initial amount of fructose to carry out the remaining reactions. To further evidence the advantage of using DES as reaction media over conventional organic solvents, we carried out the reaction, under the same experimental condition in typical solvents for this reaction like ethanol and DMSO. We obtained maximum yields of 13 % in DMSO and lower than 3% and in ethanol, which are much lower compared with the ones found in DES.

After setting the optimal reaction conditions, we proceeded to investigate the effect of the HBA component of the solvent media used, by carrying out the reactions in two other DES, Bu_4PCl:EG and ChCl:EG.

The results obtained are reported in Figure 2a and Table S3.

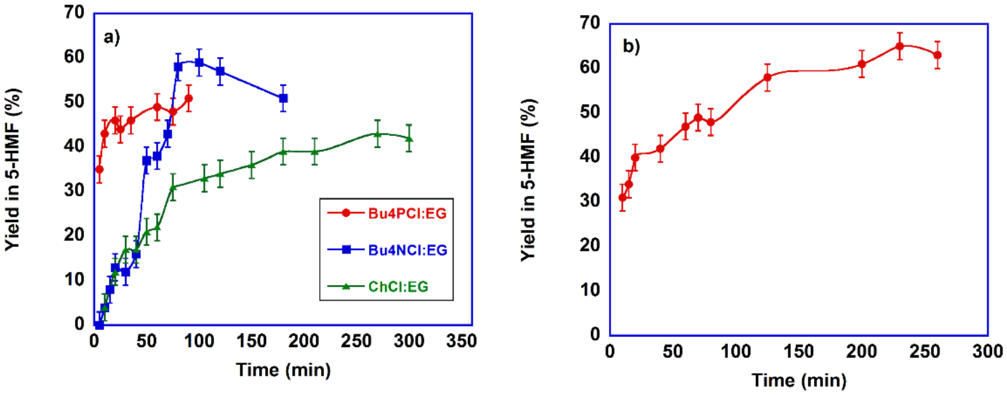


Figure 2. Yields in 5-HMF as a function of time obtained from fructose, at 60 °C, in a) DES differing for the HBA, in the presence of 25 mg of Amberlyst 15 and b) in Bu_4PCl:EG without catalyst. Yields are reproducible within ± 3%. Lines are drawn as mere visual aid.

A first glance at results reported in Figure 2a, reveals that using Bu_4NCl:EG as solvent, led to the highest yield in 5-HMF (60% in 100 minutes). In particular, the yields obtained in the three DES increase by following the order ChCl:EG < Bu_4PCl:EG < Bu_4NCl:EG (yields in 5-HMF amount to 40% in 250 minutes, 50% in 90 minutes in ChCl:EG and Bu_4PCl:EG, respectively). A closer inspection of the plot evidences a markedly different trend of yields as a function of the DES used. Indeed, in ChCl:EG yields increased smoothly, reaching a plateau value. On the contrary, in Bu_4NCl:EG a steep increase in yields led to a maximum value, which then dropped due to secondary reactions of 5-HMF with carbohydrates forming soluble humins, widely known to occur during acid catalyzed conversion of biomass to 5-HMF,[52,53] as witnessed by the browning of the reaction mixture (Figure S3). Finally, when the reaction is conducted in Bu_4PCl:EG, the yield exceeded 30% already after 2 minutes, and reached 50% after 50 minutes.

To gain further insight on this behavior, we conducted blank tests using the same reaction conditions, in all three DES, but in the absence of catalyst. While no dehydration occurred in solution of ChCl:EG and Bu_4NCl:EG, we observed formation of 5-HMF in solution of Bu_4PCl:EG. Based on this observation, we determined the yields in Bu_4PCl:EG as a function of time, obtaining the results reported in Figure 2b and Table S4. These show that the DES Bu_4PCl:EG is acidic enough to catalyze the reaction, leading to the obtainment of a yield in 5-HMF of 65% after 250 minutes. Furthermore, comparison with the results obtained in the presence of the resin, does not evidence significant differences. This can be explained by considering that the acidity generated by the catalyst is overwhelmed by the one of the DES, which is present in a much higher amount.

The inherent acidic behavior of Bu_4PCl:EG and closely related phosphonium-based DES, has been reported in the literature.[54,55] To further support this hypothesis, we recorded UV-vis spectra of solutions of the indicator methyl orange in each DES (Figure 3).

.

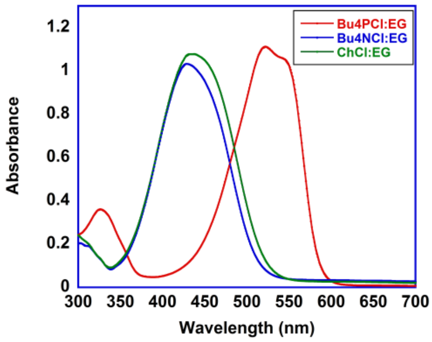


Figure 3. UV-vis spectra of methyl orange solutions ($2 \cdot 10^{-4}$ M) in the three DES.

These spectra evidence that when methyl orange is dissolved in Bu_4NCl:EG and ChCl:EG, λ_{MAX} is located at 435 nm, showing that the indicator is mainly present in solution in its non-protonated form.[56] Conversely, in solution of Bu_4PCl:EG, the absorption band shifts to 523 nm, suggestive of significant protonation of methyl orange.[57]

To obtain mechanistic information on the course of the fructose dehydration in DES, we carried out in situ ^{1}H-NMR measurements monitoring the dehydration of fructose into 5-HMF in a NMR tube in the presence of Amberlyst 15 and using ChCl:EG as solvent, under the same experimental conditions previously described. We chose to perform this experiment in ChCl:EG, because in this DES we observed the slowest reaction and, consequently, we reckoned it more suitable to follow the course of reaction by NMR. Magnified ^{1}H-NMR spectra recorded at selected times and their enlargements are reported in Figure 4.

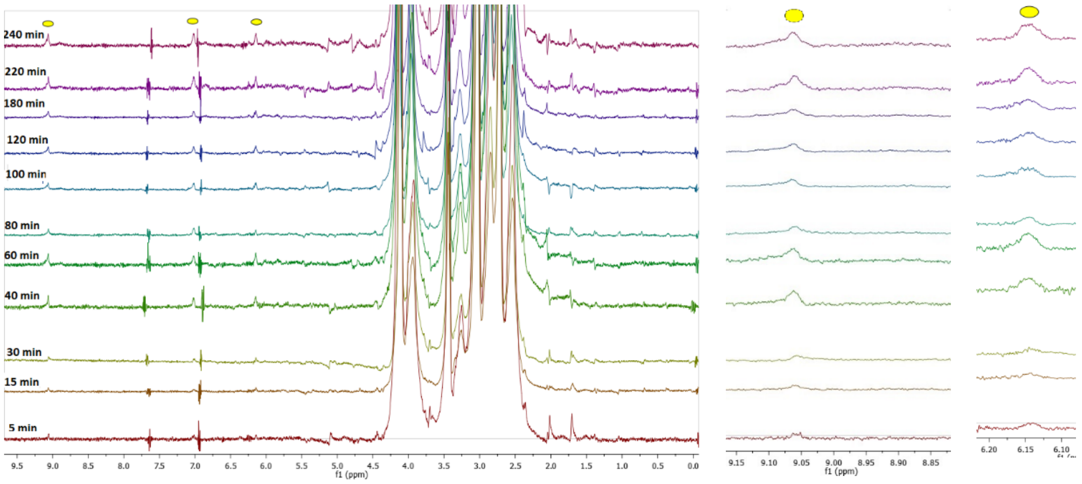


Figure 4. ^{1}H NMR spectra recorded for in situ conversion of fructose into 5-HMF in ChCl:EG, at 60 °C, at selected times (left), local enlargements of the chemical shifts region of 9.15-8.35 ppm (center) and 6.20-6.10 ppm (right).

From the spectra reported in Figure 4, we could observe only the occurrence and growth in intensity of the protons of 5-HMF, located at 9.07, 6.15 and 7.02 ppm with no obvious evidence of signals belonging to intermediates, suggesting their fast conversion into 5-HMF under the experimental conditions used. Using DES as solvent media, appears therefore to induce a faster conversion of intermediates compared to what we observed in IL mixtures, where the formation and conversion of intermediates is slow enough to be observed by ^{1}H NMR.[47]

To further investigate the effect of the nature of the DES components on the reaction, we conducted the dehydration of fructose also in DES sharing the same HBA, ChCl, differing for the HBD. For each DES bearing an acid component, we firstly carried out blank tests in the absence of added catalyst, at 60 °C. We observed different outcomes: in glutaric and lactic acid-based DES, ChCl:GA and ChCl:LA, poor yields in 5-HMF, lower than 10%, were obtained. Conversely, in solution of

ChCl:MA, the yield in 5-HMF reached 37% in 4 h. With this in mind, we carried out the dehydration of fructose in these DES in the presence of Amberlyst 15. The results obtained are reported in Figure 5 and Table S5.

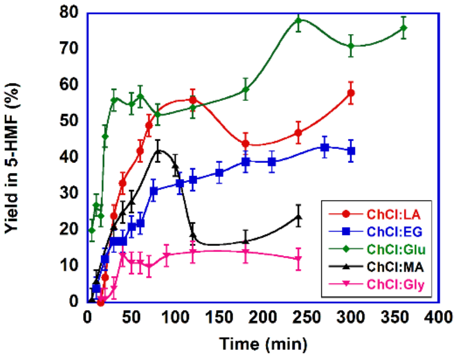


Figure 5. Yields in 5-HMF as a function of time obtained from fructose, in DES differing for the HBD in the presence of 25 mg of Amberlyst 15, at 60 °C. Yield are reproducible within ± 3%. Lines are drawn as mere visual aid.

As expected, the reaction performed in the acid-containing DES gave the highest yields in 5-HMF. However, some observations can be made. Firstly, in the case of ChCl:GA, the presence of Amberlyst significantly boosts the reaction, as the yields increased to 78% and is much higher than that found without catalyst. A similar behavior occurred in solution of ChCl:LA, where a yield of 56% was achieved in 2.5 h. On the other hand, using the DES composed by the other dicarboxylic acid, ChCl:MA, the yield obtained was 42%, close to what obtained in the absence of catalyst, with a concomitant degradation of the product. Furthermore, we can infer that, for HBD with a similar structure, the presence of a further hydroxyl group exerts a detrimental effect on the reaction outcome. In particular, comparing the polyalcohol-based HBD, passing from ChCl:EG to ChCl:Gly as solvent, induces a drastic reduction in the yield of 5-HMF, from 40% to only 10%, respectively. This poor performance arises from a pronounced degradation of 5-HMF, as accounted for by the marked darkening of the reaction mixture. A similar conclusion can be drawn by comparing the results found in the dicarboxylic acids-containing DES: once again, the presence of a hydroxyl group results in a drop in yield which almost halves, going from 78% in ChCl:GA to 42% in ChCl:MA. The marked effect of such a subtle structural variation can be a hint of the influence of the structural organization of the solvent on the reaction. Indeed, similarly to ILs, DES can be characterized by a distinct and resilient nanostructure, underpinned by hydrogen bonds.[58] On this regard, it has been recently shown that the number of hydroxyl groups in the HBD significantly impacts on the strength of hydrogen bond network of ChCl-based DES.[59] Finally, the use of the phenol-based DES, ChCl:PhOH, did not give the best results, with a yield of 40% (Figure S4, Table S6), suggesting a marginal influence of π-interactions in the reaction.

Then, to assess the sustainability of this protocol, we tested the recyclability of our catalytic system, using the best performing DES, ChCl:GA, as solvent. We also used this DES to assess the recyclability for the reaction of sucrose, since the best performing DES for this substrate, ChCl:MA (see later) is so viscous at room temperature that extraction becomes impractical. To this aim, at the end of the reactions we extracted 5-HMF with ethyl acetate, and then reused the ensuing DES phase and the catalyst. The recovered DES showed no obvious change in structure as verified by FTIR spectroscopy (Figure S1). The results obtained are shown in Figure 6.

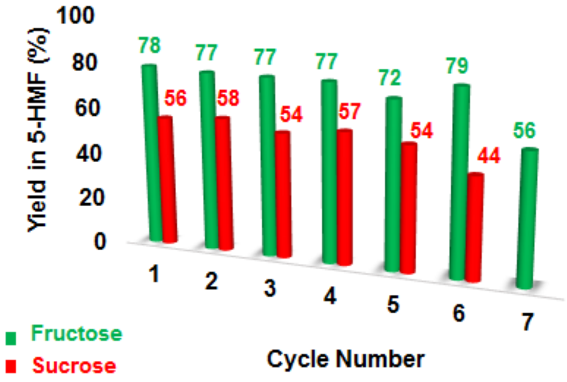


Figure 6. Yields in 5-HMF obtained after 4h at 60 °C from fructose and after 100 minutes at 80 °C from sucrose, in the presence Amberlyst 15, in ChCl:GA, upon recycling the catalytic system. Yields are reproducible within ± 3%.

Results reported in Figure 6 show that the catalytic system could be reused with no significant decrease in yield for six and five cycles in the case of fructose and sucrose, respectively. After these, yield dropped to 56% and 44 % is detected.

We also investigated the use of 2-methyltetrahydrofuran as extraction solvent. However, after the extraction, a solid phase was left instead of the DES (Figure S4), due to the solubility of glutaric acid in this solvent, and the concomitant crystallization of choline chloride.[40]

Finally, to assess the potential to scale-up of our protocol, we carried out the reaction of fructose in ChCl:GA, for 4h at 60 °C using 1 g of substrate, maintaining the same mass ratios with solvent and catalyst. We obtained a yield of 72 % which is very close to the value obtained using 50 mg as initial amount of substrate. Thus, this protocol showed promising potential to be scaled-up.

Dehydration of sucrose in DES

For the dehydration of sucrose, we firstly set out to find the best catalyst loading, by carrying out the reaction in the DES Bu_4NCl:EG, using an initial amount of 25 mg of sucrose, in the presence of increasing amounts of Amberlyst 15, at 80 °C. The results obtained are reported in Figure 7 and Table S7.

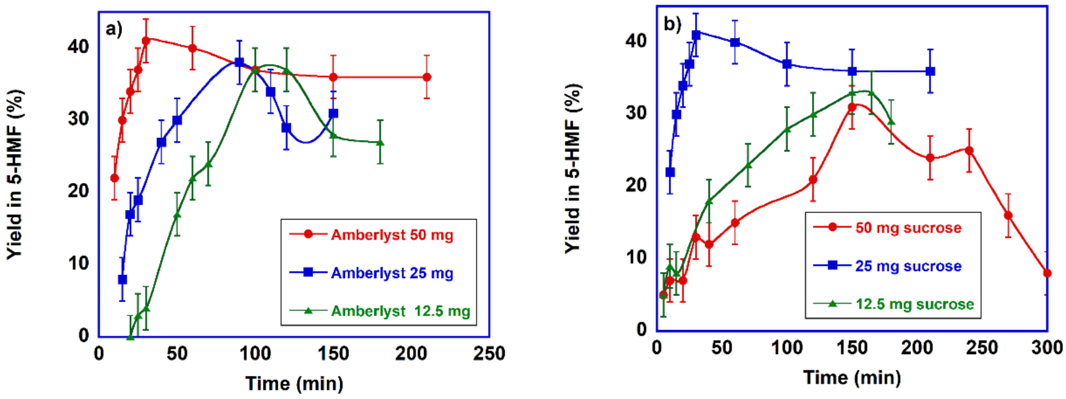


Figure 7. Yields in 5-HMF as a function of time obtained from sucrose, in Bu_4NCl:EG at 80 °C a) in the presence of increasing amounts of Amberlyst 15, b) using increasing initial amounts of sucrose. Yields are reproducible within ±3%. Lines are drawn as mere visual aid.

Differently from what observed in the case of fructose, increasing the catalyst loading consistently led to a faster reaction, and the best conditions were found using 50 mg of Amberlyst 15. In this case, a yield of 40% was achieved in only 30 minutes and stayed practically unchanged over 4 hours. Conversely, employing lower amounts of Amberlyst 15, led to comparable yields but after longer reaction times (37% after 2 hours and 38% after 90 minutes in the presence of 12.5 mg and 25 mg of Amberlyst 15, respectively). Furthermore, in the latter two cases, the trend of yields as a function of time hints at a more pronounced degradation of 5-HMF, likely due to the prolonged heating.

Also in this case, we examined the effect of the initial concentration of sucrose. To this purpose, we carried out the reaction in the DES Bu_4NCl:EG, employing increasing initial amounts of substrate and maintaining the same catalyst:substrate mass ratio, as well as all the other experimental conditions. The results obtained are reported in Figure 7b and Table S8. They show that, similarly to what happens with fructose, the best results were found using an intermediate amount of substrate, 25 mg. Indeed, raising the initial concentration of sucrose to 50 mg resulted in lower yields and a more pronounced degradation due to secondary reactions. Based on these findings, the following reactions were carried out using 25 mg of sucrose in the presence of 50 mg of Amberlyst 15.

Subsequently, we looked at how the nature of HBA affects the dehydration of sucrose, by conducting the reaction in ChCl:EG, Bu_4NCl:EG and Bu_4PCl:EG. The results obtained are reported in Figure 8a and Table S9.

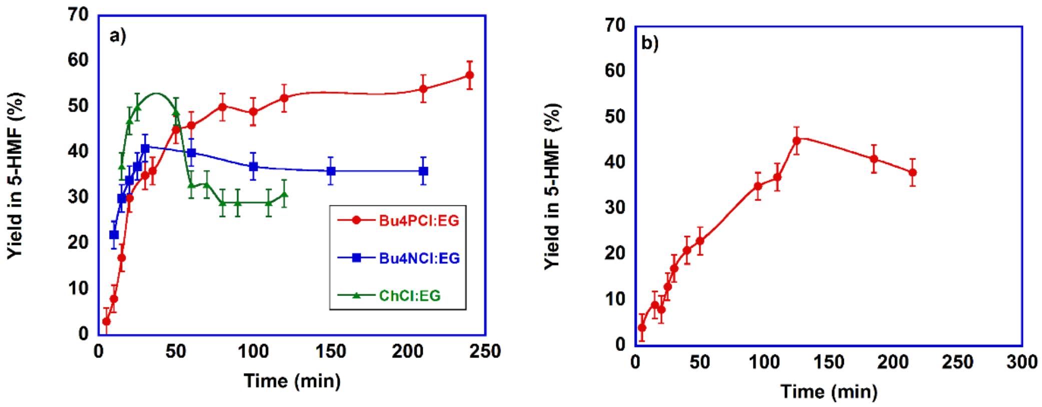


Figure 8. Yields in 5-HMF as a function of time obtained from sucrose, at 80 °C, in a) Bu_4NCl:EG, Bu_4PCl:EG and ChCl:EG, in the presence of 50 mg of Amberlyst 15 and b) Bu_4PCl:EG, without catalyst. Yields are reproducible within ±3%. Lines are drawn as mere visual aid.

In all cases, we obtained good yields in 5-HMF from sucrose. In particular, conducting the reaction in ChCl:EG, afforded a yield of 50% in 50 minutes. Notably, the yield approached the maximum value after only 10 minutes. However, after this time, it rapidly declined.

Conversely, in Bu_4NCl:EG, the yield reached 40% after 30 minutes, with a less pronounced drop and then plateaued at 36%. Finally, in Bu_4PCl:EG, yield in 5-HMF increased regularly, reaching a remarkable value of 57% in 4 hours. It is worth noting that converting sucrose into 5-HMF requires its previous hydrolysis into glucose and fructose, so that this substrate practically behaves like an equimolar mixture of these two monosaccharides.[60] Consequently, a yield in 5-HMF significantly higher than 50% suggests the occurrence of partial dehydration of the glucose unit. Considering the acidic nature of this DES, also in this case we carried out a blank test, to verify whether any formation of 5-HMF takes place from sucrose in the absence of Amberlyst 15. The results reported in Figure 8b and Table S10, show that this is indeed the case, and the acidity of the medium is sufficient to promote also the dehydration of sucrose.

Notably, unlike what happens with fructose, in this case the trends of yields detected in Bu_4PCl:EG with and without Amberlyst, are different. In particular, in the absence of catalyst, the yield reaches a lower value, 45%. This is in keeping with the lower reactivity of sucrose as compared to fructose and consequently, the extra acidity provided by the resin boosts the formation of the product. Furthermore, the absence of reduction in yield observed in this instance, agrees with the finding that a higher acidity enhances the selectivity in 5-HMF.[8] Although both processes are acid catalyzed, the acidity of the reaction medium influences their rates to different extents. Accordingly, when the dehydration is considerably faster than the degradation, no drop in yield occurs.

Also in this case, we looked at the effect of varying the nature of the HBD component, by performing the reaction in ChCl-based DES. The reactivity of sucrose in the acid-containing DES, was firstly assessed in the absence of Amberlyst 15. In all cases, no 5-HMF was formed, with the exception of ChCl:GA where a yield as low as 12% was found.

In the light of these findings, we then investigated the reactivity of sucrose in these DES upon adding Amberlyst 15, obtaining the results reported in Figure 9 and Table S11.

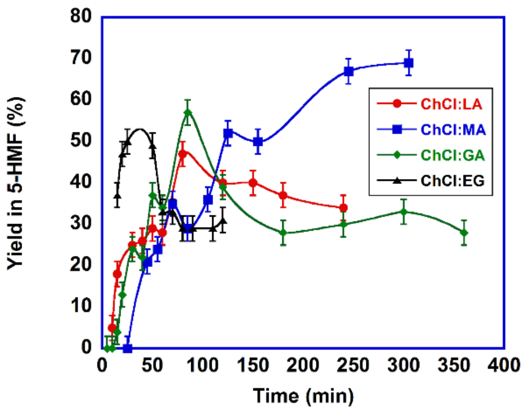


Figure 9. Yields in 5-HMF as a function of time obtained from sucrose, in ChCl-based DES differing for the HBD, at 80 °C, in the presence of 50 mg of Amberlyst 15. Yields are reproducible within ± 3%. Lines are drawn as mere visual aid.

Unlike what happens in the case of fructose, the highest yield in 5-HMF is obtained in ChCl:MA, where it reached 69% in 4 h, entailing a substantial conversion of the glucose unit. Conversely, in ChCl:GA, the yield peaked at 57% and then dropped to 30%, due to secondary reactions, whereas in ChCl:LA the yield in 5-HMF amounted to 47%. Also in this case, the worst results were found in ChCl:Gly, in which case no 5-HMF formation was detected. Indeed, the reaction mixture quickly turned dark brown, indicating extensive degradation of the substrate or 5-HMF.

In the case of sucrose, the effect exerted by changing the HBD appears more complex than that observed for fructose. Indeed, with HBD bearing two identical hydrogen bonding donating groups, such as EG and GA, the maximum yield in 5-HMF is reached faster, but then a likewise fast degradation occurs. Differently, the presence of different hydrogen bonding donating groups in LA leads to an improved performance. Finally, the presence of three hydroxyl groups as hydrogen bonding donating sites on the HBD, (Gly), has a detrimental effect on the reaction, compared with EG, similarly to what we found in the case of fructose. Summarizing, in the case of sucrose, the presence of three mixed hydrogen bonding sites like in MA appears to be the best compromise, leading to higher yields in 5-HMF from sucrose. With regard to the phenol-based DES, ChCl:PhOH very poor yield were obtained, never higher than 15%.

To assess the performance of our catalytic system, it is useful to compare it with related examples reported in the literature, dealing with the conversion of these carbohydrates into 5-HMF in DES. These are reported in Table 1, together with our best results.

Table 1. Comparison of our results with DES-based systems reported in the literature.

Dehydration of fructose				
Entry	**Catalyst**	**Time (h)**	**T (°C)**	**Yield (%)**
1[a]	Glutaric acid + Amberlyst 15	2	60	78
2[41]	Malic acid	1	90	80
3[39]	In situ generated H_2CO_3	1.5	120	74
4[43]	Heteropolyacid	0.016	110	92
5[40]	HCl	4	100	90
6[42]	*p*-toluenesulfonic acid	1	80	85
7[61]	Citric acid	1	80	78
8[62]	Betaine hydrochloride	0.5	110	57
9[63]	Acid-functionalized silica	4	110	67
10[64]	Acidic ionic liquid	3	25	89
Dehydration of sucrose				
10[a]	Malic Acid + Amberlyst 15	4	80	69
11[65]	Heteropolyacid	0.5	130	11
12[40]	$CrCl_3$	0.5	150	70
13[46]	Amberlyst 15[b]	2	90	20

[a] This work. [b] Reaction conducted in IL mixture $[bmim][Cl]_{0.5}[BF_4]_{0.5}$.

Results in Table 1 bring out that coupling Amberlyst 15 with dicarboxylic acid-containing DES, gives results competitive with what currently reported in literature. In particular, for the dehydration of fructose, our system afforded comparable yields with other systems employing weak acids[39,41] (entries 1-3 and 7) or superior to that of systems employing homogeneous[62] or heterogeneous[63] acidic catalysts (entries 1, 8-9). Furthermore, our highest yield is slightly inferior to systems using strong or mineral acids[40,42,43] (entries 1,4,5 and 6). However, it is worth noting that, with the only exception of one report in which employing an acidic ionic liquid as catalyst a higher yield is obtained at 25 °C,[64] in our case the transformation is carried out at a much lower temperature and using less acidic, and therefore safer conditions without employing potentially corrosive media. All these considerations are important to assess the overall greenness of the process.

An even better picture arises considering the conversion of sucrose. In particular, we obtained a much higher yield in 5-HMF compared with a system employing an heteropolyacid as catalyst[65] (entries 10 and 11). Notably, the present protocol also greatly improves the result obtained by us studying the conversion of sucrose promoted by Amberlyst 15 in ILs, in terms of yield, reaction time and temperature[46] (entries 10 and 13).

On the other hand, our yield is comparable with the one obtained by Lin et al.[40] (entries 10 and 12). In that case though, they employed a Cr(III) salt catalyst and a much higher temperature, once again evidencing that using Amberlyst in DES leads to a good compromise among yield, safety and sustainability of the process.

Stability of the DES

It has been very recently reported that DES formed by choline chloride and carboxyilic acid may undergo degradation when heated, due to ester formation between the two components.[66] Considering that NMR spectra of the DES show no obvious signs of degradation after being prepared (Figure S2), we checked the stability of our DES as a result of heating in the presence of the catalyst. To the best of our knowledge, this is the first time that such issue is addressed in when using this kind of DES in a reaction. To this aim, ChCl:GA, ChCl:MA and ChCl:LA were heated under stirring in the presence of Amberlyst 15, using the same mass ratios and experimetal conditions leading to the maximum yields for fructose and sucrose. Then, we obtained the ^{1}H NMR spectra and quantified (see Supporting Information) the extent of esterification using the method reported by Rodriguez *et al.*[66] Spectra obtained are reported in Figure S6. Examination of this spectra reveals the appearance of signals at 4.47, 3.65, and 3.12 ppm, relevant to the ester. In the case of ChCl:GA, after 4 h of contact with Ambelyst 15 at 60 °C, the extent of esterification amounts to 17%, while when treated at 80 °C for 100 minutes it reaches 30%. Similar conclusions can be made for the other DES with ChCl:MA showing a molar fraction of choline ester of 10% and 29 % after 90 minutes at 60 °C, and 4 h at 80 °C,respectively. Similarly, for ChCl:LA it amounts to 10% and 19% after 2.5 h at 60 °C, and 100 minutes at 80 °C.

Considering the whole of results, ChCl:GA offers the best compromise between catalytic ability and stability, since cholinium esters are biocompatible species.[67] This evidences the need to use mild reaction conditions, and our protocol is suitable to obtain the conversion of sugars in DES, given the low temperatures utilized.

Conclusions

We studied the dehydration of fructose and sucrose into 5-HMF, in the presence of Amberlyst 15, using eight DES as solvent media, differing for the HBA and HBD. By optimizing the reaction conditions, we obtained a yield in 5-HMF of 78 % at 60 °C and 69 % at 80 °C for fructose and sucrose respectively, which are competitive or superior to those of related systems currently reported in the literature. Pleasantly, in the case of the reaction of fructose the yield kept constant even by conducting the process in the gram scale, evidencing significant potential for scale-up. In general, we observed a distinct beneficial effect of coupling Amberlyst 15 with dicarboxylic acid-based DES.

The analysis of how the structure of the DES components affects the reaction, unveiled a prominent influence of the HBD. Moreover, the presence of a hydroxyl group between the two carboxylic moieties acts differently for the two substrates, favoring the reaction in the case of sucrose, whereas for fructose it exerts a detrimental effect. The catalytic system could be recycled and used for at least five cycles without loss in yields for both reactions. Finally, this is the first work in which the issue of stability of carboxyilic acid-based DES is addressed in the context of such a reaction.

We found that our carboxylic acid-based DES, under the experimental conditions used, undergo a limited extent of esterification, and ChCl:GA represents the best compromise between catalytic ability and stability. Along these premises, we state that the event of esterification of this kind of DES does not undermine the use of these kind of DES in sustainable chemistry, provided that relatively mild reaction conditions are used, also in the light of the biocompatibility of choline esters.

ASSOCIATED CONTENT

Supporting Information. The following files are available free of charge. Tables yields in 5-HMF for the studied reactions, representative pictures of reaction mixtures, FTIR and NMR spectra of DES.

Funding

We thank MIUR (PJ_RIC_FFABR_2017_160575) and University of Palermo (FFR 2018 Fund).

Declaration of interest

The authors declare no competing financial interest

References

(1) Gallezot, P. Conversion of biomass to selected chemical products. *Chem. Soc. Rev.* **2012**, *41*, 1538-1558, DOI 10.1039/C1CS15147A.

(2) Li, C.; Zhao, X.; Wang, A.; Huber, G. W.; Zhang, T. Catalytic Transformation of Lignin for the Production of Chemicals and Fuels. *Chem. Rev.* **2015**, *115*, 11559-11624, DOI 10.1021/acs.chemrev.5b00155.

(3) Ragauskas, A. J.; Beckham, G. T.; Biddy, M. J.; Chandra, R.; Chen, F.; Davis, M. F.; Davison, B. H.; Dixon, R. A.; Gilna, P.; Keller, M.; Langan, P.; Naskar, A. K.; Saddler, J. N.; Tschaplinski, T. J.; Tuskan, G. A.; Wyman, C. E. Lignin Valorization: Improving Lignin Processing in the Biorefinery. *Science* **2014**, *344*, 1246843, DOI 10.1126/science.1246843.

(4) Zhou, C.-H.; Xia, X.; Lin, C.-X.; Tong, D.-S.; Beltramini, J. Catalytic conversion of lignocellulosic biomass to fine chemicals and fuels. *Chem. Soc. Rev.* **2011**, *40*, 5588-5617, DOI 10.1039/C1CS15124J.

(5) Varma, R. S. Biomass-Derived Renewable Carbonaceous Materials for Sustainable Chemical and Environmental Applications. *ACS Sustainable Chem. Eng.* **2019**, *7*, 6458-6470, DOI 10.1021/acssuschemeng.8b06550.

(6) Sheldon, R. A. The Road to Biorenewables: Carbohydrates to Commodity Chemicals. *ACS Sustainable Chem. Eng.* **2018**, *6*, 4464-4480, DOI 10.1021/acssuschemeng.8b00376.

(7) Kucherov, F. A.; Romashov, L. V.; Galkin, K. I.; Ananikov, V. P. Chemical Transformations of Biomass-Derived C6-Furanic Platform Chemicals for Sustainable Energy Research, Materials Science, and Synthetic Building Blocks. *ACS Sustainable Chem. Eng.* **2018**, *6*, 8064-8092, DOI 10.1021/acssuschemeng.8b00971.

(8) Svenningsen, G. S.; Kumar, R.; Wyman, C. E.; Christopher, P. Unifying Mechanistic Analysis of Factors Controlling Selectivity in Fructose Dehydration to 5-Hydroxymethylfurfural by Homogeneous Acid Catalysts in Aprotic Solvents. *ACS Catal.* **2018**, *8*, 5591-5600, DOI 10.1021/acscatal.8b01197.

(9) Akien, G. R.; Qi, L.; Horváth, I. T. Molecular mapping of the acid catalysed dehydration of fructose. *Chem. Commun.* **2012**, *48*, 5850-5852, DOI 10.1039/C2CC31689G.

(10) Portillo Perez, G.; Mukherjee, A.; Dumont, M.-J. Insights into HMF catalysis. *J. Ind. Eng. Chem.* **2019**, *70*, 1-34, DOI 10.1016/j.jiec.2018.10.002.

(11) Tsilomelekis, G.; Orella, M. J.; Lin, Z.; Cheng, Z.; Zheng, W.; Nikolakis, V.; Vlachos, D. G. Molecular structure, morphology and growth mechanisms and rates of 5-hydroxymethyl furfural (HMF) derived humins. *Green Chem.* **2016**, *18*, 1983-1993, DOI 10.1039/c5gc01938a.

(12) Perego, C.; Bosetti, A.; Ricci, M.; Millini, R. Zeolite Materials for Biomass Conversion to Biofuel. *Energy Fuels* **2017**, *31*, 7721-7733, DOI 10.1021/acs.energyfuels.7b01057.

(13) Ramírez, E.; Bringué, R.; Fité, C.; Iborra, M.; Tejero, J.; Cunill, F. Role of ion-exchange resins as catalyst in the reaction-network of transformation of biomass into biofuels. *J. Chem. Technol. Biotechnol.* **2017**, *92*, 2775-2786, DOI 10.1002/jctb.5352.

(14) Mika, L. T.; Cséfalvay, E.; Németh, Á. Catalytic Conversion of Carbohydrates to Initial Platform Chemicals: Chemistry and Sustainability. *Chem. Rev.* **2018**, *118*, 505-613, DOI 10.1021/acs.chemrev.7b00395.

(15) Zhang, Z.; Song, J.; Han, B. Catalytic Transformation of Lignocellulose into Chemicals and Fuel Products in Ionic Liquids. *Chem. Rev.* **2017**, *117*, 6834-6880, DOI 10.1021/acs.chemrev.6b00457.

(16) Hallett, J. P.; Welton, T. Room-Temperature Ionic Liquids: Solvents for Synthesis and Catalysis. 2. *Chem. Rev.* **2011**, *111*, 3508-3576, DOI 10.1021/cr1003248.

(17) Plechkova, N. V.; Seddon, K. R. Applications of ionic liquids in the chemical industry. *Chem. Soc. Rev.* **2008**, *37*, 123-150, DOI 10.1039/B006677J.

(18) Sun, N.; Rodríguez, H.; Rahman, M.; Rogers, R. D. Where are ionic liquid strategies most suited in the pursuit of chemicals and energy from lignocellulosic biomass? *Chem. Commun.* **2011**, *47*, 1405-1421, DOI 10.1039/C0CC03990J.

(19) D'Anna, F.; Marullo, S.; Vitale, P.; Noto, R. The Effect of the Cation π-Surface Area on the 3D Organization and Catalytic Ability of Imidazolium-Based Ionic Liquids. *Eur. J. Org. Chem.* **2011**, *2011*, 5681-5689, DOI 10.1002/ejoc.201100763.

(20) D'Anna, F.; Noto, R. Di- and Tricationic Organic Salts: An Overview of Their Properties and Applications. *Eur. J. Org. Chem.* **2014**, *2014*, 4201-4223, DOI 10.1002/ejoc.201301871.

(21) Rizzo, C.; D'Anna, F.; Marullo, S.; Noto, R. Task Specific Dicationic Ionic Liquids: Recyclable Reaction Media for the Mononuclear Rearrangement of Heterocycles. *J. Org. Chem.* **2014**, *79*, 8678-8683, DOI 10.1021/jo501451t.

(22) Rizzo, C.; D'Anna, F.; Noto, R. Functionalised diimidazolium salts: the anion effect on the catalytic ability. *RSC Adv.* **2016**, *6*, 58477-58484, DOI 10.1039/c6ra12037g.

(23) Chatel, G.; Pereira, J. F. B.; Debbeti, V.; Wang, H.; Rogers, R. D. Mixing ionic liquids – "simple mixtures" or "double salts"? *Green Chem.* **2014**, *16*, 2051-2083, DOI 10.1039/C3GC41389F.

(24) Villar-Garcia, I. J.; Lovelock, K. R. J.; Men, S.; Licence, P. Tuning the electronic environment of cations and anions using ionic liquid mixtures. *Chem. Sci.* **2014**, *5*, 2573-2579, DOI 10.1039/C4SC00106K.

(25) Matthews, R. P.; Villar-Garcia, I. J.; Weber, C. C.; Griffith, J.; Cameron, F.; Hallett, J. P.; Hunt, P. A.; Welton, T. A structural investigation of ionic liquid mixtures. *Phys. Chem. Chem. Phys.* **2016**, *18*, 8608-8624, DOI 10.1039/C6CP00156D.

(26) D'Anna, F.; Marullo, S.; Vitale, P.; Noto, R. Binary Mixtures of Ionic Liquids: A Joint Approach to Investigate their Properties and Catalytic Ability. *ChemPhysChem* **2012**, *13*, 1877-1884, DOI 10.1002/cphc.201100878.

(27) Marullo, S.; D'Anna, F.; Campodonico, P. R.; Noto, R. Ionic liquid binary mixtures: how different factors contribute to determine their effect on the reactivity. *RSC Adv.* **2016**, *6*, 90165-90171, DOI 10.1039/C6RA12836J.

(28) Xiao, Y.; Huang, X. The physicochemical properties of a room-temperature liquidus binary ionic liquid mixture of [HNMP][CH3SO3]/[Bmim]Cl and its application for fructose conversion to 5-hydroxymethylfurfural. *RSC Adv.* **2018**, *8*, 18784-18791, DOI 10.1039/C8RA03604G.

(29) Smith, E. L.; Abbott, A. P.; Ryder, K. S. Deep Eutectic Solvents (DESs) and Their Applications. *Chem. Rev.* **2014**, *114*, 11060-11082, DOI 10.1021/cr300162p.

(30) Alonso, D. A.; Baeza, A.; Chinchilla, R.; Guillena, G.; Pastor, I. M.; Ramón, D. J. Deep Eutectic Solvents: The Organic Reaction Medium of the Century. *Eur. J. Org. Chem.* **2016**, *2016*, 612-632, DOI 10.1002/ejoc.201501197.

(31) Wazeer, I.; Hayyan, M.; Hadj-Kali, M. K. Deep eutectic solvents: designer fluids for chemical processes. *J. Chem. Technol. Biotechnol.* **2018**, *93*, 945-958, DOI 10.1002/jctb.5491.

(32) Hayyan, M.; Hashim, M. A.; Hayyan, A.; Al-Saadi, M. A.; AlNashef, I. M.; Mirghani, M. E. S.; Saheed, O. K. Are deep eutectic solvents benign or toxic? *Chemosphere* **2013**, *90*, 2193-2195, DOI 10.1016/j.chemosphere.2012.11.004.

(33) Paiva, A.; Craveiro, R.; Aroso, I.; Martins, M.; Reis, R. L.; Duarte, A. R. C. Natural Deep Eutectic Solvents – Solvents for the 21st Century. *ACS Sustainable Chem. Eng.* **2014**, *2*, 1063-1071, DOI 10.1021/sc500096j.

(34) Vanda, H.; Dai, Y.; Wilson, E. G.; Verpoorte, R.; Choi, Y. H. Green solvents from ionic liquids and deep eutectic solvents to natural deep eutectic solvents. *C. R. Chim.* **2018**, *21*, 628-638, DOI 10.1016/j.crci.2018.04.002.

(35) Liu, Y.; Friesen, J. B.; McAlpine, J. B.; Lankin, D. C.; Chen, S.-N.; Pauli, G. F. Natural Deep Eutectic Solvents: Properties, Applications, and Perspectives. *J. Nat. Prod.* **2018**, *81*, 679-690, DOI 10.1021/acs.jnatprod.7b00945.

(36) Tang, X.; Zuo, M.; Li, Z.; Liu, H.; Xiong, C.; Zeng, X.; Sun, Y.; Hu, L.; Liu, S.; Lei, T.; Lin, L. Green Processing of Lignocellulosic Biomass and Its Derivatives in Deep Eutectic Solvents. *ChemSusChem* **2017**, *10*, 2696-2706, DOI doi:10.1002/cssc.201700457.

(37) Ilgen, F.; Ott, D.; Kralisch, D.; Reil, C.; Palmberger, A.; König, B. Conversion of carbohydrates into 5-hydroxymethylfurfural in highly concentrated low melting mixtures. *Green Chem.* **2009**, *11*, 1948-1954, DOI 10.1039/B917548M.

(38) Jérôme, F.; De Oliveira Vigier, K. Catalytic Conversion of Carbohydrates to Furanic Derivatives in the Presence of Choline Chloride. *Catalysts* **2017**, *7*, 218, DOI 10.3390/catal7070218.

(39) Liu, F.; Barrault, J.; De Oliveira Vigier, K.; Jérôme, F. Dehydration of Highly Concentrated Solutions of Fructose to 5-Hydroxymethylfurfural in a Cheap and Sustainable Choline Chloride/Carbon Dioxide System. *ChemSusChem* **2012**, *5*, 1223-1226, DOI 10.1002/cssc.201200186.

(40) Zuo, M.; Le, K.; Li, Z.; Jiang, Y.; Zeng, X.; Tang, X.; Sun, Y.; Lin, L. Green process for production of 5-hydroxymethylfurfural from carbohydrates with high purity in deep eutectic solvents. *Ind. Crops Prod.* **2017**, *99*, 1-6, DOI 10.1016/j.indcrop.2017.01.027.

(41) Istasse, T.; Bockstal, L.; Richel, A. Production of 5-Hydroxymethylfurfural from D-Fructose in Low-Transition-Temperature Mixtures Enhanced by Chloride Anions and Low Amounts of Organic Acids. *ChemPlusChem* **2018**, *83*, 1135-1143, DOI 10.1002/cplu.201800416.

(42) Assanosi, A.; Farah, M. M.; Wood, J.; Al-Duri, B. Fructose dehydration to 5HMF in a green self-catalysed DES composed of N,N-diethylethanolammonium chloride and p-toluenesulfonic acid monohydrate (p-TSA). *C. R. Chim.* **2016**, *19*, 450-456, DOI 10.1016/j.crci.2015.11.004.

(43) Zhao, Q.; Sun, Z.; Wang, S.; Huang, G.; Wang, X.; Jiang, Z. Conversion of highly concentrated fructose into 5-hydroxymethylfurfural by acid–base bifunctional HPA nanocatalysts induced by choline chloride. *RSC Adv.* **2014**, *4*, 63055-63061, DOI 10.1039/C4RA10121A.

(44) Carrión-Prieto, P.; Martín-Ramos, P.; Hernández-Navarro, S.; Sánchez-Sastre, L. F.; Marcos-Robles, J. L.; Martín-Gil, J. Furfural, 5-HMF, acid-soluble lignin and sugar contents in C. ladanifer and E. arborea lignocellulosic biomass hydrolysates obtained from microwave-assisted treatments in different solvents. *Biomass Bioenergy* **2018**, *119*, 135-143, DOI 10.1016/j.biombioe.2018.09.023.

(45) Sert, M.; Arslanoğlu, A.; Ballice, L. Conversion of sunflower stalk based cellulose to the valuable products using choline chloride based deep eutectic solvents. *Renewable Energy* **2018**, *118*, 993-1000, DOI 10.1016/j.renene.2017.10.083.

(46) D'Anna, F.; Marullo, S.; Vitale, P.; Rizzo, C.; Lo Meo, P.; Noto, R. Ionic liquid binary mixtures: Promising reaction media for carbohydrate conversion into 5-hydroxymethylfurfural. *Appl. Catal., A* **2014**, *482*, 287-293, DOI 10.1016/j.apcata.2014.05.039.

(47) Marullo, S.; Rizzo, C.; Meli, A.; D'Anna, F. Ionic Liquid Binary Mixtures, Zeolites, and Ultrasound Irradiation: A Combination to Promote Carbohydrate Conversion into 5-Hydroxymethylfurfural. *ACS Sustainable Chem. Eng.* **2019**, *7*, 5818-5826, DOI 10.1021/acssuschemeng.8b05584.

(48) Lansalot-Matras, C.; Moreau, C. Dehydration of fructose into 5-hydroxymethylfurfural in the presence of ionic liquids. *Catal. Commun.* **2003**, *4*, 517-520, DOI 10.1016/S1566-7367(03)00133-X.

(49) Passos, H.; Tavares, D. J. P.; Ferreira, A. M.; Freire, M. G.; Coutinho, J. A. P. Are Aqueous Biphasic Systems Composed of Deep Eutectic Solvents Ternary or Quaternary Systems? *ACS Sustainable Chem. Eng.* **2016**, *4*, 2881-2886, DOI 10.1021/acssuschemeng.6b00485.

(50) Menges, F.: Spectragryph, Optical spectroscopy software, Version 1.2.11, 2019.

(51) D'Anna, F.; Vitale, P.; Noto, R. Determination of Basic Strength of Aliphatic Amines through Ion Pair Formation in Some Ionic Liquid Solutions. *J. Org. Chem.* **2009**, *74*, 6224-6230, DOI 10.1021/jo901172j.

(52) van Zandvoort, I.; Wang, Y.; Rasrendra, C. B.; van Eck, E. R. H.; Bruijnincx, P. C. A.; Heeres, H. J.; Weckhuysen, B. M. Formation, Molecular Structure, and Morphology of Humins in Biomass Conversion: Influence of Feedstock and Processing Conditions. *ChemSusChem* **2013**, *6*, 1745-1758, DOI 10.1002/cssc.201300332.

(53) Cheng, Z.; Everhart, J. L.; Tsilomelekis, G.; Nikolakis, V.; Saha, B.; Vlachos, D. G. Structural analysis of humins formed in the Brønsted acid catalyzed dehydration of fructose. *Green Chem.* **2018**, *20*, 997-1006, DOI 10.1039/C7GC03054A.

(54) Kareem, M. A.; Mjalli, F. S.; Hashim, M. A.; AlNashef, I. M. Phosphonium-Based Ionic Liquids Analogues and Their Physical Properties. *J. Chem. Eng. Data* **2010**, *55*, 4632-4637, DOI 10.1021/je100104v.

(55) Ghaedi, H.; Ayoub, M.; Sufian, S.; Hailegiorgis, S. M.; Murshid, G.; Khan, S. N. Thermal stability analysis, experimental conductivity and pH of phosphonium-based deep eutectic solvents and their prediction by a new empirical equation. *J. Chem. Thermodyn.* **2018**, *116*, 50-60, DOI 10.1016/j.jct.2017.08.029.

(56) Masoud, M. S.; Hammud, H. H. Electronic spectral parameters of the azo indicators: methyl red, methyl orange, PAN, and fast black K-salt. *Spectrochim. Acta, Part A* **2001**, *57*, 977-984, DOI 10.1016/S1386-1425(00)00416-9.

(57) Kaur, P.; Rajani, N.; Kumawat, P.; Singh, N.; Kushwaha, J. P. Performance and mechanism of dye extraction from aqueous solution using synthesized deep eutectic solvents. *Colloids Surf., A* **2018**, *539*, 85-91, DOI 10.1016/j.colsurfa.2017.12.013.

(58) Hammond, O. S.; Bowron, D. T.; Jackson, A. J.; Arnold, T.; Sanchez-Fernandez, A.; Tsapatsaris, N.; Garcia Sakai, V.; Edler, K. J. Resilience of Malic Acid Natural Deep Eutectic Solvent

Nanostructure to Solidification and Hydration. *J. Phys. Chem. B* **2017**, *121*, 7473-7483, DOI 10.1021/acs.jpcb.7b05454.

(59) Wang, H.; Liu, S.; Zhao, Y.; Wang, J.; Yu, Z. Insights into the Hydrogen Bond Interactions in Deep Eutectic Solvents Composed of Choline Chloride and Polyols. *ACS Sustainable Chem. Eng.* **2019**, *7*, 7760-7767, DOI 10.1021/acssuschemeng.8b06676.

(60) Qi, L.; Mui, Y. F.; Lo, S. W.; Lui, M. Y.; Akien, G. R.; Horváth, I. T. Catalytic Conversion of Fructose, Glucose, and Sucrose to 5-(Hydroxymethyl)furfural and Levulinic and Formic Acids in γ-Valerolactone As a Green Solvent. *ACS Catal.* **2014**, *4*, 1470-1477, DOI 10.1021/cs401160y.

(61) Hu, S.; Zhang, Z.; Zhou, Y.; Han, B.; Fan, H.; Li, W.; Song, J.; Xie, Y. Conversion of fructose to 5-hydroxymethylfurfural using ionic liquids prepared from renewable materials. *Green Chem.* **2008**, *10*, 1280-1283, DOI 10.1039/B810392E.

(62) Vigier, K. D. O.; Benguerba, A.; Barrault, J.; Jérôme, F. Conversion of fructose and inulin to 5-hydroxymethylfurfural in sustainable betaine hydrochloride-based media. *Green Chem.* **2012**, *14*, 285-289, DOI 10.1039/C1GC16236E.

(63) Tran, P. H.; Tran, P. V. A highly selective and efficient method for the production of 5-hydroxymethylfurfural from dehydration of fructose using SACS/DES catalytic system. *Fuel* **2019**, *246*, 18-23, DOI 10.1016/j.fuel.2019.02.112.

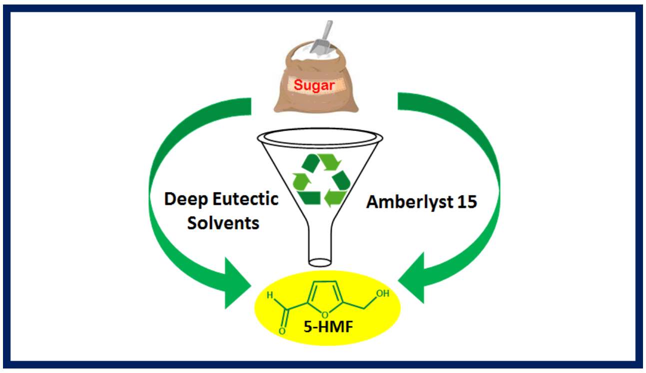
(64) Zhang, J.; Xiao, Y.; Zhong, Y.; Du, N.; Huang, X. Alcohol Effect and the Related Mechanism on Fructose Dehydration into 5-Hydroxymethylfurfural in the Deep Eutectic Solvent of [Emim]Cl/Alcohol. *ACS Sustainable Chem. Eng.* **2016**, *4*, 3995-4002, DOI 10.1021/acssuschemeng.6b00882.

(65) Sun, Z.; Wang, S.; Wang, X.; Jiang, Z. Lysine functional heteropolyacid nanospheres as bifunctional acid–base catalysts for cascade conversion of glucose to levulinic acid. *Fuel* **2016**, *164*, 262-266, DOI 10.1016/j.fuel.2015.10.014.

(66) Rodriguez Rodriguez, N.; van den Bruinhorst, A.; Kollau, L. J. B. M.; Kroon, M. C.; Binnemans, K. Degradation of Deep-Eutectic Solvents Based on Choline Chloride and Carboxylic Acids. *ACS Sustainable Chem. Eng.* **2019**, DOI 10.1021/acssuschemeng.9b01378.

(67) Lopes, J. M.; Paninho, A. B.; Môlho, M. F.; Nunes, A. V. M.; Rocha, A.; Lourenço, N. M. T.; Najdanovic-Visak, V. Biocompatible choline based ionic salts: Solubility in short-chain alcohols. *J. Chem. Thermodyn.* **2013**, *67*, 99-105, DOI 10.1016/j.jct.2013.07.025.

TOC



Synopsis: We studied the conversion of fructose and sucrose into 5-HMF, in Deep Eutectic Solvents, catalyzed by Amberlyst 15.