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High yield and isolation of 2,5-furandicarboxylic acid from HMF and sugars in ionic liquids, a new prospective for the establishment of a scalable and efficient catalytic route†

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The synthesis of 2,5-furandicarboxylic acid (FDCA) for the production of the sustainable bioplastic poly-ethylenefuroate (PEF) represents a topic of strong scientific and commercial interest. However, despite extensive research, the development of an efficient process for the synthesis of FDCA still faces difficult challenges. The principle cause is the strong dependence of the reactions involved on the solvent employed and difficulties in isolating the intermediate 5-HMF, leading to issues in performing the oxi-dation step which is favoured only in water, while 5-HMF formation is promoted in ionic liquids and other organic solvents. In this study we exploited ionic liquids as efficient solvents for the synthesis of HMF from sugars with MnO_2 as catalysts for the *in situ* oxidation of HMF into a dialkylimidazolium furan carboxylate ([dbmim]-FDC). The advantage in forming the imidazolium salt instead of the diacid form lies in the easier separation of this compound from the reaction mixture at low concentration (<2%) through antisolvent addition (ethanol) and its conversion into FDCA through acidification. This process represents a new efficient methodology to isolate FDCA directly from sugars such as glucose and fructose at isolated yield higher than 80% from these substrates, representing a step forward for the development of a techno-economically efficient process for the production of biobased plastics.

Background

The establishment of an efficient catalytic process to produce the biobased monomer 2,5-furandicarboxylic acid (FDCA) has represented a huge challenge over the past 20 years, resulting in over 1000 scientific publications focused in optimising the yield and catalyst design.[1] However, in order to establish a techno-economically efficient process, the synthesis of FDCA needs to be conducted starting from sugars or cellulose since the isolation of the intermediate 5-hydroxymethyl furfural (HMF) is not feasible, leading to prohibitive costs for a monomer intended for use in commodity products such as bioplastics.[2,3] Most of the literature has focused on studying separately the conversion of sugars into HMF and the catalytic conversion of HMF into FDCA, but rarely these two steps are compatible.[4] Indeed, the transformation of HMF into FDCA has proven to be efficient only in water while the formation of

HMF has proven to be limited in this solvent due to the formation of side products.[5] Other solvents such as DMSO, ionic liquids or biphasic water/organic solvent systems produce HMF more efficiently.[6,7]

In one of our recent publications, we demonstrated that the establishment of a two-step, one-pot process using ionic liquids, such as [bmim]Cl, can lead to remarkable advantages in the flexibility of the feedstock used and the price of the final product if a catalyst was developed for the conversion of HMF into FDCA in this solvent.[2] However this process seems far away due to the high sugar loadings required to achieve a techno-economically feasible process, which strongly disfavours high yields of HMF from sugars or the oxidation step, where current state of the art doesn't report satisfactory yields.[8,9] Some studies have demonstrated the oxidation of HMF into FDCA in ionic liquids but the separation of FDCA was not reported. Chen and co-workers developed a vanadium-based catalyst to convert glucose into FDCA at very low concentration of HMF (<0.1%).[10] Another paper reported iron and zir-conium mixed oxide catalyst, achieving 60% yield at 160 °C starting from HMF.[9]

Here we report that the isolation of FDCA from the ionic liquid [bmim]Cl can be achieved at very low concentration

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(<2%) by precipitation through antisolvent addition with ethanol. This process is favoured by the formation of the di-alkylimidazolium furan carboxylate ([dbmim]FDC), which has more favourable properties for separation. The isolation of the product enables the recycling of the solvent which is a fundamental aspect for the establishment of a green process. By exploiting this aspect and the high efficiency of the ionic liquids in converting sugars into HMF at high yield, we established a two-step, one-pot process to convert sugars into the [dbmim]FDC which can be converted into FDCA through acidification (Scheme 1).

The use of noble metal catalysts was discarded since these lose oxidation activity once halogen ions are present in the reaction mixture, shifting their selectivity towards etherification.[11] Our attention was directed to non-noble metals which already have shown promising results when the oxidation is carried out in water.[12] In the literature, different non-noble metal catalysts have shown potential activity in performing the oxidation of HMF into FDCA with the aid of a homogeneous base even if turnover numbers were not reported due to the unclear nature of the active sites.[13–15] However, in an attempt to achieve the transformation of HMF into FDCA, manganese oxide was exploited for this purpose as multiple reports have highlighted the beneficial activity for this type of reaction. In this study, we analysed γ-MnO$_2$, which has previously shown good activity for the conversion of the alcohol moiety of HMF into an aldehyde to obtain the dialdehyde 2,5-diformylfuran.[16] Other work reports reactions where manganese oxide-based catalysts proved to be effective for the conversion of the alcohol into aldehyde under water free conditions and to carboxylic acids under water-basic environment. According to these observations, we hypothesize that the high basicity of the halogenated ionic liquids would favour the oxidation of HMF into FDCA at low water content. The high efficiency of these materials in performing such oxidations at high yield (98%), allowed us to back-integrate the production of HMF using fructose or glucose as substrate, obtaining high yields through a two-step, one pot process. This is the first study which reports such high isolated yields of FDCA starting from sugars, opening a new avenue of research and development in this field.

Results and discussion

Solvent selection and optimization

In this study we focused on dialkylimidazolium ionic liquids as solvents since these have been reported to be high performing in converting sugars into HMF.[17–19] While noble metals are inefficient for this type of transformation,[8] manganese oxide gives promising yields and leaves room for improvement for further optimization. Our analysis begins by analysing the effect of the solvent anion on the yield and selectivity of reaction (Fig. 1). Under dry conditions, bromide-based ionic liquids proved to be more efficient compared with chloride but in both cases the reactions exhibited a loss in the total carbon balance (unidentified byproducts). Therefore, we repeated the experiments by adjusting the water content to 20%. We found that in case of [bmim]Br the selectivity is shifted towards FFCA rather than FDCA, possibly due to water slowing the reaction kinetics. When [bmim]Cl was used as solvent, the carbon
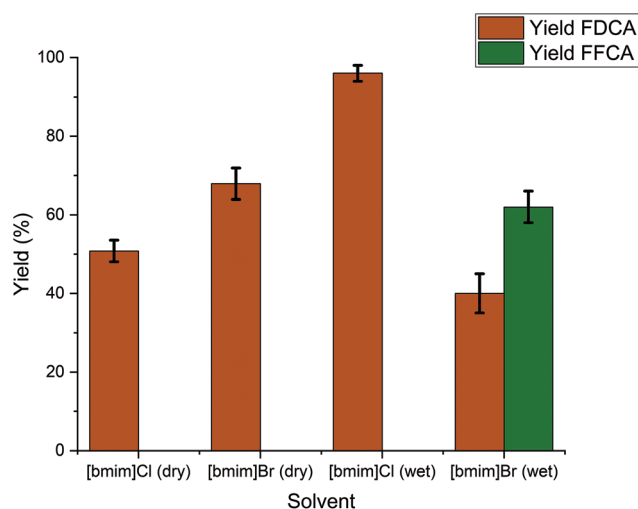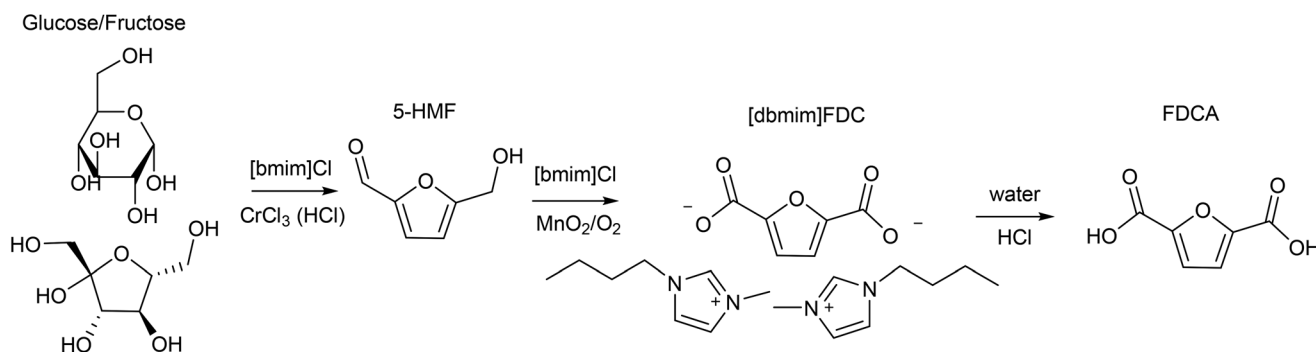

Fig. 1 Ionic liquid selection and effect of the water content. Wet is equivalent to 20 % in weight of water content. Conditions: HMF loading 1.26 %, 130 °C, 10 bar O$_2$, 6 h. All reactions reached 100% conversion of HMF.

Scheme 1 Reaction path followed in this study to obtain [dbmim]FDC and FDCA from sugars.

balance improved remarkably through the addition of water, reaching a yield of FDCA of over 98%.

The role of water can have multiple effects such as favouring the formation of geminal diols as intermediate products to favour the thermodynamics of the overall reaction and increase the solubility of oxygen, which is known to be very low in ionic liquids[20,21] and the differing selectivity behaviour between Br^- and Cl^- ionic liquids indicates a strong dependence of the β value of the Kamlet–Taft parameters on the mechanism of reaction.[22] Further optimization was carried through varying time, oxygen pressure and manganese oxide content and reported in table Table 1.

Oxygen pressure has a significant effect on the reaction. Low (1) and high oxygen pressures (3) lead to a decrease in the carbon balance. In particular, the decrease in furan selectivity at 2 bar (1) and at low MnO_2 (entries 4 and 5) content suggests that the reaction needs to be performed as quickly as possible since the oxidation products are more stable compared to HMF as demonstrated in one of our previous publications[23] and prolonged reaction times at high MnO_2 content (entries 6 and 7) didn't lead to any consistent change in the yield of HMF.

We selected [bmim]Cl with 20% water at 10 bar and 5 mg MnO_2 content as optimum conditions; moreover [bmim]Cl allows a better versatility of a further back integration towards sugars and cellulose, since this solvent has been reported to favour the direct conversion of cellulose and glucose to HMF.[24]

It is surprising that the addition of ethanol to the reaction mixture leads to the precipitation of a white solid which analysis by NMR and mass spectrometry confirmed is the furan carboxylate dialkylimidazolium salt. The formation of this complex was unexpected since the pK_a of FDCA has been reported at around 2, which is not acidic enough to be deprotonated by the chloride anions. This was further confirmed by dissolving commercial FDCA in pure ionic liquids, which did not show any formation of the salt upon ethanol addition. We postulate that the hydrogen is removed by the manganese oxide and retained in its matrix and then released through reaction with oxygen, favouring the formation of the dialkylimidazolium salt. The formation of this complex proved to be highly beneficial for the separation of the final product due to differences in its properties compared with FDCA. Solubility test showed a completely different physical behaviour, exhibiting high solubility in water and low solubility in ethanol for the dialkylimidazolium salt, contrary to FDCA. In one of our

previous publications, we showed that a minimum of 40% (by mass) FDCA in [bmim]Cl is required to make the separation feasible which is more than one order of magnitude above our current operating procedure.[25] The formation of the dialkylimidazolium salt has multiple benefits since it overcome the hydrogen bonding of the chloride anions with the OH group of the carboxylic acid which is responsible for the difficult separation of FDCA from ionic liquids.[26] After water removal (<5 %), the separation of [dbmim]-FDC was achieved through ethanol addition at a 1 : 1 ratio compared with ionic liquid and cooling to 3 °C. In this process we observed a strong dependency of the precipitation efficiency with the water content since the imidazolium salts showed high solubility in water on the contrary of FDCA.

[dbmim]FDC was obtained as a white powder at high purity which was confirmed by HPLC (>98%), mass spectrometry and NMR. Analysis of the solvent by NMR and mass spectrometry did not exhibit any signs of ionic liquid degradation (ESI†). Further confirmation of the integrity (and inertness) of the ionic liquid was assessed by repeating the oxidation experiment by redissolving HMF in the solvent and re-loading fresh manganese oxide and oxygen. The reuse of the ionic liquid gave the same yield, suggesting that [bmim]Cl didn't undergo significant degradation.

Synthesis of FDCA from sugars

The possibility of separating the dialkylimidazolium salt at low concentrations opens up the possibility of establishing a chemical pathway to FDCA starting from sugars by producing in one step HMF and then loading the system with MnO_2 and oxygen to convert the HMF to FDCA *in situ*. In our process, fructose is converted into HMF at 89% yield using HCl as a Brønsted acid resin, then manganese oxide is loaded into the reaction mixture which is pressurized to 10 bar with O_2. We performed the dehydration from fructose using HCl and $CrCl_3$ when glucose was used. The reaction starting from fructose achieved yields over 85% while the dehydration from glucose did not reach more than 55% yield to HMF at low concentration. In the second step, the water content was adjusted to achieve 20% and the pH eventually corrected with [bmim]OH when fructose was used, followed by loading of MnO_2 and pressurization with O_2. The neutralization step was needed since residual HCl proved to be detrimental for the oxidation step, decreasing drastically the yield (<40%). This can be due to a multiple effects since acidic conditions can inhibit the for-

Table 1 Optimization of the reaction parameters. HMF loading 1.26%, 250 mg [bmim]Cl (20% water content), 130 °C

Entry	P O_2 (bar)	MnO_2 (mg)	Time (h)	Conversion (%)	Yield FDCA (%)	Yield FFCA (%)	Total furan selectivity (%)
1	2	5	6	87.9 ± 2.9	46.2 ± 9.85	15.1 ± 0.95	69.7
2	10	5	6	100	95.8 ± 0.25	0	95.8
3	20	5	6	100	76.5 ± 0.5	0	76.5
4	10	1	6	82.2 ± 0.8	30.3 ± 0.3	11.6 ± 0.6	51
5	10	3	6	96.5 ± 3.5	76.3 ± 11.25	8.2 ± 4.1	87.5
6	10	5	6	100	95.8 ± 0.3	0	95.8
7	10	5	3	100	92.5 ± 1.5	0	92.5

mation of the geminal diol, which are the intermediate in the aldehyde oxidation, or enhancing the leaching of the manganese oxide.

The isolation of [dbmim]-FDC was then achieved through the addition of ethanol. The results shown in Table 2 suggest that MnO_2 is a robust catalyst which can efficiently perform the conversion of the second step starting from sugars. In particular the catalyst is capable of boosting the yield of [dbmim]-FDC, suggesting that oligomeric side products[23] can be recovered through the oxidation and agglomerated into the final product, which has already been reported for other catalytic systems,[27] representing a further advantage for this type of reaction. By not relying on an isolated yield of HMF from sugars, but instead on the aggregate yield of furanic content, this approach yields better versatility of the whole process.

Recyclability of MnO_2

While high activity was observed on the first cycle, the MnO_2 catalyst lost 80% of its activity upon the second cycle (20% yield). The spent catalyst was analysed by XRD, XPS, SEM, BET and TPD in combination with an ICP analysis of the ionic liquid phase. The XRD spectra showed that the manganese has changed its crystalline structure from the original gamma form. This was further confirmed by morphological analysis (SEM) which showed that the material changed from a cubic structure to a rod like feature after reaction, even if this did not lead to any change in surface area (which remained at $55 \ m^2 \ g^{-1}$). This change in the morphology accompanied with the change in the crystalline structure suggests that the manganese has entered an inactive form which cannot be regenerated through simple application of oxygen. This is consistent with a study done by Hayashi and co-workers[14] which demonstrated that different crystalline structure of manganese oxide strongly impacts the activity and selectivity of these catalysts. Temperature programmed desorption further confirmed a drastic reduction in the basic sites, which can be related to the main activity of the catalyst. The change in morphological structure upon contact of a metal oxide with ionic liquids was further observed in other studies in our group using zinc and it open the prospective for further research on the influence of these solvents on the morphological and chemical structure of the final solid oxide.[28]

Table 2 Results of the synthesis of [dbmim]-FDC starting from sugars. Overall yield is referred to the sugar loading. Procedure to perform the 1st and 2nd step is reported in the ESI.† Purity was assessed after acidification and confirmed to be over 98%

Substrate	Catalyst	Yield HMF (1st step)	Overall yield [dbmim]-FDC (HPLC)	Overall isolated yield [dbmim]-FDC
Fructose (2% loading)	HCl (5% loading)	80 ± 4%	93 ± 0.2%	80 ± 7%
Glucose (2% loading)	CrCl$_3$·6H$_2$O (7% loading)	55 ± 0.3%	91 ± 3%	81 ± 3%

This observation is consistent with the extensive literature studies with manganese oxide-based catalysts in water where most of the reactions were conducted at catalyst loadings higher than 10 : 1 with respect to HMF, undermining the catalyst recyclability.[13,29,30] Different regeneration methodologies are reported to restore the manganese activity based on the treatment with stoichiometric oxidants at high pH.[31]

Further analysis of the liquor by ICP showed a consistent leaching of manganese into the solvent (12 ± 4%). This amount could be recovered by diluting the ionic liquid solution and adjusting the pH of the solution to 10 through addition of [bmim]OH, followed by neutralization with HCl and water evaporation. However, the large water addition required for such steps undermines the economic feasibility of the ionic liquid recovery due to the high energy required for the regeneration.[2,32] Further studies are underway in our laboratories to study the nature of the active sites in the MnO_2, limit the leaching and regenerate the catalyst activity.

Conclusions

This study reports an innovative reaction pathway to isolate FDCA starting from sugars. We exploited [bmim]Cl as an efficient solvent to carry out the transformation of glucose and fructose into HMF and then performed the HMF oxidation step *in situ* using manganese oxide at 10 bar O_2 pressure. This catalyst proved to be very efficient, giving high yield, selectivity and robustness, including demonstrating the ability to recover oligomeric furanic compounds derived from the dehydration of sugars and convert them into the final product. The formation of the dialkylimidazolium furan carboxylate ([dbmim]-FDC) proved to be very efficient for this process since it enables an efficient separation of the final product at very low concentration (<2%) by addition of ethanol as an antisolvent at a ratio of 1 : 1 compared to the ionic liquid. FDCA could be obtained by treating [dbmim]-FDC under acidic conditions and the ionic liquid recovered without any observable degradation. We achieved an overall isolated yield of more than 98% from HMF and 80% starting from sugars, which is a unique achievement in this field. Further work is underway to optimize the catalyst recyclability and achieve a closed loop system for competitive economic production of FDCA.

Conflicts of interest

The authors have no conflicts of interest to report.

Acknowledgements

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