Conversion of carbohydrates into 5-hydroxymethylfurfural in highly concentrated low melting mixtures

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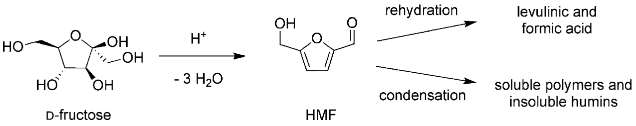
Received 23rd April 2009, Accepted 25th August 2009
First published as an Advance Article on the web 29th September 2009
DOI: 10.1039/b917548m

Highly concentrated melt systems consisting of choline chloride (ChCl) and up to 50 wt% of carbohydrates, corresponding to carbohydrate concentrations of 2.9 to 3.1 mol/L, have been used for the conversion of the carbohydrate content into 5-hydroxymethylfurfural (HMF) in the presence of catalysts. Apart from the monosaccharides D-fructose and D-glucose, the disaccharide sucrose and the polyfructan inulin were successfully converted into HMF. The reported conditions with short reaction times at high concentrations may allow for high space-time yields, which may be of interest for the development of efficient continuous processes for the conversion of carbohydrates into HMF. In a preliminary ecological evaluation, the ChCl/D-fructose system is compared to other representative solvents for the synthesis of 5-hydroxymethylfurfural. The melts have an inherent low toxicological impact due to their negligible vapour pressure.

Introduction

Declining fossil fuel reserves steadily increase the need to develop sustainable sources for chemical production in the near future.[1] Hence, the utilisation of biomass for the industrial production of chemicals is required to address the need for fine chemicals and commodities.[2] Renewable and vastly abundant biomass is a promising alternative for the sustainable supply of precious intermediates and platform chemicals to the chemical industry.[3]

With more than 75%, carbohydrates are the largest part of all biomass[4] and therefore of particular interest for conversion into fine chemicals. Amongst many possible biomass-derived chemicals, 5-hydroxylmethylfurfural (HMF) is considered to have the potential to be a sustainable substitute for petroleum-based building blocks.[5] Intermediates like 2,5-furandicarboxylic acid, 2,5-dihydroxymethylfuran, 2,5-bis(hydroxymethyl)tetrahydrofuran and dimethylfuran are derived from HMF by oxidation, hydrogenation, hydrogenolysis or aldol condensation.[6] The most convenient and efficient method in terms of chemical yield for the preparation of HMF is the acid catalysed dehydration of D-fructose. For fructose conversion, traditionally highly polar organic solvents, namely DMSO,[7] DMF[8] and sub-critical or high-temperature water[9] are used. High boiling solvents, however, require significant energy input during the separation process of HMF from the solvent. Further, HMF molecules, generated under aqueous acidic conditions partially rehydrate to the undesired side products levulinic and formic acid, which is a major challenge in the synthesis of HMF (Scheme 1). Another significant side reaction is the self-condensation of the reactive HMF to form both soluble polymers and insoluble humins.



Scheme 1 Acid catalysed dehydration of D-fructose to HMF and possible subsequent side reaction by rehydration to levulinic and formic acid and the self-condensation to soluble polymers and humins.

Due to the increased interest and demand for industrial application, more efficient catalytic systems were recently developed. Biphasic systems are used to continuously or intermittently remove the produced HMF from the reactive phase and thus reduce the side reactions.[10] Róman-Leshkov *et al.* developed a system where DMSO and PVP (poly(1-vinyl-2-pyrrolidinone) were added to the aqueous phase in order to enhance the dehydration, while the extraction phase (methyl isobutyl ketone, MIBK) was modified with 2-butanol for better separation from the aqueous phase. At 89% fructose conversion, a maximum selectivity of 85% was achieved.[1] Excellent yields (92%) from D-fructose were obtained by Stark *et al.* with a biphasic reactor based on 1-butyl-3-methylimidazolium methylsulfonate and MTBE (methyl tert-butyl ether) as extracting reagent.[11] Comparable yields (90%) were obtained by Smith *et al.* using microwave heating of D-fructose in a 70:30 (wt/wt) acetone/DMSO mixture.[12] Xie *et al.* could show that a biphasic system consisting of EtOAc and choline chloride/citric acid/D-fructose melt can be used for the preparation of HMF at 80 °C in yields as high as 90%.[13] Recent reports focus on the formation of HMF from glucose rather than from fructose, since the former one is cheaper in production as it is obtained from the hydrolysis of cellulose. Zhao *et al.* demonstrated the use of metal chlorides reporting best results for $CrCl_2$ and $CrCl_3$ with $[C_2mim]Cl$ as solvent. HMF yields as high

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as 68% were obtained from glucose. The initial loading of glucose was 10 wt%.[14] Recently, a new concept using N-heterocyclic carbene-metal (NHC/M) complexes in ionic liquids (ILs) was introduced by Ying *et al.* This new methodology enabled the group to obtain HMF in yields of 96% and 81% for fructose and glucose, respectively. The NHC/M/IL system is reported to be tolerant towards carbohydrate concentrations as high as 20% by weight.[15]

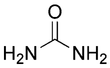
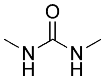
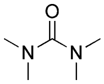
The use of diluted solutions for the conversion of carbohydrates into HMF, however, limits the efficacy of the process.[16] A more desired approach would allow the conversion of highly concentrated liquids or neat substances to gain larger product amounts in a minimal volume and to avoid solvents and concentration steps. Such a solvent system tolerating diverse carbohydrates would make the HMF preparation more efficient and thus be a premise to meet the increasing demand for HMF and its derivatives.

Here, we report the use of highly concentrated carbohydrate melts (up to 50 wt%) for the selective conversion of D-fructose, D-glucose and other di- and oligosaccharides into HMF. Different reaction conditions as well as homogeneous and heterogeneous catalysts were investigated. In addition, a preliminary ecological evaluation was performed for the preparation of HMF in ChCl/fructose melts compared to other solvents.

Results and discussion

The low melting carbohydrate/urea mixtures recently developed in our group[17] allow converting biomass derived renewables at high concentration into valuable intermediates. To obtain HMF, a D-fructose/*N*,*N*′-dimethyl urea (DMU) melt was tested for acid catalysed dehydration. In preliminary experiments, $CrCl_2$ and $CrCl_3$ (10 mol% each) were used as catalysts, because they were reported to have very high activities in dehydration reactions. The reactions were conducted with 40 wt% of fructose over 2 h at 110 °C. Extraction of the still liquid melt with EtOAc gave HMF in only low yields of 6% and 2%, respectively. Catalysts like $FeCl_3$ and $AlCl_3$ gave similar results. The only catalyst which gave HMF in acceptable yield was Amberlyst 15, an ion-exchange resin (27%). Upon extraction, the organic phase was evaporated, weighed and analysed by NMR to find no side products besides HMF. In a further series of experiments, different urea derivatives, urea, DMU and TMU (*N*,*N*′-tetramethyl urea), were compared as melt components in the D-fructose to HMF conversion (Table 1). $FeCl_3$ (10 mol%) was used as catalyst in all cases and the reactions were run at 100 °C for 1 h. Under these conditions, the urea and DMU containing reaction mixtures gave urea-fructose condensation products explaining the low HMF yields. The TMU based melt, in which a condensation of fructose and TMU is not possible, gave HMF in 89% yield. However, TMU can not be considered as a suitable additive as its separation is energy intensive similar to the use of DMSO and it is inherently toxic.

Table 1 HMF formation from D-fructose in low melting mixtures with urea (2:3, D-fructose : urea ratio, wt/wt), *N*,*N*′-dimethyl urea (DMU) (2:3, D-fructose : DMU, wt/wt) and *N*,*N*′-tetramethyl urea (TMU) (9:1, D-fructose : TMU, wt/wt). $FeCl_3$ (10 mol%) was used as catalyst in all cases; the reaction temperature was 100 °C; reaction time 1 h

$FeCl_3$			
HMF	no prod.	8%	89%

Therefore, new melts had to be found meeting the requirements of having a high sugar content, low melting point, low viscosity and low toxicity. Table 2 shows the results for mixtures of carbohydrates and sugar alcohols with melt additives expected to have melting point depressing properties. Glucosamine was tested, too, because it can be obtained from the second most abundant biopolymer chitin.

To obtain a mixture close to the eutectic point, the components were blended using compositions of 1:9, 2:8 *etc.* up to 9:1 (wt/wt) and the melting point was determined. The pH values were measured in aqueous solutions (1.13 M for fructose : imidazole 1:1) and the results are summarised in Fig. 1.

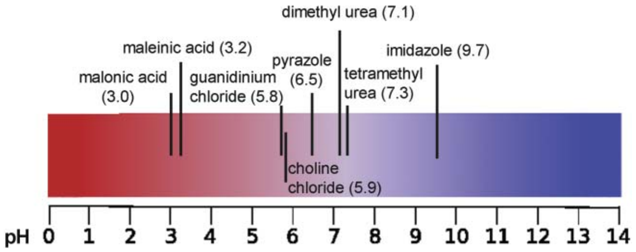


Fig. 1 pH values of different melt systems with fructose as carbohydrate component.

The low melting mixtures show different pH values, from acidic to basic, which can be used to establish the desired reaction conditions. In addition, the melts were tested for dehydration of fructose by Amberlyst 15 and $FeCl_3$ as catalysts. Neither

Table 2 Eutectic mixtures of carbohydrates and sugar alcohols with several H-bond donor and acceptor additives

	Urea	DMU	Imidazole	4-Me-imidazole	Pyrazole	Choline chloride	Guanidinium HCl	Malonic acid
D-Glucose	b	80 °C (3:7)	60 °C (4:6)	50 °C (2:8)	80 °C (5:5)	80 °C (4:6)	70 °C (4:6)	b
D-Mannose	b	80 °C (4:6)	80 °C (4:6)	50 °C (2:8)	50 °C (4:6)	50 °C (4:6)	80 °C (4:6)	90 °C (5:5)
D-Fructose	70 °C (6:4)	70 °C (4:6)	70 °C (5:5)	50 °C (2:8)	70 °C (5:5)	70 °C (4:6)	70 °C (4:6)	100 °C (7:3)
D-Sorbitol	70 °C (5:5)	80 °C (4:6)	80 °C (3:7)	50 °C (2:8)	60 °C (3:7)	70 °C (4:6)	a	c 70 °C
Sucrose	a	b	80 °C (7:3)	70 °C (4:6)	60 °C (4:6)	80 °C (5:5)	b	80 °C (6:4)
Isomaltose	b	90 °C (4:6)	80 °C (4:6)	70 °C (3:7)	70 °C (5:5)	90 °C (4:6)	60 °C (4:6)	a
Glucosamine	b	b	a	50 °C (3:7)	90 °C (1:9)	100 °C (1:9)	b	b

Melting point of mixtures (carbohydrate : additive weight fraction), a = not determined, b = no melt at 100 °C, c = decomposition.

imidazole nor pyrazole-based melts gave conversion to HMF with the above mentioned catalysts at 100 °C for 1 h. In the case of malonic and maleinic acid under the same conditions, only levulinic acid was identified in the organic phase by ^{1}H- and ^{13}C-NMR after workup (23% and 26% yield; see the experimental part for workup conditions), indicating conditions prone for rehydration of HMF due to the low pH value. Guanidinium chloride leads to a product mixture which was difficult to analyse. Choline chloride is the only melt component which gave HMF in 25% and 40% yield for Amberlyst 15 and $FeCl_3$ as catalysts under the described conditions. For comparison, a neat melt consisting of fructose exclusively was investigated resulting in the formation of levulinic acid (20%) as the single product. This shows the beneficial effect of the melt additives for synthesis of HMF.

As choline chloride was found to be a suitable additive for melts with very high carbohydrate content, the melting point of mixtures was investigated in more detail with differential scanning calorimetry (DSC). The lowest melting point was found for the ratio 2:3 of fructose : choline chloride with a melting range of 79-82 °C (Fig. 2). The choline chloride melt component is water soluble and not extractable by organic solvents as in the case of DMU. Choline chloride is less expensive than most ionic liquids,[18] has a very low toxicity to humans[19] and the environment,[20] is non-flammable[20] and can be considered as thermally stable.[21] Hence, these properties can make choline chloride a suitable media for this specific task.[22]

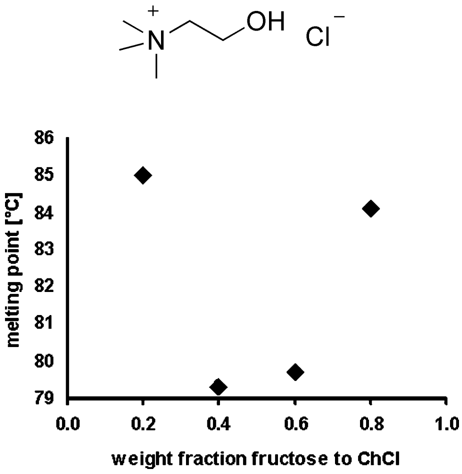


Fig. 2 Chemical structure of choline chloride and melting points determined by DSC of different fructose ChCl mixtures.

Heterogeneous catalysts can be easily recycled by filtration or centrifugation. Therefore, the heterogeneous catalysts Amberlyst 15 and Montmorillonite, a weakly acidic phyllosilicate, were selected for dehydration reactions of diverse carbohydrates in ChCl melts. An optimal catalyst loading of 50 mg per 1 g of melt was found and used for all carbohydrate conversions discussed in the following. For homogenous catalysts 10 mol% were used.[9,23] The performance of the different catalysts is summarized in Table 3.

The reaction conditions for D-fructose conversion in ChCl using $FeCl_3$ (10 mol% based on sugar) as catalyst were optimised and found to be best for a short reaction time of 0.5 h at a reaction temperature of 100 °C (59% yield).[24] The best yield for this melt system was achieved using pTsOH as catalyst (Table 3). Longer reaction times or temperatures above 100 °C lead to the formation of significant amounts of humins as black insoluble solids. The high sugar concentration may lead to a high local HMF concentration which favours subsequent condensation reactions.

Table 3 Conversion of different carbohydrates into HMF using different reaction conditions and catalysts. Yields were determined by HPLC analysis

	Yield of HMF [%] from			
Catalysts	D-Fructose/ ChCl (4:6)[a]	D-Glucose/ ChCl (4:6)[b]	Sucrose/ ChCl (5:5)[c]	Inulin/ ChCl (5:5)[d]
Amberlyst 15	40*	9*	27*	54*
$FeCl_3$	59	15	27	55
$ZnCl_2$	8	6	6	3
$CrCl_2$	40	45	62	36
$CrCl_3$	60	31	43	46
*p*TsOH	67	15	25	57
$Sc(OTf)_3$	55	9	28	44
Montmorillonite	49*	7*	35*	7*

Reaction conditions: 10 mol% catalyst used (*Montmorillonite: 50 mg, Amberlyst 15:50 mg)[a] 400 mg fructose, 600 mg ChCl, 100 °C, 0.5 h. [b] 400 mg glucose 600 mg ChCl, 110 °C, 0.5 h. [c] 500 mg sucrose, 500 mg ChCl, 100 °C, 1 h. [d] 500 mg inulin 500 mg ChCl, 90 °C, 1 h.

D-Glucose is of relevance for the preparation of 5-hydroxymethylfurfural, due to its higher abundance and lower price. For glucose conversion, the same ratio of sugar to ChCl (4:6) was used and the reaction conditions were tested and found to give the highest HMF yields after 0.5 h at 110 °C. $CrCl_2$ was found to be the best catalyst for the conversion of D-glucose (45% yield).

To further expand the scope of monosaccharide starting materials, an eutectic mixture of D-glucosamine hydrochloride and ChCl (1:9 wt/wt) was developed with a melting point of 100 °C.[25] The dehydration of D-glucosamine to HMF in this mixture using Amberlyst 15 and $FeCl_3$ as catalysts was tested. However, even prolonged reaction times at 120 °C did not result in the formation of the desired product. The dehydration reaction of D-glucosamine to HMF was reported in pure AcOH by Zivanovic *et al.*[26]

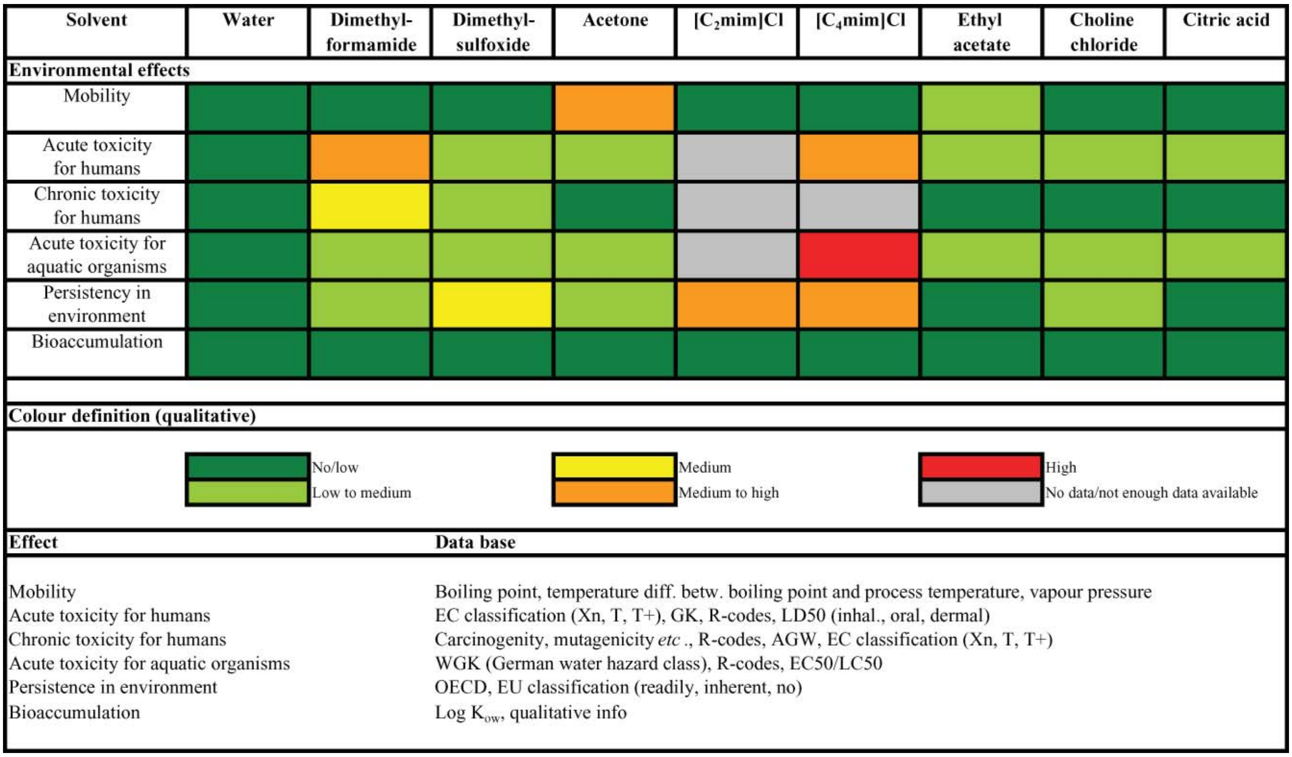
Next, the more complex carbohydrates sucrose (5:5, wt/wt sucrose : ChCl) and inulin (5:5, wt/wt inulin : ChCl) were used as starting materials for HMF synthesis in the melt. Sucrose is supposed to react around 18 times faster than glucose. Inulin is an abundant polyfructan with an average of 100 fructose units per molecule.[27] The direct conversion of both sucrose and inulin into HMF combines the hydrolysis step to monosaccharides and the elimination of water in one process, thus saving one reaction step in the synthesis. The formation of HMF, levulinic acid and humins was monitored for different reaction times (0.5 to 2 h) and temperatures (80-100 °C): The best HMF yields were found for sucrose at 100 °C and 1 h reaction time. Longer reaction times at this temperature led to the formation of insoluble humins. Reactions at 110 °C gave in less than 30 min high amounts of humins. For sucrose, the chromium catalysts gave the best HMF yields, while for inulin pTsOH as catalyst gave the highest HMF yields (see Table 3).

Preliminary ecological evaluation of carbohydrate–ChCl melts for carbohydrate conversion

In a first ecological screening, we compared the environmental effects of selected solvent mixtures used for the conversion of carbohydrates to 5-hydroxymethylfurfural, as discussed in the introduction (water, dimethylformamide, DMSO, acetone/DMSO, AcOEt/ChCl/citric acid, [C_2mim]Cl, [C_4mim]Cl),[28] with the herein investigated choline chloride system (see Fig. 3). The assessment is mainly based on safety data sheets.[29] Concerning the mobility, solvents with lower boiling points might enter the environment more likely, especially by working under higher reaction temperatures as in the case of the HMF formation. Therefore, especially the ionic liquids [C_2mim]Cl and [C_4mim]Cl as well as choline chloride and choline chloride/citric acid and water might be suitable media reducing the environmental impact into air due to their negligibly low vapour pressure as well as the inherent low toxicological impact in the case of water, citric acid and choline chloride. Accordingly, the potential impact on human health can be reduced. However, especially in the case of the ionic liquids, often not enough data for the assessment of the toxicological risks for human and ecosystems are currently available.

Taking into consideration the bioaccumulation potential, the selected solvents feature log K_{OW} values < 1, indicating that no bioaccumulation can be expected and the bioaccumulation potential can be stated as low, respectively. However, the persistence also influences the environmental fate and toxicity potential of the solvents. For determining the biodegradation properties, safety data sheets as well as the software BioWIN[30] were consulted. Dimethyl sulfoxide is not readily biodegradable, while for the studied ionic liquids only limited information are available, indicating that they are not readily biodegradable. Recently reported results indicate that for imidazolium based ionic liquids with short alkyl (≤ 6) and short functionalised side chains no biological degradation can be expected, while ionic liquids consisting of imidazolium and pyridinium cations with octyl chains are biodegradable.[31,32] Therefore, the persistence of the ionic liquids in the environment was classified as "medium to high". The factors of bioaccumulation and persistence influence the ecological effects and toxicity on aquatic organisms. Hence, the entry into the water pathway should be avoided, especially in the case of the ionic liquids where disposal strategies are still rare.[31,33]

Concerning EHS issues of the solvents considered for the ecological evaluation, the solvent systems choline chloride/citric acid and water as well as the herein investigated low melting mixture choline chloride/fructose feature preferable properties making them more suitable media for a "greener" reaction process. However, a conclusive statement requires a more holistic examination, including *e.g.* the performance, energy requirements, auxiliary materials, catalysts as well as costs under consideration of upstream and downstream chains. For instance, the workup of the conversions we report here uses, similar to the procedure by Hu *et al.*,[10] ethyl acetate to extract the product phase from choline chloride, resulting in an additional solvent demand and exposure risks as well as time and energy consuming



Solvent	Water	Dimethyl-formamide	Dimethyl-sulfoxide	Acetone	[C_2mim]Cl	[C_4mim]Cl	Ethyl acetate	Choline chloride	Citric acid
Environmental effects									
Mobility	🟩	🟩	🟩	🟧	🟩	🟩	🟢	🟩	🟩
Acute toxicity for humans	🟩	🟧	🟢	🟢	▨	🟧	🟢	🟢	🟢
Chronic toxicity for humans	🟩	🟨	🟢	🟩	▨	▨	🟩	🟩	🟩
Acute toxicity for aquatic organisms	🟩	🟢	🟢	🟢	▨	🟥	🟢	🟢	🟢
Persistency in environment	🟩	🟢	🟨	🟢	🟧	🟧	🟩	🟢	🟩
Bioaccumulation	🟩	🟩	🟩	🟩	🟩	🟩	🟩	🟩	🟩

Colour definition (qualitative)

🟩 No/low	🟨 Medium	🟥 High
🟢 Low to medium	🟧 Medium to high	▨ No data/not enough data available

Effect	**Data base**
Mobility	Boiling point, temperature diff. betw. boiling point and process temperature, vapour pressure
Acute toxicity for humans	EC classification (Xn, T, T+), GK, R-codes, LD50 (inhal., oral, dermal)
Chronic toxicity for humans	Carcinogenity, mutagenicity *etc* ., R-codes, AGW, EC classification (Xn, T, T+)
Acute toxicity for aquatic organisms	WGK (German water hazard class), R-codes, EC50/LC50
Persistence in environment	OECD, EU classification (readily, inherent, no)
Bioaccumulation	Log K_{ow}, qualitative info

Fig. 3 Qualitative assessment of the environmental effects of selected solvent systems used in the conversion of carbohydrates to 5-hydroxymethylfurfural: water, dimethylformamide, dimethyl sulfoxide, acetone/dimethyl sulfoxide, [C_2mim]Cl, [C_4mim]Cl, ethyl acetate/choline chloride/citric acid and choline chloride, respectively.

distillation steps. In contrast, the use of high boiling solvents like dimethyl sulfoxide, water and dimethylformamide might also have the drawback of high energy consumption or the use of additional solvents during the separation process. We previously discussed the ecological performance of [C_6mim][BF_4] and citric acid/DMU (wt/wt 40/60) in the Diels–Alder reaction of cyclopentadiene with methyl acrylate in comparison to molecular solvents. At this, we could show that the development of efficient recycling strategies should be addressed for further work, and the use of multiphase reaction systems might be beneficial concerning ecological as well as economic issues.[17] At the moment, investigations are extended to optimise the reaction performance, to study the possibility of recycling the reaction medium and to facilitate the product separation. Then, a more accurate statement especially concerning ecological improvements will be possible. In addition, the use of heterogeneous catalysts, like Amberlyst 15 and Montmorillonite for the conversion of biomass, or the possibility of biphasic reaction systems while the catalyst remains in the solvent phase, should be addressed in further research.

Conclusions

Low melting carbohydrate mixtures are suitable to convert carbohydrates into 5-hydroxymethylfurfural. The melts are non-toxic, based on bulk renewables, have high sugar contents (up to 50 wt%) and a negligibly low vapour pressure. In an optimisation study, choline chloride was found to be the most suitable melt additive since it is chemically inert under the reaction conditions used. For D-fructose, an eutectic point at 4:6 (fructose : ChCl, wt/wt) with a melting region of 79-82 °C (DSC) was determined. A reaction time of 1 h at 100 °C gave best results for HMF using $CrCl_2$ (10 mol% based on sugar). Apart from D-fructose, D-glucose, sucrose and inulin were tested with different catalysts at individually optimised conditions. The best HMF yields from the carbohydrate-ChCl systems were 67% for fructose (*p*TsOH, 100 °C, 0.5 h), 45% for glucose ($CrCl_2$, 110 °C, 1 h), 42% for sucrose ($CrCl_2$, 100 °C, 1 h) and 57% for inulin (*p*TsOH, 90 °C, 1 h), respectively.

In a screening study, a comparison of the environmental impact of different conventional and alternative solvents for the conversion of carbohydrates into HMF indicates advantages of the melt systems in terms of low toxicity and reduced mobility. However, these investigations have to be extended by a more holistic ecological as well as economic evaluation under consideration of upstream and downstream chains to provide a final comparison.

Experimental

General

All chemicals were used for syntheses as received without further purification. For DSC measurements, the compounds were dried under vacuum at 90 °C for 5 h. The dried compounds were kept under nitrogen and transferred to a glove box. HMF was purchased from Sigma Aldrich and stored under nitrogen at 4 °C.

Preparation of the melts

Unless otherwise stated, the constituents of the melts were ground with a mortar and pestle, filled into a resealable vial equipped with a stirring bar and placed into an oil bath. Upon formation of the melt, the catalysts were loaded under nitrogen (unless otherwise stated) before the vial was sealed.

NMR spectroscopy

NMR spectra were recorded on a Bruker Avance 300 (^{1}H: 300.1 MHz, ^{13}C: 75.7 MHz, $T = 300$ K). The spectra are referenced against the internal NMR-solvent standard and chemical shifts are reported in ppm.

Determination of the pH value

For the measurements, a 691 pH-meter from Metrohm was used which was calibrated with pH 4.0 and 7.0 buffer solutions prior to use. Determination of the pH value is conducted by measuring a solution (1.13 M for fructose : imidazole 1:1) of 100 mg melt in distilled water (0.9 mL). The pH value reported represents the average of three independent measurements.

Melting point and DSC measurements

The melting points were determined in a first approximation with a Büchi SMP 20. More exact measurements were conducted by differential scanning calorimetry. The pre-dried samples were blended, transferred to aluminium pots and sealed in a glove box. Two heating cycles were recorded with a temperature range of −15 to 100 °C within 5 minutes time.

Synthesis of 5-hydroxymethylfurfural (HMF)

D-Fructose (0.40 g, 2.20 mmol) and choline chloride (0.60 g, 4.30 mmol) were molten in a 50 mL reaction flask at 100 °C until a clear melt was formed. Amberlyst 15 (50 mg) was added and the reaction was stirred for 0.5 h. Afterwards, water (20 mL) was added and the mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated to give HMF (166 mg, 40%). The ^{1}H and ^{13}C NMR-spectroscopic data complied with the literature.[34]

HPLC measurements

The HPLC measurements were conducted with a LabID 86/Phenomenex Luna 3u HILIC 200 A, 150 × 2.00 mm column with PL-ELS 2100 evaporative light scattering detection and run with ACN/H_2O/100 mM NH_4OAc: 90:5:5 as eluent. The column temperature was 40 °C, the injection volume 0.1 µL, while a flow rate of 0.3 mL/min and both sucrose (for glucose and fructose) and acetanilide (for sucrose and inulin) as internal standard were used. For monitoring and evaluation of the chromatographic results, the program ChemStation for LC 3D Systems Rev. B.03.02 was used.

List of abbreviations

ACN	Acetonitrile
AGW	Arbeitsplatzgrenzwert (Threshold limit value)

ChCl	Choline chloride
$[C_4mim]Cl$	1-Butyl-3-methylimidazolium chloride
DMF	Dimethylformamide
DMSO	Dimethyl sulfoxide
DMU	*N*,*N′*-Dimethyl urea
EC50	Half maximal effective concentration
EHS	Environment, health, safety
$[C_2mim]Cl$	1-Ethyl-3-methylimidazolium chloride
EtOAc	Ethyl acetate
GK	Giftklasse (Swiss poison class)
$[C_6mim][BF_4]$	1-Hexyl-3-methylimidazolium tetrafluoroborate
HPLC	High performance liquid chromatography
IL	Ionic liquid
LC50	Median lethal concentration
LD50	Median lethal dose
Log K_{OW}	Log octanol-water partitioning coefficient
Me	Methyl-
NMR	Nuclear magnetic resonance
PE	Petrol ether
*p*TsOH	*Para*-toluene sulfonic acid
$Sc(OTf)_3$	Scandium (III) triflate
T_{dec}	Decomposition temperature
TGA	Thermogravimetric analysis
TMU	*N*,*N′*-Tetramethyl urea
WGK	Wassergefährdungsklasse (German water hazard class)
Wt	Weight

Acknowledgements

We thank the Südzucker AG and the Fachagentur Nachwachsende Rohstoffe for the support of the project. F. I. thanks the German Federal Environmental Foundation (DBU) for a graduate scholarship and A. P. thanks the Fonds der Chemischen Industrie for a thesis fellowship.

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