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Dehydration of Highly Concentrated Solutions of Fructose to 5-Hydroxymethylfurfural in a Cheap and Sustainable Choline Chloride/Carbon Dioxide System

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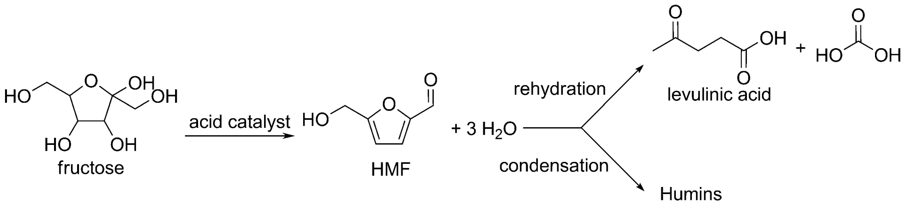
With the depleting of fossil carbon reserves together with a continuous increase of the per-barrel price, utilization of biomass as raw material for the production of fuels and chemicals has become of growing interest.[1,2] In this context, much effort has been devoted to the acid-catalyzed dehydration of hexoses to 5-hydroxymethylfurfural (HMF). HMF is a platform chemical especially used for the fabrication of renewably sourced and potentially safer polymers.[3] The efficiency of this reaction is mainly governed by the nature of the solvent used. In particular, the solvent has to be capable of dissolving a large amount of carbohydrates while diluting released water in order to limit the side-reaction of rehydration of HMF to levulinic and formic acids (Scheme 1).



Scheme 1. Dehydration of fructose.

In the current literature, DMSO, water, mixtures of water and organic solvents, and ionic liquids have been extensively investigated as solvents for the synthesis of HMF.[4] Although promising results have been reported, these systems still have shortcomings such as price/toxicity (ionic liquids), reactivity (water), or energy-consuming extraction processes (DMSO) that clearly hamper their industrial suitability. Recently, König and co-workers smartly reported that fructose was capable of forming a deep eutectic solvent (DES)[5] when mixed with choline chloride; a cheap, nontoxic, and biodegradable quaternary ammonium salt.[6] They showed that in the presence of a metal salt, hexoses such as fructose can be dehydrated in such DESs affording HMF with yield up to 60%. Since then, several groups have attempted to optimize these neoteric systems and significant advances have been recently reported in this field. In particular, DES-derived fluids have been proven to provide similar results to those collected in imidazolium-based ionic liquids while offering a lower ecological and economical footprint, thus opening a new strategy for the production of HMF in a more rational way.[7] In DESs, Brønsted or Lewis acids are used to catalyze the dehydration of hexoses to HMF.[8] Although few studies have pointed out that HMF can be selectively extracted from DES with an organic solvent such as methylisobutylketone (MIBK) or ethylacetate, slight contamination of HMF with Lewis (metal salts) or Brønsted acid is nearly unavoidable, complicating the synthesis of HMF with the required industrial specifications.

On the other hand, the addition of CO_2 to a choline chloride (ChCl)-derived DES is known to decrease the pH of this system through the formation of carbonic acid.[9] Additionally, Han and co-workers have shown that the pK_a of carbonic acid is sufficient to catalyze the dehydration of fructose to HMF.[10] Considering that (1) the fructose contained 1.2 wt% of water (determined by means of Karl Fisher analysis), and (2) water is released when HMF is produced, it occurred to us that fructose could be conveniently dehydrated to HMF in ChCl upon addition of CO_2. In this context, we show here that up to 70% yield of HMF can be obtained in a ChCl/CO_2 system. The main advantages of this work stem from (1) the absence of work-up required for removing trace amounts of catalyst contained in HMF after extraction; (2) the use of cheap and safe CO_2 as a reservoir of acid; (3) the low ecological footprint of the ChCl/CO_2 system; and (4) that the system is still efficient when using high loadings of fructose (100 wt%), which is one of the main disadvantages of current procedures.

In a first set of experiments, ChCl containing 20 wt% of fructose was heated at 120 °C under 4 MPa of CO_2. The reaction progress (conversion, yields) was monitored by HPLC. As shown in Figure 1, under these conditions, a 60% yield of HMF was obtained after only 15 min of reaction, demonstrating that CO_2 can indeed react with water contained in fructose to generate carbonic acid and then to promote the formation of HMF. After prolonged reaction time, the yield of HMF reached a maximum of 74% at 90 min of reaction before gradually decreasing due to the degradation/condensation of HMF to insoluble and soluble black materials (presumably, humins). At the end of the reaction (after release of the CO_2 pressure),

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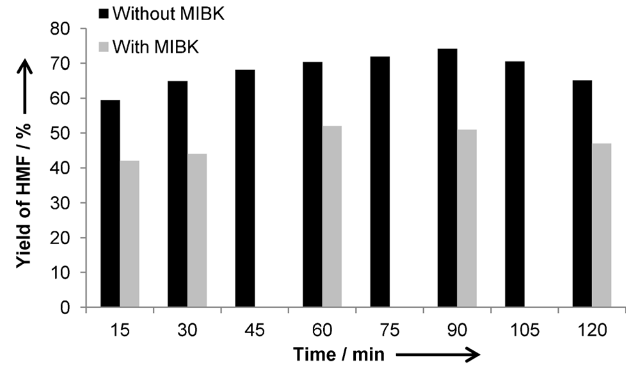

Figure 1. Hydrolysis of fructose to HMF versus time, with or without MIBK. Conditions: 20 wt % fructose, $T = 120\,^{\circ}C$, $P_{CO_2} = 4$ MPa, $t = 90$ min, in choline chloride (25 g).

HMF was selectively extracted from the reaction medium with MIBK. Due to the high selectivity of the reaction and the insolubility of ChCl in MIBK, HMF was recovered with a purity of 98 % (HPLC titration, see ^{1}H NMR spectrum of recovered HMF in the Supporting Information). Using this procedure, more than 88 % of produced HMF was extracted from ChCl (i.e., 62 % isolated yield).

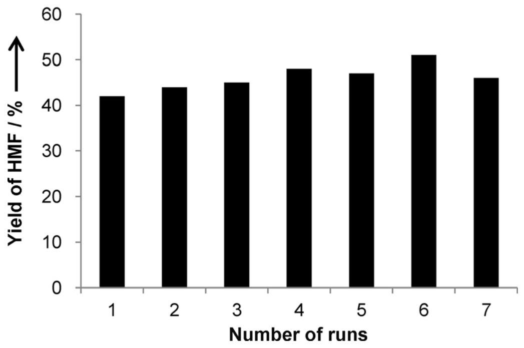

Figure 2. Recycling tests. Conditions: 20 wt % fructose, 20 mL MIBK, $T = 120\,^{\circ}C$, $P_{CO_2} = 4$ MPa, $t = 90$ min.

It was possible to perform the catalytic reaction in a biphasic ChCl-fructose/MIBK system, which allowed continuous and selective extraction of HMF from the catalytic mixture. At the end of the reaction, the MIBK phase containing HMF was recovered by decantation. In such a configuration, ChCl could be successfully recycled at least 7 times without appreciable decrease of the yield of HMF, further demonstrating the usefulness of this methodology (Figure 2). However, after the 7th run a drop of the HMF yield was observed, which may be attributed to the accumulation of water in ChCl. Increase of the content of water in ChCl-derived DES is, indeed, known to drastically decrease the solubility of CO_2 in such DESs.[9]

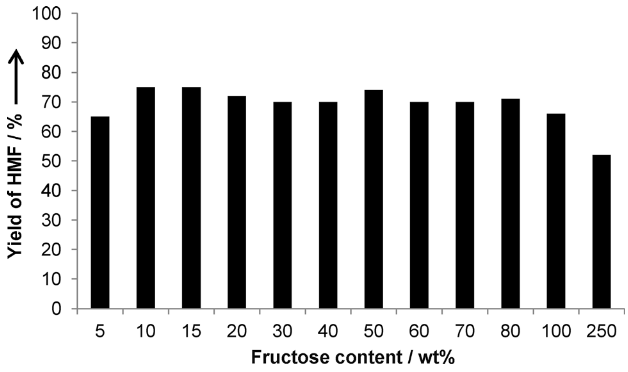

Figure 3. Effect of the fructose content on the HMF yield. Conditions: $T = 120\,^{\circ}C$, P_{CO_2}4 MPa, $t = 90$ min.

It should be pointed out that catalysis in a biphasic ChCl-fructose/MIBK system should normally lead to an enhancement of the yield of HMF because of its continuous extraction, which is known to limit its degradation in the catalytic phase. However, conversely to current methods, a significant drop of the yield of HMF from 74 % to 52 % was observed in the presence of MIBK (Figure 3). As observed above, after 90 min of reaction, the degradation of HMF became the dominant reaction over dehydration of fructose (Figure 1). We may assume that the inhibition of the HMF yield in the presence of MIBK might be due to the higher solubility of CO_2 in MIBK than in the ChCl-fructose phase, thus limiting the formation of carbonic acid. This hypothesis is supported by three independent works of Sato,[11] Wong,[9a] and Han,[9b] which tend to show that solubility of CO_2 is much higher in MIBK than in ChCl-derived DES. Hence, one can conclude that in our system it is better to extract HMF only at the end of the reaction prior to recycling ChCl.

Having all these results in hand, we next changed the temperature and the CO_2 pressure in order to find the optimal conditions for our system (Table 1). As expected, a decrease of the reaction temperature from 120 °C to 110, 100, and 90 °C led to a decrease of reaction rate since after 90 min of reaction HMF was obtained in 72, 64, 54 and 33 % yield, respectively. In a similar way, a decrease of the CO_2 pressure below 2 MPa lowered the reaction rate, which is consistent with the formation of carbonic acid in a lower amount as previously observed by Han and co-workers.[10]

Table 1. Effect of temperature and CO_2 pressure on the yield of HMF.[a]

Entry	T [°C]	P_{CO_2} [MPa]	Yield of HMF [%]
1	120	4	72
2	110	4	64
3	100	4	54
4	90	4	33
5	20	2	66
6	20	1	30

[a] 20 wt % fructose, $t = 90$ min

Next, we investigated the possible increase of the fructose content (Figure 3). This point is of particular interest for industrial applications and is currently a limiting factor in most reported strategies. It is well established that an increase of the fructose content generally lowers the selectivity of the reaction. Hence, most works are only applicable for a fructose content ranging between 5 and 20 wt%.[3] To this end, the fructose content in ChCl was varied from 5 to 250 wt% (Figure 3). Remarkably, 100 wt% of fructose could be dehydrated to HMF in ChCl/CO_2 without appreciable loss of yield (66%), increasing again the interest of such a system for the eco-efficient synthesis of HMF.

This surprising tolerance of the ChCl/CO_2 system to a high content of fructose can be attributed to a change of the physico-chemical properties of the ChCl/fructose mixture. As previously reported, ChCl is capable, even in the presence of water, of forming various DESs with a wide range of hydrogen-bond donors such as urea, polyols, or carboxylic acid. One may suspect that when fructose is converted, ChCl and HMF tend to form a new DES explaining the remarkable stability of HMF under our conditions. Indeed, previous studies have clearly shown that when a component is engaged in the formation of a DES, its reactivity is drastically reduced.[12] To check this hypothesis, various mixtures of ChCl and HMF were heated at 110 °C for 10 min and then cooled to room temperature. Interestingly, from a HMF content of 60 wt% in ChCl, a liquid phase was obtained at room temperature further pushing forward the possible formation of a ChCl–HMF eutectic mixture when working at high concentration of fructose (Figure 4).

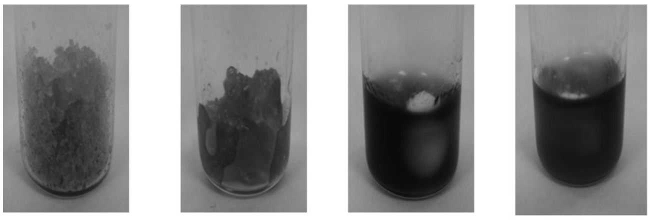
HMF = 20 wt% HMF = 40 wt% HMF = 60 wt% HMF = 100 wt%

Figure 4. Pictures of various ChCl/HMF mixtures at room temperature.

This change of physico-chemical properties can be also observed during the extraction stage of HMF with MIBK. In particular, whereas HMF can be easily extracted from a ChCl/fructose mixture (fructose content <40 wt%) or from neat water with MIBK, the use of ultrasound was required when the fructose content was higher than 40 wt%, supporting that a strong interaction between ChCl and HMF occurred when working with a high content of fructose. It should be noted that the more difficult extraction of HMF when it is produced at high concentration unfortunately led to a concomitant decrease of the purity of recovered HMF. Indeed, the purity of HMF recovered after extraction with MIBK decreased from 98% to 93% and 80% when the fructose content was increased from 20 wt% to 80 wt% and 100 wt%, respectively. This change of purity is also consistent with the formation of a ChCl/HMF DES. Because of the stabilization of HMF in ChCl, the extraction of impurities competes with the extraction of HMF.

Having demonstrated that the ChCl/CO_2 system was very convenient for the dehydration of fructose to HMF, we next investigated the ability of this system to promote the tandem hydrolysis/dehydration of inulin, a biopolymer of fructose, to HMF (Table 2). In the presence of 20 wt% of inulin dissolved in ChCl (120 °C, 4 MPa CO_2, 90 min), the yield of HMF was rather disappointing (12%). This low yield can be ascribed to the low content of water at the initial stage of the reaction that does not favor the hydrolysis of inulin to fructose. Hence, we decided to initially add 16 wt% of water. Under these conditions, the yield of HMF was improved up to 22%, confirming that water was not present in a sufficient amount in the ChCl/inulin system. Upon prolonged reaction time, the yield of HMF was significantly increased and reached 38% after 6 h of reaction. HMF was also recovered with 41% yield after 14 h of reaction further demonstrating the stability of HMF in ChCl as compared to other solvents. Notably, and in accordance with previous reports, this strategy was not applicable to the dehydration of glucose, mainly because carbonic acid was not capable of isomerizing glucose to fructose, a step required prior to dehydration to HMF.

Table 2. Acid-catalyzed production of HMF from inulin (20 wt%) in choline chloride (25 g) under 4 MPa CO_2 at 120 °C.

Entry	H_2O added [mL]	t[a] [h]	Yield of HMF [%]
1	–	1.5	12
2	5	1.5	22
3	5	6	38
4	5	15	41

[a] Time of the experiment.

In conclusion, we report that fructose can be conveniently dehydrated to HMF in a ChCl/CO_2 system with a yield of up to 72%. In addition to the environmental benefits of this strategy, we found that HMF is highly stable in the presence of ChCl, presumably through the formation of a eutectic mixture. This aspect allows to perform the catalytic process with a high content of fructose (up to 100 wt%) as compared to traditional procedures, in which HMF is obtained in yields higher than 60% only from a fructose content lower than 20 wt%. Additionally, whereas after extraction HMF is unavoidably partly contaminated with traditional Lewis and Brønsted acids, the possible decrease of pH upon addition of CO_2 allows circumventing this problem because carbonic acid is readily converted to CO_2 and water when the CO_2 pressure is released. Finally, we have shown that this system is capable of promoting the tandem hydrolysis/dehydration of inulin to HMF, further increasing the interest of such methodology. The further application of this reaction medium to the conversion of renewable raw materials is the topic of current investigations in our group.

Experimental Section

Analytical methods: Yields of HMF were determined by external calibration at 25 °C using an HPLC equipped with a Nucleosil 100–5C18 column (250×4.6 mm), a Shimadzu LC-20AT pump, a Shimadzu RID-10A detector, and an acetonitrile/water (10:90) mixture as mobile phase (0.8 mL min^{-1}). Fructose was quantified by external calibration at 25 °C using a HPLC equipped with a Varian NH$_2$ column, a Varian Prostar RID detector, Varian Prostar pumps (model 210), and an acetonitrile/water (90:10) mixture as mobile phase (0.8 mL min^{-1}).

General procedure for the dehydration of fructose to HMF: Fructose was dissolved in 25 g of choline chloride in a batch reactor. Then the mixture was heated under air at 120 °C. When the desired temperature was reached, air was replaced by CO$_2$ (4 MPa). All reaction times provided in the manuscript correspond to the reaction time under CO$_2$ and do not take into account the heating period of the reactor. At the end of the reaction the autoclave was cooled to room temperature and the pressure was released. Although CO$_2$ was not recycled here, it should be noted that recycling of CO$_2$ is clearly possible and does not represent a technical obstacle to the scale-up of this work. The yield of HMF was determined by analysis of the reaction medium by HPLC. HMF was then extracted from the reaction medium with MIBK. After removal of MIBK under vacuum, HMF was recovered with 98 % purity (determined by HPLC)

In the case of a continuous extraction of HMF with MIBK, 20 mL of MIBK was added at the beginning of the process prior to heating the reactor. The MIBK phase containing HMF was then separated from the medium by simple phase decantation. Then, MIBK was removed under vacuum affording HMF as a dark-brown chemical. Because the extraction with MIBK is highly selective to HMF, the distilled MIBK could be recycled for other extraction cycles.

Recycling experiments: Recycling experiments were performed in choline chloride–MIBK mixture (25 g–20 mL) using a fructose content of 20 wt %. The temperature was 120 °C and the reaction time was 15 min. After the first extraction of HMF with MIBK, fructose was directly reloaded to the recovered choline chloride. The reaction was then heated again at 120 °C for 15 min. This procedure was repeated up to the 7th cycle.

Acknowledgements

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Keywords: biomass · carbohydrates · carbon dioxide · catalysis · renewable resources

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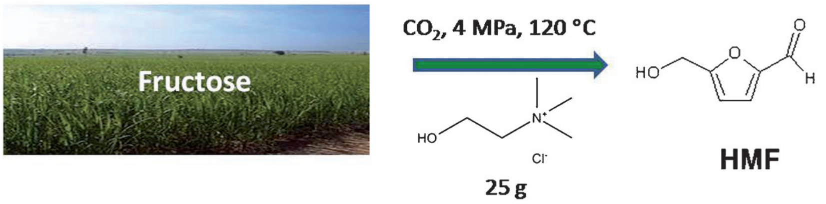

Fête DES sciences: The dehydration of fructose and inulin to HMF is conveniently performed in a cheap and sustainable choline chloride/CO$_2$ deep eutectic solvent (DES) system. The medium is capable of converting high contents of fructose ($>$100 wt %) without affecting the yield of HMF (up to 72 %). The purity of the recovered HMF is $>$98%, and the reaction medium can be recycled.

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