

PRODUCTION OF 5-HYDROXYMETHYLFURFURAL (HMF) VIA FRUCTOSE DEHYDRATION: EFFECT OF SOLVENT AND SALTING-OUT

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Abstract - 5-Hydroxymethylfurfural (HMF) is a key renewable platform compound for production of fuels and chemical intermediates. The production of 5-hydroxymethylfurfural (HMF) from fructose dehydration was studied using H_3PO_4 as catalyst, in organic/water system with different solvents (acetone, 2-butanol and ethyl ether). The effect of fructose concentration, temperature and acid concentration was investigated in acetone/water medium. The increase in fructose concentration favors the formation of condensation products and rehydration products are favored at high acid concentration. The solvents exhibited similar performance when the volume ratio of organic to aqueous phase was 1:1, but when this ratio increases to 2:1, the HMF yield obtained with ether was much lower. NaCl addition to the aqueous phase promoted the extraction of HMF to the organic phase, with an HMF yield of 80% in the case of 2:1 acetone/water medium.

Keywords: 5-hydroxymethylfurfural; Dehydration; Fructose; Biphasic system; Salting-out.

INTRODUCTION

The interest in renewable resources as chemical feedstocks has grown considerably in recent years. The production of fine chemicals, polymer precursors and petrol-derived commodities from biomass can contribute to diminish our current dependence on non-renewable energy sources. Furanic derivatives can be used as the starting materials for new products as well as for replacement of oil-derived chemicals, establishing a new set of chemical compounds based on biomass (Tong *et al.*, 2010). In particular, 5-hydroxymethylfurfural (HMF) has been considered an important platform chemical in a bio-refinery because it is a precursor for the production of various high-volume plastics and biofuels (Boisen *et al.*, 2009; Bozell and Petersen, 2010; Corma *et al.*,

2007). HMF is a versatile and multi-functional compound used as intermediate for polymers, pharmaceuticals, fine chemicals, liquid fuels and for the synthesis of dialdehydes, ethers, amino alcohols and other organic derivatives (Boisen *et al.*, 2009; Tong *et al.*, 2010).

Despite the versatile application profile of HMF-derived intermediate chemicals, HMF is not yet produced on an industrial scale, mainly because of the high production costs (Zakrzewska *et al.*, 2011). HMF can be obtained by acid-catalyzed dehydration of different carbohydrates such as fructose, glucose, sucrose, cellulose or inulin (Rosatella *et al.*, 2011). Glucose, which is the most abundant and the cheapest monosaccharide, has been considered as the preferred feedstock for the production of HMF. However, HMF is typically produced from glucose with low

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yields, which is attributed to the stable pyranoside ring structure of glucose (Hu *et al.*, 2012). Thus, current technologies in general include an additional isomerization step of glucose to fructose, since dehydration of fructose to HMF takes place with better selectivity and higher rates (Chheda *et al.*, 2007; Grande *et al.*, 2012). The isomerization step can be done either enzymatically or by using aqueous bases or solid catalysts, such as hydrotalcites, zeolites and different oxides.

Efficient HMF production requires the minimization of side reactions that yield soluble and insoluble polymers and HMF rehydration to levulinic and formic acids (Corma *et al.*, 2007; Roman-Leshkov *et al.*, 2006; Chheda *et al.*, 2007; Roman-Leshkov and Dumesic, 2009). Dehydration of fructose in pure water using solid or mineral acids is generally non-selective due to degradation of HMF via rehydration reactions. Different strategies have been used in HMF synthesis to decrease the formation of by-products. The use of aprotic solvents, such as dimethylsulfoxide (DMSO), has been investigated by many authors to suppress unwanted side reactions and generate high yields of HMF (Roman-Leshkov *et al.*, 2006; Chheda *et al.*, 2007; Musau and Munavu, 1987). However, the separation of HMF from these high-boiling point solvents is difficult, leading to thermal degradation of the HMF product. Some interesting results have been presented on the dehydration of carbohydrates in ionic liquids, which have unique properties such as negligible vapor pressure and comparative thermal stability (Van Putten *et al.*, 2013; Zakrzewska *et al.*, 2011). Nevertheless, the high costs of ionic liquids, the limited data about toxicity and complicated HMF separation and purification still limit their industrial application.

Biphasic systems, in which a water-immiscible organic solvent is added to extract continuously HMF from the aqueous phase, offer an important advantage in that the product is separated from the reactant and reaction intermediates and is thereby protected against degradation reactions (Boisen *et al.*, 2009; Chheda *et al.*, 2007; Roman-Leshkov *et al.*, 2006; Van Putten *et al.*, 2013). This extraction shifts the equilibrium reaction to favor HMF production. However, this method requires a large amount of solvent due to the high HMF solubility in water and poor partitioning into the organic phase. Roman-Leshkov *et al.* (2006) reported a two-phase reaction system with HCl as the catalyst. In that work DMSO and poly(1-vinyl-2-pyrrolidone)(PVP) were added to the aqueous phase to suppress the undesired side reactions and HMF was continuously

extracted into an organic phase of methylisobutylketone (MIBK) modified with 2-butanol to enhance the partitioning from reactive aqueous solution. It was reported that an 80% HMF selectivity at 90% conversion was achieved for 30 wt% fructose solution at 180 °C.

The salting-out technique can be used to change the partition coefficient of HMF in a biphasic system and thus improve the HMF yield (Roman-Leshkov and Dumesic, 2009; Hansen *et al.*, 2011). The use of salting-out for carbohydrate dehydration has been known since the 1930s (Fulmer *et al.*, 1935). The ions in solution alter the intermolecular forces between the liquids in equilibrium, resulting in an increased immiscibility. The decreased mutual solubility of the aqueous and organic phases enhances the extraction of HMF from the aqueous phase (Roman-Leshkov and Dumesic, 2009). Roman-Leshkov and Dumesic (2009) studied the effect of different inorganic salts (LiCl, KCl, NaCl, CsCl, CaCl₂, MgCl, KBr, NaBr and Na₂SO₄) in biphasic systems using 1-butanol as the extracting solvent and HCl as catalyst. Na⁺ and K⁺ showed the best combination of extracting power and HMF selectivity of the monovalent and divalent chloride salts tested. Using NaCl an 82% HMF selectivity at 87% fructose conversion was achieved at 180 °C, with a partition coefficient of 3.1. Hansen *et al.* (2011) also studied the effect of different salts in water:MIBK system, using boric acid as catalyst. They reported 65% HMF selectivity at 70% fructose conversion, using NaCl at 150 °C, with a partition coefficient of only 1.0.

This paper studies the effect of different solvents and the use of the salting-out technique in HMF production by dehydration of fructose. The solvents chosen were acetone, 2-butanol and ethyl ether. Acetone has the advantage of being a biomass-derived solvent, 2-butanol showed the highest HMF selectivity of all solvents studied by Roman-Leshkov and Dumesic (2009), and ethyl ether is a very volatile solvent, favoring HMF separation by distillation without degradation. The reaction conditions were evaluated in the water/acetone system, and then these conditions were applied to the other solvents, with or without NaCl addition to the aqueous phase.

EXPERIMENTAL

Fructose, phosphoric acid, organic solvents and NaCl were obtained from Sigma-Aldrich in reagent grade.

All fructose dehydration reactions were carried out in a 600 mL SS reactor (Parr) with 450 rpm of agitation and H_3PO_4 as catalyst, under autogeneous pressure. The reaction time was maintained constant at 10 min. The first experiments were performed with 100 mL of water and 100 mL of acetone, varying fructose concentration (25, 75 and 125 g L^{-1}), temperature (120, 150, 180 and 200 $^\circ\text{C}$), and H_3PO_4 concentration (0.5, 1.0 and 1.5 wt%).

Once the reaction conditions were defined, other solvents were tested (2-butanol and ethyl ether), with the ratios of volumes of both phases (Vorg:Vaq) at 1:1 or 2:1 (100 mL of water and 100 or 200 mL of organic solvent). In some experiments, NaCl was added to saturate the water phase (300 g L^{-1}).

All products were analyzed by high performance liquid chromatography (HPLC) on a Shimadzu Prominence system, equipped with UV and RI detectors and an Aminex HPX-87H column (Biorad), using 0.01 M H_2SO_4 as the mobile phase at a flow rate of 0.8 mL min^{-1} .

The fructose conversion (C_f) and the HMF selectivity (S_{HMF}) and yield (Y_{HMF}) are described by Eq. (1)-(3), respectively.

$$C_f(\%) = \frac{\text{moles of fructose reacted}}{\text{moles of fructose initial}} \times 100 \quad (1)$$

$$S_{\text{HMF}}(\%) = \frac{\text{moles of HMF produced}}{\text{moles of fructose reacted}} \times 100 \quad (2)$$

$$Y_{\text{HMF}}(\%) = \frac{\text{moles of HMF produced}}{\text{moles of fructose initial}} \times 100 \quad (3)$$

For biphasic systems, the partition coefficient (R) is defined in Eq. (4).

$$R = \frac{\text{HMF concentration in organic phase}}{\text{HMF concentration in aqueous phase}} \quad (4)$$

RESULTS AND DISCUSSION

Effect of Reaction Conditions Using Water/Acetone

Figure 1 depicts a generalized reaction scheme for production of HMF by elimination of three water molecules from fructose. Cross-polymerization of HMF, fructose and reaction intermediates can lead to condensation products, such as soluble polymers and insoluble humins, and HMF rehydration produces

levulinic and formic acids. Dehydration of fructose was carried out using H_3PO_4 as homogeneous catalyst. The choice of H_3PO_4 was based on its low corrosivity towards stainless steel reactors, as compared to HCl, and the good results presented by some authors in the literature using this catalyst. Takeuchi *et al.* (2008) compared HCl, H_3PO_4 and H_2SO_4 as catalysts for glucose dehydration in water: the higher HMF yields were obtained using H_3PO_4 . According to them, the use of a strong acid such as HCl accelerates the rehydration of HMF to levulinic and formic acids. High HMF selectivities were also obtained when using H_3PO_4 in glucose dehydration performed in biphasic system (Chheda *et al.*, 2007) and in fructose dehydration in subcritical water (Asghari and Yoshida, 2006).

Firstly, the influence of fructose concentration, temperature, and H_3PO_4 concentration was analyzed in water/acetone medium, with results summarized in Table 1. The reaction time was kept at 10 min because previous experiments (unpublished) showed that longer times increase the degradation and rehydration reactions. Many studies in the literature, using organic solvents and homogeneous catalysts, have employed similar reaction times (van Putten *et al.*, 2013). When the initial fructose concentration was increased from 25 to 125 g L^{-1} the HMF conversion remained almost constant at 100%; however, the HMF yields decreased from 66 to 55%. This result is in agreement with reports in the literature that increasing the fructose concentration leads to higher rates of condensation reactions, with formation of larger amounts of humins (Rosatella *et al.*, 2011; Roman-Leshkov *et al.*, 2006; Cao *et al.*, 2011). The option for working with 125 g L^{-1} of fructose in the further experiments was based on the greater productivity of a higher feed concentration for an industrial process, measured by the amount of HMF produced per unit reactor volume and thus a more favorable process economics (Cao *et al.*, 2011).

It was observed that an increase of the temperature favored fructose conversion and HMF yield, as shown in Table 1. The best result was obtained at the temperature of 180 $^\circ\text{C}$, reaching 98% of fructose conversion and a HMF yield of 55%, since a further increase to 200 $^\circ\text{C}$ only increased the HMF yield to 57%. According to Jiang *et al.* (2012), when the reaction temperature is in the range of 170-190 $^\circ\text{C}$ there is no significant influence on the fructose conversion and HMF yield (in the water/n-butanol system). Kuster (1990) reported that HMF selectivity increases with temperature because the activation energy for HMF formation is higher than for HMF degradation. The same was measured by Moreau *et*

al. (2006). The formation rate of HMF is increased by a higher enolization rate, as well as by a higher proportion of the acyclic and furanose forms of fructose at higher temperature (Kuster, 1990). On the other hand, Ranoux *et al.* (2013) reported that the formation of rehydration products from HMF increases exponentially with reaction temperature (from 170 to 200 °C) in aqueous media without any catalyst. Above 200 °C several significant fragmentation products can be formed from fructose, such as acetaldehyde, acetic acid, glycolaldehyde and propeionic acid (Daorattanachai *et al.*, 2012).

The H_3PO_4 concentration was evaluated in the range of 0 - 1.5 wt%, with the results shown in Table 1. The blank test (without H_3PO_4) showed low fructose conversion and almost no HMF formation. Some works reported good HMF yields from fructose in the absence of catalyst, such as Brown *et al.* (1982) in DMSO solvent, or Ranoux *et al.* (2013) in aqueous media, but with much longer reaction times (at

least several hours). The use of 0.5% catalyst resulted in an increased fructose conversion and HMF yield; increasing the acid concentration to 1.0%, the conversion and HMF yield improved significantly (98% and 55%, respectively). However, a further increase to 1.5% did not show any benefit; on the contrary, the conversion and HMF yield decreased to 92 and 52%, respectively. According to Takeuchi *et al.* (2008), the increase in acid concentration accelerates the rehydration of HMF, which explains the decrease in HMF yield. In fact, the formation of levulinic and formic acids was higher when the H_3PO_4 concentration was 1.5%. Kuster and Temmink (1977) investigated the role of pH in fructose dehydration using formic acid for pH adjustment, showing that HMF formation is favored at pH 2.7-3.9; below pH 2.7 rehydration products are favored. The ideal pH range found by Souza *et al.* (2012) was 1.5-2.15, using HCl as catalyst for fructose dehydration in water, at 150 °C.

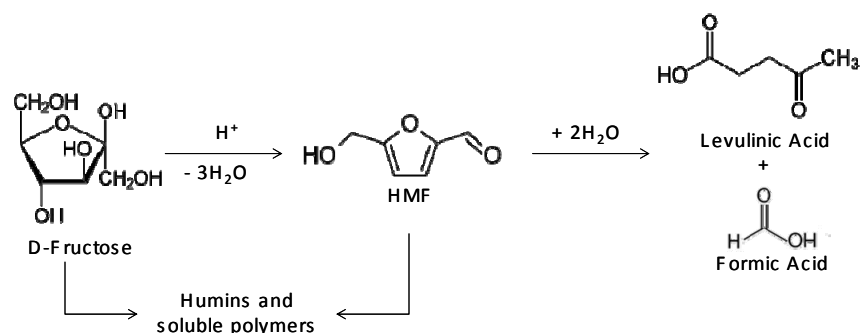


Figure 1: Reaction scheme for fructose dehydration to HMF and parallel reactions.

Table 1: Results of fructose dehydration in water/acetone (Vorg:Vaq=1:1), under different reaction conditions.

Fructose concentration (g L ⁻¹)	Temperature (°C)	H ₃ PO ₄ concentration (%)	[HMF] (g L ⁻¹)	C _f (%)	S _{HMF} (%)	Y _{HMF} (%)
25	180	1.0	11.6	100	66	66
75	180	1.0	32.8	94	66	62
125	180	1.0	48.4	98	56	55
125	120	1.0	1.2	14	9.7	1.4
125	150	1.0	10.6	24	50	12
125	200	1.0	50.2	100	57	57
125	180	0	1.6	18	10	1.9
125	180	0.5	32.1	84	43	37
125	180	1.5	45.8	92	57	52

Effect of Different Solvents

Once the reaction conditions had been defined using water/acetone medium, these conditions (125 gL⁻¹ of fructose, 180 °C and 1% of H₃PO₄) were used to test other solvents (2-butanol and ethyl ether), and also varying the volume ratio of both phases (Vorg:Vaq=1:1 and 2:1). The results of fructose dehydration with different solvents, as well as with only an aqueous phase, are displayed in Figure 2. The fructose conversion was almost 100% in all reactions. The benefit of using an organic solvent, even if it is completely miscible with water, is clearly shown when analyzing the HMF yields: in aqueous medium the HMF yield is only 34%, and with water/organic mixture it increases to 50-60% (when the volume ratio is 1:1). Thus, the presence of organic solvent in the reaction system decreases the possibility of HMF contact with water that leads to HMF degradation and rehydration. The 1:1 ether:water system is biphasic (the solubility of ether in water is very low) and the partition coefficient was very low, only 0.3, showing a poor migration of HMF to the organic phase.

The HMF yields were similar for all three solvents when the volume ratio was 1:1, with a slightly lower value for ethyl ether. The HMF yield with acetone was 55%, close to that obtained with 2-butanol (59%). According to Bicker *et al.* (2003), acetone favors the furanoid form of fructose, from which HMF is preferably obtained. Roman-Leshkov and Dumesic (2009) found higher HMF selectivity

with 2-butanol than with acetone, but the tests were only performed with the aqueous phase saturated with NaCl. When the volume ratio Vorg:Vaq was increased to 2:1 the HMF yields were almost the same as with the 1:1 ratio in the case of acetone and 2-butanol, showing that, with totally miscible solvents, the increase in organic content does not result in an increase in HMF formation. However, when using ethyl ether in a 2:1 ratio there was extensive formation of humins and the HMF yield was only 27%, with a partition coefficient of 0.4. The use of a very low boiling point solvent is not adequate in biphasic systems, because the solvent goes preferentially to the vapor phase during the reaction, without the desired effect of extracting HMF from the aqueous phase.

Effect of Salting-Out

The salting-out technique was applied using NaCl and its concentration (300 g L⁻¹) was obtained by saturation tests. The use of NaCl promotes the phase separation, creating biphasic systems with solvents that are completely miscible with water in the absence of salt. The benefit of using a biphasic medium is that the organic solvent acts as an extraction phase of the HMF formed in the aqueous phase, i.e., the HMF generated in the water migrates continuously to the organic medium. Thus, the residence time of HMF in water is decreased and side reactions are therefore minimized.

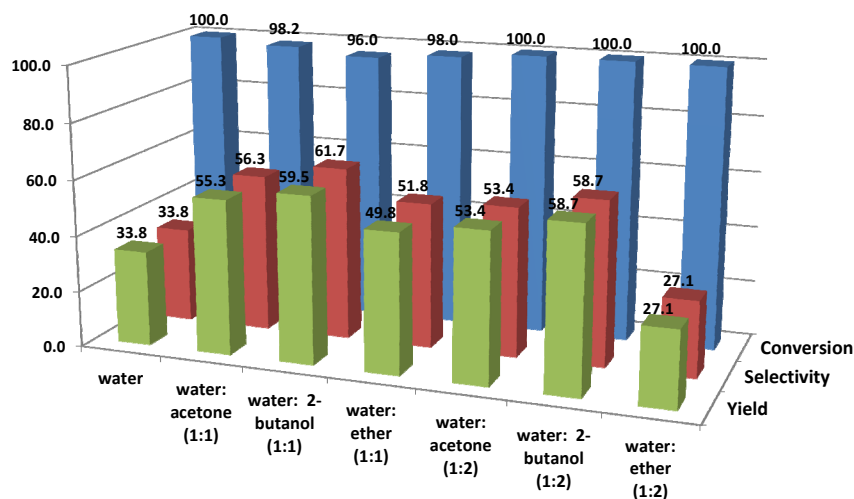


Figure 2: Results of the fructose dehydration reaction with different solvents. Reaction conditions: 125 g L⁻¹ of fructose, 180 °C and 1% of H₃PO₄.

Figure 3 shows the fructose conversion and HMF selectivity and yield in the reactions performed with NaCl addition, using different solvents and two different volume ratios Vorg:Vaq (1:1 and 2:1). The corresponding distribution of HMF between the organic and aqueous phases, and the values of the partition coefficient R, is shown in Figure 4. The extent of the salting-out effect depends on the nature of the ionic interactions between all components of the system. For acetone and 2-butanol, with a volume ratio of 1:1, the addition of NaCl did not provide any significant benefit as compared to the same system without salt. On the other hand, the HMF yield obtained in the water/ether medium was less than half of that without salt (maintaining the volume ratio at 1:1), with a low value of the partition coefficient ($R=0.6$) and high formation of rehydration and degradation products.

When the volume ratio Vorg:Vaq was increased to 2:1, HMF yields increased significantly for ether and acetone systems, while there was only a slight increase for 2-butanol. In general, a higher R-value is correlated with a higher HMF yield. However, the higher R value (4.4) was obtained with 2-butanol, while the higher HMF yield (80%) was provided when using acetone ($R=3.4$). It is noteworthy that this R-value was measured at room temperature and it can be different from the value at the reaction temperature. Comparing this result in acetone medium with that of Roman-Leshkov and Dumesic (2009) (79% of HMF selectivity at 62% of conversion, $R=3.6$, using an acetone:water ratio of 3.2, HCl as catalyst, at 150 °C), an equivalent HMF selectivity with higher fructose conversion was obtained using a lower proportion of organic phase, 180 °C and 1% of H_3PO_4 .

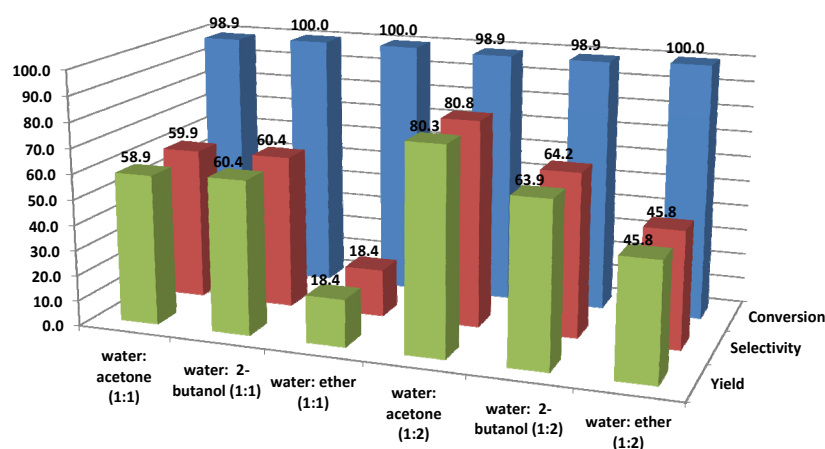


Figure 3: Results of the fructose dehydration reaction with different solvents and the aqueous phase saturated with NaCl. Reaction conditions: 125 g L⁻¹ of fructose, 180 °C and 1% of H_3PO_4 .

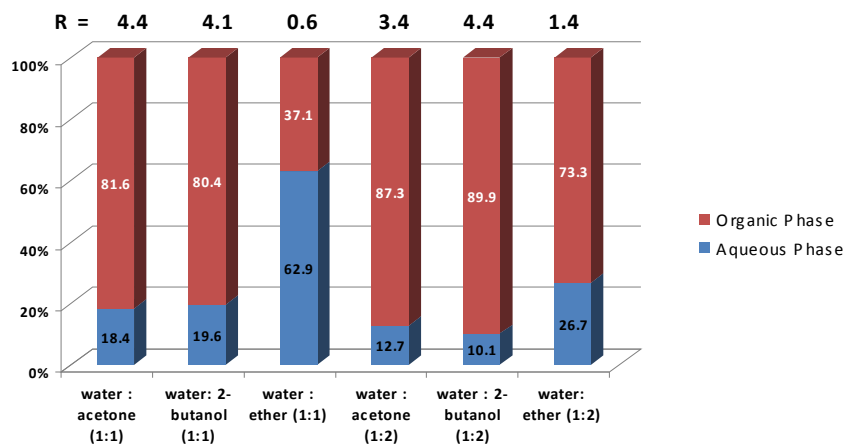


Figure 4: Distribution of HMF between the organic and aqueous phases, and values of the partition coefficient R for the fructose dehydration reaction with different solvents and the aqueous phase saturated with NaCl. Reaction conditions: 125 g L⁻¹ of fructose, 180 °C and 1% of H_3PO_4 .

CONCLUSIONS

The evaluation of reaction conditions using the water/acetone system revealed that the HMF yield decreased with increasing fructose concentration due to the higher contribution of condensation reactions. The HMF yield increased with temperature (in the range of 120-200 °C) and showed a maximum value with a H₃PO₄ concentration of 1 wt%. With increasing acid concentration rehydration reactions were favored.

Using an organic system the HMF yield was significantly higher than in aqueous medium alone. Comparing the three solvents used in this study, it was clearly observed that acetone and 2-butanol lead to better reaction results than ethyl ether, which forms biphasic systems even without salt. The addition of NaCl created biphasic systems with acetone and 2-butanol, and the benefit of the salting-out effect was more pronounced when the volume ratio of water to organic phase was 1:2. The best result was obtained with the 1:2 water:acetone system containing NaCl, i.e., an 80% of HMF yield with a partition coefficient of 3.4, which is very promising compared to other studies in the literature.

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