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OPTIMIZATION OF PRODUCTION OF 5-HYDROXYMETHYLFURFURAL FROM GLUCOSE IN A WATER: ACETONE BIPHASIC SYSTEM

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Abstract - 5-Hydroxymethylfurfural (HMF) is considered to be an important building block for biorefineries and has a high potential for the production of chemicals and fuels. Production of HMF from glucose was studied using phosphoric acid as catalyst, in a water:acetone system with volume ratio of 1:2 and NaCl. An experimental design was applied to examine the influence of temperature, time and concentration of catalyst on the HMF yield. HMF yields of more than 50 % were obtained when using 200 °C, 8.4 min and 0.8% of catalyst. The temperature is the main factor influencing the HMF yield.

Keywords: 5-hydroxymethylfurfural; Glucose; Acetone; Design of experiments.

INTRODUCTION

There is a growing interest in fuels and chemicals from renewable sources and furan compounds are an alternative platform for biorefinery processes (Román-Leshkov and Dumesic, 2009; Huang *et al.*, 2010). This versatile family of compounds may result in derivatives which can replace fossil fuels as the source of traditional chemical intermediates for the production of polyesters, polyamides and polyurethanes (Moreau *et al.*, 2004).

One of the most attractive furan compounds is 5-hydroxymethylfurfural (HMF), which occurs naturally as a product of thermal degradation of sugars and nowadays is considered to be a biorefinery building block, or a key compound for the development of an advanced biorefinery (Rasrendra *et al.*, 2010). From this compound, 2,5-dimethylfuran (Román-Leshkov *et al.*, 2007), esters of levulinic acid and HMF ethers (Yang. *et al.*, 2012, Peng *et al.*, 2011, Peng *et al.*, 2012) can be obtained, for possible use in Otto cycle or diesel engines, besides furan dicarboxylic acid (FDCA), applied in the production of polyesters (Ribeiro and Schuchardt, 2003).

The main route for obtaining HMF is the dehydration of monosaccharides, like glucose and fructose, catalyzed by acids. However, many other products can be obtained from sugars in acidic aqueous medium, such as furfural, levulinic acid, formic acid, lactic acid, mannose and glycolaldehyde (Antal *et*

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*To whom correspondence should be addressed *al*., 1990, Lecomte *et al*., 2002, Moliner *et al*., 2010, Watanabe *et al*., 2005). Other important point to note is that yields from fructose are not reproduced by using glucose in aqueous medium, due to the higher ring stability that causes a higher rate of enolization of fructose (ketose) in relation to glucose (aldose), which is an important step to facilitate the dehydration reaction (Pidko *et al*., 2010, Zakrzewska *et al*., 2011). Zakrzewska (2011) reported several studies using ionic liquids for conversion of hexoses, Simeonov and coworkers (2013) studied integrated chemo-enzymatic systems for glucose conversion and the yields were higher than obtained with aqueous medium, but the trend to lower yields with glucose that with fructose was also observed. Biphasic systems can improve the yields because HMF is continuous extracted from the aqueous phase to the organic phase, avoiding rehydration and condensation reactions, and the use of solvent with low boiling point is desirable to facilitate the product separation. Water:acetone mixtures have been used as reaction medium for HMF production to promote the rearrangement of fructose to the furanoid form (Biker *et al*., 2003). Roman-Leshkov and Dumesic (2009) tested a biphasic system water (saturated with NaCl):acetone at 150 °C for 35 min, with HCl as catalyst and obtained 62% of fructose conversion with 79% of HMF selectivity, however, the system was not tested for glucose. Acetone can also be used as solvent for HMF extraction after reaction (Zhang *et al*., 2010). Phosphoric acid was used as catalyst in aqueous media and the maximum glucose conversion was approximately 60% at 220 °C for 5 min, with HMF yield of 9.6% (Daorattanachai *et al*., 2012).

In general, most of the studies use a dilute solution of glucose, resulting in low product concentrations, increasing the cost of separation and purification. Despite their efforts, the industrial production of HMF is not yet a reality. It is still necessary to find a process that is highly selective with high isolated yields of HMF so that the final price is competitive. According to Putten *et al*. (2013), the use of glucose or cellulose and starch for the production of HMF is still a challenge because the more extreme conditions of conversion are also possible degradation conditions for HMF, a barrier that must be overcome to make the process economically more favorable. The purpose of this study was to evaluate different reaction conditions (temperature, time and catalyst concentration) in acetone/water systems saturated with NaCl, using H_3PO_4 as catalyst and concentrated solutions of glucose for HMF production. For this, response surface methodology (RSM) was applied in order to obtain an optimum condition for HMF production from glucose.

EXPERIMENTAL

Dehydration Procedure

For the tests 1-17, 100 mL of glucose solution (250 g.L^{-1}), 200 mL of acetone and 30 g of sodium chloride were used, and the temperature, time and catalyst concentration (H_3PO_4) were varied in accordance with the experimental design matrix. All experiments were performed in a stainless steel reactor (450 mL) with agitation at 350 rpm. The salt promotes the phase separation water:acetone by saturation of the aqueous phase. The pressure was the result of system dynamics (20-21 bar). After cooling the reactor the two phases were separated using a separatory funnel and the products were analyzed by high performance liquid chromatography (HPLC) using a Shimadzu Prominence instrument with Aminex HPX-87H column at 55 °C, an injection loop of 20 μL and 5mM sulphuric acid at 0.8 mL.min^{-1} as the mobile phase. Glucose residue was detected by refractive index (RID-10A) and HMF by the UV detector at 210 nm (SPD-20AV). Acetone was recovered using a rotary evaporator at 30 °C and reused.

Glucose conversion (X), HMF yield (Y) and HMF selectivity (S) were calculated according to Eqs. (1)-(3):

$$X=\frac{\text{moles of glucose reacted}}{\text{moles of glucose initial}} \text{ x } 100 \tag{1}$$

$$Y=\frac{\text{moles of HMF produced}}{\text{moles of glucose initial}} \text{ x } 100 \tag{2}$$

$$S=\frac{Y}{X} \text{ x } 100 \tag{3}$$

Three tests to verify the autocatalysis possibility as reported by Ranoux *et al* (2013) and to evaluate the influence of each system component were performed. First an aqueous solution of glucose was heated from room temperature to 200 °C, removing aliquots from 120 °C every twenty degrees. In the second, added acetone 1:1 and 30 g of NaCl and, last, using glucose solution with 1% of phosphoric acid, with the same sampling procedure.

Experimental Design

The central composite design (CCD) was used to evaluate the effects of three independent variables or factors: temperature (x_1), time (x_2) and concentration of catalyst (x_3). The design consisted of 8 factorial points ($2n = 2^3 = 8$), 6 axial points and 3 central points, totaling 17 trials. The glucose conversion (X), the HMF yield (Y) and the HMF selectivity (S) are the dependent variables. The studied levels for each factor are described in Table 1. STATISTICA version 6 was utilized to estimate the approach of RSM with CCD.

Table 1: The range and levels of the independent variables for CCD.

Factors	Levels				
	-α	-1	0	+1	+α
Temperature (°C) – x_1	183.2	190	200	210	216.8
H_3PO_4 (% v/v) – x_2	0.33	0.5	0.75	1.0	1.17
Time (min) – x_3	1.6	3.0	5.0	7.0	8.4

RESULTS AND DISCUSSION

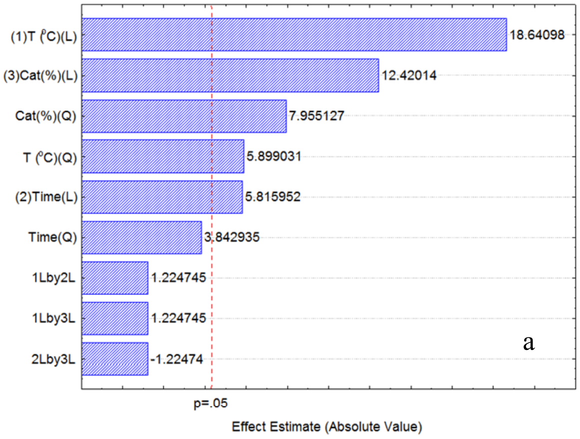
Glucose can form true oligosaccharides that still contain reactive reducing groups, resulting in a greater risk of cross-polymerisation with reactive intermediates and HMF (Rosatella *et al*., 2011), coupled with the fact that the stability of the ring limits the yield in aqueous media. In many reactions the formation of black solid residues was observed, especially in tests conducted at high temperatures, as reported in Shi *et al*. (2013). The high concentration of glucose could favor the reverse reaction to form oligosaccharides that can be dehydrated and form char. For the tests 1-17, the conversions were greater than 89% (Table 2). Yield values ranged from 19% to 49 %, and the selectivity from 21 % to 52 %; the worst results were obtained in test 9, which was carried out at the lowest temperature, 183 °C. The effect of temperature on yield is observed when comparing this test with the ones at the central point (tests 15-17), where the conditions were the same except that the temperature was 200 °C: the HMF yield obtained was almost double that of test 9. In addition to HMF, levulinic acid, formic acid and furfural have been identified as products in a few tests.

The statistical analysis was performed in four steps: significance test of the factors, graphical analysis of the residuals, ANOVA and application of F test to subsequently trace the response surface. The magnitude of the effects of the factors temperature, time and catalyst concentration on the response variables is shown in the diagrams of Figure 1, which presents Pareto charts for glucose conversion (a), HMF yield (b) and selectivity (c). For the conversion, the temperature was the most influential factor, which is consistent with the natural tendency of glucose to be converted with increasing temperature, and all of the other factors were significant. On the other hand, the major influence on the yield was the catalyst concentration, for which the Pareto diagram indicates a reduction in the initial concentration of acid. The time factor was statistically significant for the conversion factor, and not significant for yield and selectivity, for the range of values studied. Since the yield is the main parameter of the study, all subsequent analysis will be directed to evaluate the optimization of this factor.

Table 2: Experimental design matrix and results for CCD.

Test	Factors			Response variables		
	Temperature (°C) x_1	Time (min) x_2	% H_3PO_4 x_3	X (%)	Y (%)	S (%)
1	-1	-1	-1	90	22	24
2	-1	-1	+1	92	31	34
3	-1	+1	-1	91	29	32
4	-1	+1	+1	92	34	37
5	+1	-1	-1	96	42	43
6	+1	-1	+1	99	33	33
7	+1	+1	-1	98	36	37
8	+1	+1	+1	100	24	24
9	0	0	-1.68	90	30	33
10	0	0	+1.68	97	32	33
11	0	-1.68	0	90	40	44
12	0	+1.68	0	95	49	52
13	-1.68	0	0	89	19	21
14	+1.68	0	0	100	40	40
15	0	0	0	92	40	43
16	0	0	0	91	42	46
17	0	0	0	91	40	44

X = Conversion, S = Selectivity and Y = Yield (molar)



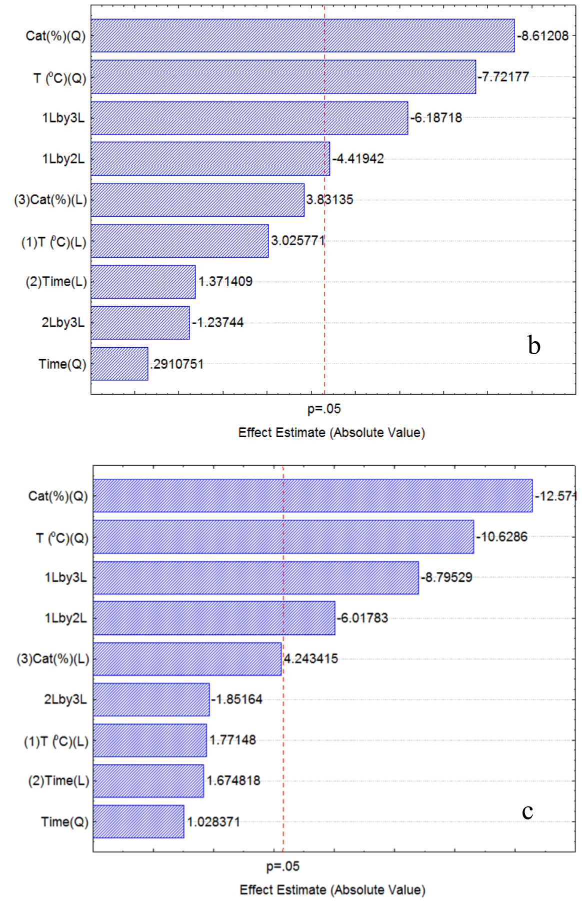


Figure 1: Pareto charts of CCD. Glucose dehydration for glucose conversion (a) HMF yield (b) and selectivity (c).

The graphical analysis of the residuals was used to assess the normality of the data, which is indicated in Figure 2a. The expected behavior for a normal sample is observed in the graph, for which the points approximate a straight line. Once verified the normality of the data, other tests can be performed in order to assess the statistical model generated by the program. One important analysis is shown in Figure 2b, comparing the values predicted *versus* values observed, in which the deviation from the straight line through the origin is small and the points show a linear trend, indicative of model fit.

Table 3 summarizes the regression analysis for HMF yield. Analysis of variance (ANOVA) was applied to test the mathematical modeling with $\alpha = 0.05$ (level of significance) and is presented in a simplified form. The F test was used to verify that the change of the independent variable had a significant influence on the variation of the dependent variable; if so, the calculated value of F (F_{calc}) is greater than the tabulated F (F_{value}). This hypothesis was verified for the three response variables, indicating that the model generated adequately described the phenomenon. The F test was used to verify that the change of the independent variable had a significant influence on the variation of the dependent variable; since $F_{calc} = 17.3074$ is greater than $F_{value} = 3.63$, this hypothesis was verified, indicating that the model generated describes adequately the phenomenon.

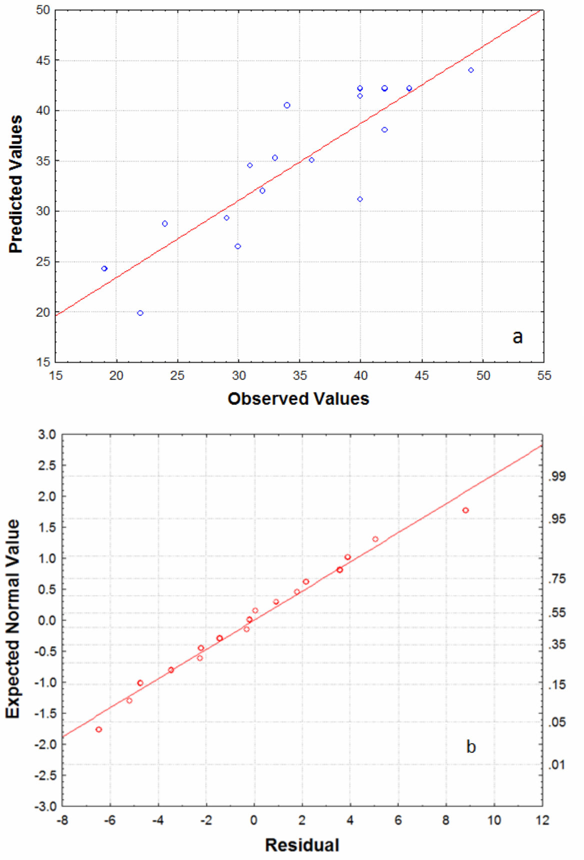


Figure 2: Graphical analysis of residuals. a) comparison of normal probability to residuals; b) Observed vs. predicted values for HMF yield.

Table 3: ANOVA of glucose conversion, HMF yield and selectivity.

Mode	Sum of squares	Degrees of freedom	Mean Squares	F_{Value}	F_{Table}
HMF Yield					
Regression	875.75	9	925.207	17.3074	$F_{0.05}$=3.63
Residual	255.286	7	53.4573		
Total	1131.036	16			

The model Equation (Eq. (4)) was obtained for the HMF yield, in which the variables x_1 and x_3 are the temperature and catalyst concentration, respectively, and Y is the HMF yield. The quadratic fit of the model should satisfy R^2 greater than 0.75 featuring an acceptable degree of agreement between the predicted and the observed values. For the response variable in question the R^2 obtained was 0.75165 and the lack of fit with $p = 0.099531$, greater than 0.05, therefore not significant and is within of significance level established. The equation is obtained for the coded values of the variables.

$$Y = 42.428 + 1.638x_1 - 4.651(x_1)^2 + 2.074x_3 \\ -5.181(x_3) - 4.375x_1x_3 \quad (4)$$

The model generates the response surface of Figure 3, in which the relation between the HMF yield and the significant response variables, temperature and catalyst concentration, is shown graphically. For this, the time at the central point, 5 min, was set. Despite the borderline fit of the model, it is possible to verify the advantage of modeling the data showing clearly that the HMF yield is optimized for the system studied. This result is consistent because at higher temperatures, the yield decreases due to the occurrence of side reactions, and at higher catalyst concentrations the same effect occurs.

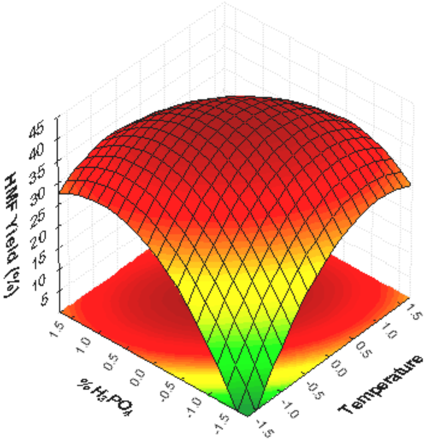


Figure 3: Response surface for HMF yield based on temperature and catalyst concentration.

Effect of Biphasic System

To evaluate the effect of the two-phase system on the HMF yield and the possibility that formic and levulinic acids promote dehydration of glucose without catalyst, three tests were performed and yields are shown in Figure 4. It was observed that only at 200 °C were significant yields obtained for the three systems. Ranoux *et al.* (2013) reported a 19% conversion of glucose to HMF to 195 °C with 38% selectivity using only water. As shown in Figure 5, approximately 60% conversion was reached at 200 °C for the system water-glucose. The most probable hypothesis is that the use of the closed and agitated reactor contributed to a higher rate of mass transfer and thus increased the conversion of glucose. However, it had a negative effect on the stability of the HMF yield leading to only 0.4% in this condition. By adding the catalyst, as expected, conversion increased considerably and this trend was also observed for the yield, yet in the experiment with acetone increases to 25.3%. Therefore, there is overwhelming evidence that the addition of a solvent to form a second phase that takes up HMF is critical to achieve high yields at higher temperatures.

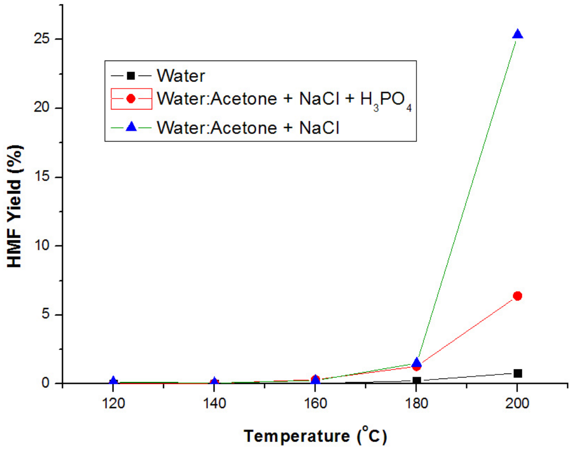


Figure 4: HMF molar yields at different temperatures. Reaction conditions: glucose solution 250 $g.L^{-1}$ for all systems, phosphoric acid 1% (v/v) when present and acetone:água 1:1 for the biphasic systems (HMF not isolated).

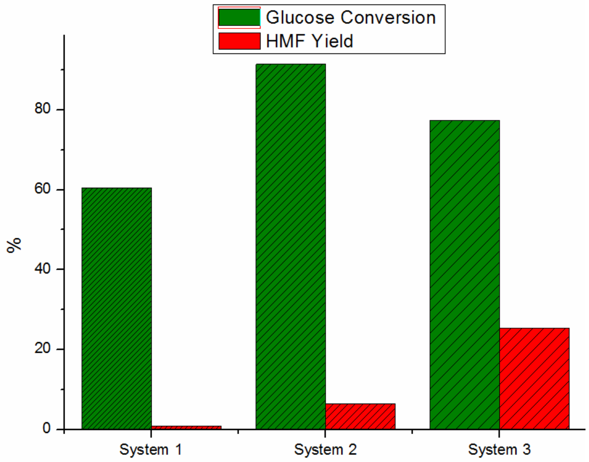


Figure 5: HMF yields and conversions at 200 °C for reactions in systems 1 (water), 2 (water:acetone + NaCl) and 3 (water:acetone + NaCl + H_3PO_4).

The formation of formic acid, levulinic acid, furfural and HMF is shown in Figure 6 for the different temperatures tested for the system glucose, water and phosphoric acid. The results corroborate the hypothesis of HMF rehydration due to the high concentration of formic acid formed. Qi *et al*. (2008) observed that the fructose conversion and HMF yield improved with an increase in acetone concentration in the acetone–water mixtures attributed to a conformational change of fructose to the furanoid form in the presence of acetone, and to the suppression of HMF dehydration. The mechanism of glucose dehydration is still unclear for this mixture. In this study, small amounts of fructose were detected as product, but were insufficient to state that isomerization had occurred. Shi *et al*. (2013) reached a 45.2% yield of HMF in a biphasic system using water:tetrahydrofuran (THF) 1:10, $NaHSO_4$ and $ZnSO_4$ as a catalyst and 0.2 g of glucose in 44 mL of solvent. However, the authors employed THF as the major solvent, which does have some disadvantages, such as high cost and environmental effects. A slightly higher yield (58%) was obtained by Caes *et al*. (2013) in a system with N, N-dimethylacetamide (ionic liquid), $CrCl_2$ and 10% glucose by weight.

Table 4 shows a comparison between HMF yields and initial concentrations of glucose using biphasic systems. McNeff *et al*. (2010) used an initial glucose concentration, time and temperature similar to those used in this study. Nikolla *et al*. (2011) obtained a yield similar to that obtained in this work, however, using an inorganic acid and a solid catalyst. However, HMF yields from glucose remain low when compared to fructose, as noted by Putten *et al*. (2013) in their recent review.

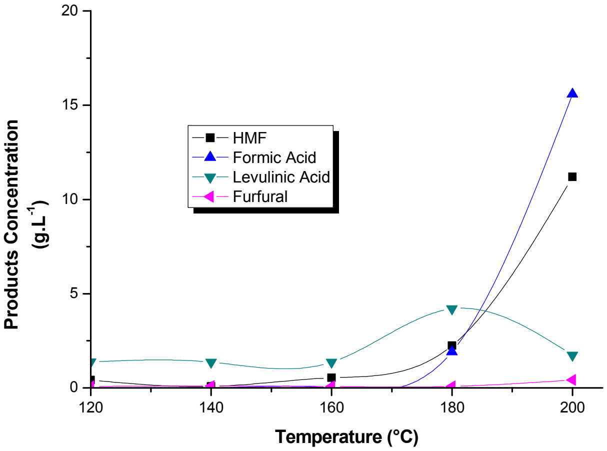


Figure 6: Product concentration versus temperature, using 1% H_3PO_4 (v/v) and initial glucose solution.

Table 4: HMF yields from glucose obtained in two-phase systems.

Initial Glucose Concentration (wt %)	Biphasic System	Catalyst	Catalyst loading	Temperature (^{o}C)	Time (min)	X %	Y %	S %	Reference
23%	Water:n-butanol	TiO_2	Fixed bed	200	3	-	13	-	McNeff *et al.* (2010)
10%	Water (26% NaCl):THF	Ti- β-Zeolite/HCl	pH=1 0.5 mol% Ti	180	105	76	53	70	Nikolla *et al.* (2011)
10%	Water (26% NaCl):n-butanol	Sn-β-Zeolite/HCl	pH=1 0.5 mol% Sn	160	90	75	41	55	Nikolla *et al.* (2011)
25%	Water (30% NaCl):acetone	H_3PO_4	0.8% (v/v)	200	8.4	95	49	52	This study

X = Conversion, S = Selectivity and Y = Yield

CONCLUSIONS

The analysis of the response surface for the variable yield, keeping the time constant at 5 minutes, demonstrated that the system was otimized, considering the inlet variables: temperature (183.2 to 216.8 °C) and catalyst (0.33 to 1.17%). The water:acetone system studied was able to convert glucose into 5-hydroxymethylfufural, using an aprotic solvent with low boiling point, enabling a less energy-intensive recovery of the solvent. The use of a biphasic system with acetone and NaCl to extract the HMF promoted an increase in the reaction yield compared to the aqueous system because HMF migrates preferentially into the organic phase, avoiding its rehydration. The statistical analysis showed that the HMF yield is optimized within the range of factors used. The best result obtained was an approximately 50% HMF yield at 200 °C, in 8.4 minutes and 0.75% of catalyst, which is appreciable when considering the low reaction time, ease of solvent recovery and low toxicity of the reagents; however, HMF was not totally isolated from the reaction medium. The relativity low cost of the reaction system (catalyst and solvent), when compared to the cost of ionic liquids or other aprotic solvents, makes this system even more attractive.

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