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Sulfonic acid heterogeneous catalysts for dehydration of C₆-monosaccharides to 5-hydroxymethylfurfural in dimethyl sulfoxide

Gabriel Morales^{a,*}, Juan A. Melero^a, Marta Paniagua^a, Jose Iglesias^b, Blanca Hernández^a, María Sanz^a

^a Department of Chemical and Environmental Technology, Universidad Rey Juan Carlos. C/ Tulipán s/n. Móstoles. E28933. Madrid, Spain

^b Department of Chemical and Energy Technology, Universidad Rey Juan Carlos. C/ Tulipán s/n. Móstoles. E28933. Madrid, Spain

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ABSTRACT

Sulfonic acid-functionalized heterogeneous catalysts have been evaluated in the catalytic dehydration of C₆ monosaccharides into 5-hydroxymethylfurfural (HMF) using dimethyl sulfoxide (DMSO) as solvent. Sulfonic commercial resin Amberlyst-70 was the most active catalyst, which was ascribed to its higher concentration of sulfonic acid sites as compared with the other catalysts, and it gave 93 mol% yield of HMF from fructose in 1 h. With glucose as the starting material, which is a much more difficult reaction, the reaction conditions (time, temperature, and catalyst loading) were optimized for Amberlyst-70 by a response surface methodology, which gave a maximum HMF yield of 33 mol% at 147 °C with 23 wt% catalyst loading based on glucose and 24 h reaction time. DMSO promotes the dehydration of glucose into anhydroglucose, which acts as a reservoir of the substrate to facilitate the production of HMF by reducing side reactions. Catalyst reuse without a regeneration treatment showed a gradual but not very significant decay in catalytic activity.

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1. Introduction

As a consequence of the declining easily accessible fossil fuel reserves and the impact of CO₂ emission on climate change, interest in renewable resources such as chemical feedstocks has grown considerably. The production of fine chemicals, polymer precursors, and petroleum derived commodities from biomass can diminish our current dependence on non-renewable energy sources. Actually, biomass offers the only renewable source of organic molecules for the manufacture of bulk, fine and speciality chemicals, and it is necessary for the future needs of society. However, to be a truly sustainable strategy, biomass feedstocks must originate from the non-edible components of crops, cellulosic material from agricultural or for-

estry waste, or short rotation non-food crops requiring minimal cultivation. In this sense, lignocellulosic furanic derivatives should be the starting materials for products as well as for the replacement of oil-derived chemicals to establish a new set of chemical compounds with sustainable biomass origin [1]. In particular, 5-hydroxymethylfurfural (HMF) is considered an important platform chemical derived from cellulosic biomass that has a potential leading role in the development of biorefineries [2–5]. The reason is that HMF is a versatile and multi-functional compound, which is an intermediate for polymers, pharmaceuticals, fine chemicals, liquid fuels and for the synthesis of dialdehydes, ethers, amino alcohols, and other organic derivatives [1,3]. HMF can be obtained from acid-catalyzed dehydration of different C₆-based carbohydrates such as fruc-

* Corresponding author. Tel: +34-914888091; Fax: +34-914887068; E-mail: gabriel.morales@urjc.es

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tose, glucose, sucrose, cellulose, or inulin [6]. However, efficient HMF production requires the minimization of side reactions to soluble and insoluble polymers commonly known as humins, and HMF rehydration to levulinic and formic acids [5,7–9]. The dehydration of C₆ sugars to HMF is frequently performed using liquid mineral acids including H₂SO₄, HCl, and H₃PO₄ as catalyst. However, the commercial implementation of HMF as a chemical intermediate is impeded by high production costs [10] because the large scale production of HMF from C₆ sugars is a low selectivity and complex process. Several aspects still remain a challenge, one of which is the utilization of glucose (inexpensive and highly available) as feedstock [8]. Hence, the control of undesired side reactions, which consume the starting monosaccharides, intermediates, and final product, is critical. One side reaction that is particularly important to prevent is the transformation of HMF in the aqueous phase to levulinic and formic acids. For this purpose, the use of organic solvents such as dimethylsulfoxide (DMSO) is a good alternative because it prevents the hydrolysis of HMF. Besides this, the use of solid acid catalysts has several advantages over the widely used mineral acids, especially in selectivity and the management of the transformation [1]. Most research has focused on the more facile conversion of fructose as a model saccharide to HMF, which avoids side products such as oligosaccharides and humins commonly reported in acid-catalyzed glucose conversion.

Different strategies have been used in HMF synthesis from fructose to suppress the formation of byproducts, such as the use of a second reaction solvent. Biphasic systems, in which a water-immiscible organic solvent is added to continuously remove the HMF from the aqueous phase, offer an important advantage because the product is separated from the reaction media and it is thereby protected from degradation reactions [3,7,8]. However, this method requires a large amount of solvent due to high HMF water solubility and poor partitioning in the organic phase although the salting-out technique can partially overcome this drawback [9,11]. Unlike the case of fructose, where the dehydration is quite easy, reactions to convert the cheaper and more abundant glucose to HMF have been much less reported and remain a challenge in several aspects. Operation in a biphasic system such as water/MIBK is still a promising approach to the continuous transformation of glucose into HMF [7,12], both when using mineral [7,8,13] or solid acids [14–16]. A tandem homogeneous Lewis/Brønsted acid catalyzed process using AlCl₃ and HCl in the water/2-sec-butylphenol biphasic system allowed the isomerization of glucose into fructose followed by its dehydration to HMF, with 62% yield of the final product [13]. Other catalytic systems such as homogeneous metal halides [17,18], including Cr(III), Zn(II), and Sn(IV) and more water tolerant lanthanide chloride [19], can also drive the conversion of glucose, but they give lower HMF selectivity. The application of the Lewis acidic Sn-β zeolite together with aqueous HCl can also convert glucose to HMF in a biphasic system at 180 °C with 60% HMF selectivity. However, the use of corrosive HCl is undesirable [20]. A tandem reaction using solid base hydrotalcites and solid acid resins in a single reactor conducted in *N,N*-dimethylformamide [21] is very

promising.

As an alternative to a biphasic system, the use of aprotic solvents like DMSO to suppress undesired side reactions [22] to give high yields of HMF [7,8,23,24] has been investigated by many authors. Amarasekara et al. [25] demonstrated the reaction mechanism of HMF production from fructose in DMSO by means of NMR spectroscopy. They explained the dehydration of the two furanose forms of D-fructose to HMF by the elimination of three water molecules and showed the participation of DMSO as a catalyst. DMSO at high temperature has the effect of modifying the tautomeric forms of fructose, increasing the presence of furanose over the pyranose forms, and making the dehydration into HMF easier. Furthermore, DMSO contributes to stabilize HMF, which significantly reduces undesired side reactions [23,26]. Other authors have proposed the heterogenization of this system by the incorporation of the thioether groups onto mesoporous silica to generate a promoting effect similar to that introduced by DMSO [27]. Despite some improvement in the selectivity towards HMF, the catalytic activity of these materials is limited by the low extent of silica functionalization. In addition, the combination of a Brønsted acid catalyst, such as sulphated zirconia modified with aluminium, and DMSO as solvent has been shown to be an efficient catalytic system that gave high yields of HMF from glucose [28]. On the other hand, several authors have brought attention to the main drawback of using DMSO in HMF production, which is the difficulty of the separation of the chemicals by conventional processes such as distillation due to the high boiling point of HMF and its sensitivity to high temperatures. However, a recent work on the room temperature separation of HMF from DMSO by selective adsorption on porous activated carbons has provided a cost-effective recovery process [29] that avoided the disadvantages of high temperature separation.

In this contribution, we present a study of the dehydration of fructose and glucose to HMF over sulfonic-modified solid catalysts using DMSO as solvent. The catalytic performance of several sulfonic-containing heterogeneous acid catalysts was benchmarked. This was followed by a multivariate analysis to assess the optimal reaction conditions (catalyst loading, temperature, and reaction time) to maximize the production of HMF.

2. Experimental

2.1. Materials

Glucose (99.5% purity), fructose (99% purity), levoglucosan, or anhydroglucose (1,6-anhydro-β-D-glucose, 99% purity), HMF (99% purity), and levulinic acid (98% purity) were purchased from Sigma-Aldrich. Formic acid (98% purity) and DMSO (99.8% purity) were obtained from Scharlab. All the chemicals were used as received without further purification.

2.2. Catalyst preparation

Several sulfonic acid-containing heterogeneous catalysts were evaluated in the dehydration of C₆-monosaccharides.

Propylsulfonic-acid and arenesulfonic-acid functionalized mesostructured silica (Pr-SO₃H-SBA-15 and Ar-SO₃H-SBA-15, respectively) were synthesized using previously reported procedures [30,31]. Different commercial acid catalysts were also evaluated in this work. Acidic macroporous resins such as Amberlyst 70 as well as Nafion®-SiO₂ composite (SAC-13; fluorosulfonic acid Nafion® polymer on amorphous silica) were supplied by Rohm&Haas and Du Pont, respectively.

2.3. Catalyst characterization

The textural properties of sulfonic acid-modified mesostructured silicas were obtained by N₂ adsorption-desorption isotherms recorded at 77 K using a Micromeritics TRISTAR 3000 system. Pore size distributions were calculated by the BJH method using the KJS correction. The total pore volume was taken at $p/p_0 = 0.975$. Structural characterization was performed by X-ray powder diffraction (XRD) patterns acquired on a PHILIPS X'PERT diffractometer using the Cu K α line. Data were recorded at $2\theta = 0.6^\circ$ – 5° with a resolution of 0.02° . Acid capacity was measured by the determination of cationic-exchange capacity using sodium as the cation exchange agent. Thermogravimetric analysis (TGA) was performed on an SDT 2960 Simultaneous DSC-TGA apparatus from TA Instruments with an air flow rate of 100 mL/min and a heating ramp of $5^\circ\text{C}/\text{min}$.

2.4. Catalytic tests

Catalyst screening was based on the comparison of the catalytic activity of the sulfonic acid-functionalized materials. Catalytic dehydration tests were performed in ACE glass reactors immersed in an oil bath under strict temperature control. After a specific reaction time, the tube was removed from the oil bath and rapidly cooled down to room temperature. Reactions were performed for 1 h for fructose and 24 h for glucose at 140°C using the appropriate amount of catalyst to achieve a constant acid site loading of 0.20 mmol H⁺. For the optimization of the reaction conditions, the catalyst loading was varied in the range from 10 to 30 wt% referred to glucose. The temperature was between 130 and 150°C . The reactions were performed for 1–24 h. Typically, the weight composition of the reaction mixture was 0.38 g of glucose and 5 g of solvent (DMSO). Under the optimized reaction conditions, the reusability of the catalyst was evaluated with three consecutive catalytic runs. In this study, after each catalytic run the catalyst was recovered by filtration, washed with methanol and hexane for 30 min at room temperature in an ultrasonic system, and finally dried overnight at 110°C before being reused under the same reaction conditions.

Reaction samples were analyzed by high performance liquid chromatography (HPLC; Varian ProStar) using a Hi-Plex H⁺ column and a refractive index detector (Varian 356-LC). Aqueous sulfuric acid (0.005 mol/L) was used as eluent (0.6 mL/min), and the column temperature was 60°C . Reaction products detected by HPLC included glucose dehydration products (anhydroglucose or levoglucosan, and HMF) and HMF

hydrolysis products (levulinic and formic acid). Catalytic results are shown either in terms of conversion of the monosaccharide (fructose or glucose, mol%) or in terms of yields towards the different products (Y_i , mol%). Product quantification was based on a previous calibration of the analysis unit with standard stock solutions of pure commercial chemicals.

3. Results and discussion

3.1. Dehydration of fructose

The sulfonic acid-based heterogeneous catalysts selected for this work were first assayed in the dehydration of fructose to HMF using DMSO as solvent. The catalysts included propyl- and arene-sulfonic acid-modified SBA-15, which have been shown to be very active catalysts in other acid-catalyzed reactions [32]. They have been benchmarked with sulfonic macroporous resins, which are commercially available and conventionally used in acid-catalyzed processes, such as Amberlyst 70 and the composite Nafion-SiO₂ SAC-13. The blank reaction experiment performed in the absence of catalyst was also included as a reference. Figure 1 depicts the results of the catalyst screening carried out under typical reaction conditions [6]. The blank test results confirmed the promoting effect of DMSO in the dehydration reaction because it provided 49% yield towards HMF in just 1 h.

For the heterogeneous sulfonic acid-based catalysts, the screening was performed by keeping constant the total number of acid sites in order to analyse the intrinsic effect of each acid site. Of course, due to differences in acid capacities (Table 1), the mass of catalyst varied significantly. As shown in Fig. 1, all the heterogeneous catalysts provided 100% fructose conversion, improving over the results of the blank test. In addition, the HMF yields were very high in all cases, with the maximum value of 93% for the sulfonic resin Amberlyst-70. The performance of the different solid acid catalysts is usually related to textural properties and availability and strength of the acid sites. However, in this case there was no clear trend. For example, mesoporous SBA-15 with the highest specific surface area

Fig. 1. Catalyst screening in the dehydration of fructose to HMF in DMSO. Reaction conditions: 140°C , 1 h, catalyst 0.20 mmol H⁺, fructose 0.38 g, DMSO 5.0 g.

Table 1Physicochemical properties of the SO₃H-based catalysts.

Catalyst	S_{BET} (m ² /g)	Pore volume (cm ³ /g)	Pore size (Å)	Acid capacity (meq H ⁺ /g)	SO ₃ H surface concentration (μeqH ⁺ /m ²)	T_{limit} (°C)
Amberlyst-70 *	36	—	220	2.55	70.83	190
Nafion SAC-13 *	>200	0.6	>100	0.12	>0.60	200
Pr-SBA-15-SO ₃ H	721	1.18	81	1.03	1.43	>200
Ar-SBA-15-SO ₃ H	712	0.97	92	0.92	1.29	>200

* Properties provided by suppliers or experimentally determined.

did not provide the highest yield to HMF. Neither did the SAC-13 catalyst, which has a superior acid strength due to its perfluorosulfonic acid groups. Therefore, in this reaction system, the superior performance of Amberlyst-70 must be due to another cause. We propose that the high surface concentration of sulfonic acid sites (Table 1), almost two orders of magnitude higher than the other acid solids, played an important role. Usually, such a high surface concentration of sulfonic acid sites is a detrimental factor when the catalyst is used in a water-rich environment due to deactivation as a consequence of the competitive adsorption of water molecules on the acid sites [33,34]. In the presence of highly hygroscopic DMSO, this detrimental effect seemed not significant, which made Amberlyst-70 the best catalyst in the screening. Therefore, Amberlyst-70 was used to analyse the effect of reaction time under the above reaction conditions (Fig. 2). It shows that the reaction is very fast, rapidly leading to the transformation of fructose into HMF without the undesired formation of levulinic acid. Nevertheless, after 1 h the yield to HMF started to decay linearly, which was most likely due to the degradation of HMF by humin formation. Interestingly, even after 24 h, the formation of levulinic acid was negligible, supporting the assumption of the ability of DMSO to prevent the hydrolytic rupture of HMF.

3.2. Dehydration of glucose

3.2.1. Catalyst screening

As with fructose, the study of the dehydration of glucose in DMSO to yield HMF over the sulfonic acid-based heterogeneous catalysts was initiated by screening the performance of several catalysts. In this case, the selected reaction conditions for the

screening were those reported by Yan et al. [28]. Catalyst comparison was possible by keeping constant the concentration of sulfonic acid sites in the reaction medium, with the aim to elucidate the true influence of the different catalytic site environment on their performance. The results are depicted in Fig. 3, which showed that the conversion of glucose was very high in every case. The main identified products were HMF, levulinic acid (LA), and anhydroglucose (levoglucosan). The appearance of anhydroglucose was attributed to the dehydrating effect of the hygroscopic DMSO. It was noted that the blank reaction experiment provided a yield to HMF of 8% after 24 h, along with a yield to anhydroglucose of 26%. This clearly indicated that under the test reaction conditions, DMSO has a promoting effect on the dehydration of glucose. The mechanism for the transformation of glucose into HMF occurs by the isomerization of glucose into fructose, and then the dehydration of fructose into HMF. This indicates that DMSO even in the absence of any catalyst can promote the transformation of glucose into fructose-related intermediates (furanose forms) that can evolve into HMF. However, our analytical techniques did not detect fructose, indicating that the transformation occurred very fast. On the other hand, when a solid catalyst was used, HMF yield clearly increased, showing the necessity for an acid catalyst to increase the desired reaction rate. As in the case of fructose dehydration, catalyst benchmarking identified the commercial Amberlyst-70 resin as the most active catalyst in the dehydration of glucose, giving a HMF yield close to 27%. Sulfonic acid-modified mesostructured catalysts (Pr-SBA-15 and Ar-SBA-15) showed similar catalytic activity to the SAC-13 catalyst, indicating that the surface area or acid strength were

Fig. 2. Effect of reaction time in the dehydration of fructose in DMSO over Amberlyst-70. Reaction conditions: 140 °C, catalyst 0.20 mmol H⁺, fructose 0.38 g, DMSO 5.0 g.

Fig. 3. Catalyst screening in the dehydration of glucose to HMF in DMSO. Reaction conditions: 140 °C, 24 h, catalyst 0.20 mmol H⁺, glucose 0.38 g, DMSO 5.0 g.

not crucial parameters, similar to fructose dehydration. Again, we attributed the superior performance of the Amberlyst-70 resin to its much higher concentration of sulfonic acid sites (70 $\mu\text{eqH}^+/\text{m}^2$). For each catalyst, some anhydroglucose and levulinic acid were formed, but these were limited as shown in Fig. 3.

3.2.2. Study of reaction conditions with Amberlyst-70

From the above catalyst screening, Amberlyst-70 was selected as the best catalyst to study the reaction variables. A preliminary analysis of the reaction time and temperature served as a reference to perform a more accurate study of the reaction conditions. As shown in Fig. 4, high temperature (150 °C) increased the rate of HMF formation, as do long reaction times. However, the combination of the longest reaction time (24 h) with the highest temperature (150 °C) did not lead to a clear improvement. This indicated some temperature-time interactions, probably due to secondary reactions. Hence, an experimental design methodology [35] was used to simultaneously analyse the effect of the three important reaction variables, i.e., temperature, catalyst loading, and time. A 2^3 factorial experimental design (three different levels for each of two factors, temperature and catalyst loading) was carried out at three different reaction times. The central point of each experiment was repeated three times in order to determine the variability of the results and assess the experimental error. The selected responses were glucose conversion (X_G) and the yields towards three relevant products, HMF (Y_{HMF}), levulinic acid (Y_{LA}), and anhydroglucose (Y_{ANHG}). The optimization of the reaction variables aimed to increase the yield to HMF and reduce the yields to LA and anhydroglucose, which were competing products. The selection of the levels for each factor (temperature and catalyst loading) was based on preliminary results (Fig. 4), while also considering the constraints imposed by the limits for the operating conditions of the different materials used, e.g. recommended temperature for the use of Amberlyst-70. The lower and upper levels of the experimental factors were: 130–150 °C for the temperature, and 10%–30% for the catalyst loading (based on glucose weight). The reaction times selected for the different design experiments were 1, 6, and 24 h. The standard

Fig. 4. Effect of reaction temperature in the dehydration of glucose to HMF in DMSO. Media compositions: Amberlyst-70 0.076 g, glucose 0.38 g, DMSO 5.0 g.

experimental matrix for the design is shown in Table 2. Experiments were run randomly to minimize errors due to possible systematic trends in the variables. Table 2 also shows the results of glucose conversion and yields to HMF, LA, and anhydroglucose.

The experimental data were analyzed by the response surface methodology using a second order polynomial equation:

$$Y = \beta_0 + \sum_{i=1}^2 \beta_i \cdot X_i + \sum_{i=1}^2 \beta_{ii} \cdot X_i^2 + \sum_{i=1}^2 \beta_{ij} \cdot X_i \cdot X_j$$

where Y is response (glucose conversion, yield to HMF, yield to levulinic acid, and yield to anhydroglucose, mol%), β_0 , β_i , β_{ii} , and β_{ij} are the regression coefficients for the intercept, linear, quadratic, and binary interactions, respectively, and X_i and X_j are the independent factors (temperature and catalyst loading). To confirm the parameter estimation and for model fitting, an estimate of the statistical error was performed. The analysis of statistical significance was based on the total error criteria with

Table 2

Experiment matrix and experimental results for the dehydration of glucose in DMSO over sulfonic acid-modified Amberlyst-70 resin.

Run	Reaction time (h)	T (°C) (X)	C (%) (Y)	I_T	I_C	X_G (%)	Y_{HMF} (%)	Y_{LA} (%)	Y_{ANHG} (%)
1	1	140	20	0	0	70.4	1.3	0.6	23.5
2		140	20	0	0	67.3	0.5	0.5	23.2
3		140	20	0	0	72.5	0.8	0.5	25.4
4		130	10	-1	-1	47.3	0.2	0.0	3.2
5		140	10	0	-1	68.6	0.4	0.5	23.2
6		150	10	1	-1	63.5	0.0	0.0	20.5
7		130	20	-1	0	69.7	0.0	0.0	23.0
8		140	20	0	0	57.1	1.8	0.4	26.7
9		150	20	1	0	87.8	2.6	0.8	32.4
10		130	30	-1	1	73.4	5.4	0.5	26.1
11		140	30	0	1	83.5	6.1	0.7	30.8
12		150	30	1	1	87.0	4.6	0.9	31.5
13	6	140	20	0	0	90.1	8.1	1.5	25.3
14		140	20	0	0	90.5	8.0	1.6	24.7
15		140	20	0	0	89.0	6.4	1.4	25.4
16		130	10	-1	-1	84.6	0.9	0.9	26.5
17		140	10	0	-1	91.8	2.9	1.4	30.2
18		150	10	1	-1	91.7	7.1	1.5	27.4
19		130	20	-1	0	90.9	2.7	1.2	26.5
20		140	20	0	0	90.1	5.6	1.5	25.4
21		150	20	1	0	91.9	19.8	1.5	16.0
22		130	30	-1	1	87.5	8.6	1.4	25.9
23		140	30	0	1	89.5	12.1	1.4	21.4
24		150	30	1	1	91.3	24.0	1.5	12.8
25	24	140	20	0	0	95.9	30.7	1.6	7.6
26		140	20	0	0	95.8	30.9	1.7	7.4
27		140	20	0	0	95.8	30.6	1.8	7.2
28		130	10	-1	-1	91.0	8.1	1.7	25.1
29		140	10	0	-1	91.6	13.6	1.7	19.6
30		150	10	1	-1	98.8	28.2	3.4	4.3
31		130	20	-1	0	90.1	17.0	1.2	21.6
32		140	20	0	0	96.5	30.5	1.7	5.9
33		150	20	1	0	99.7	30.6	3.3	1.5
34		130	30	-1	1	90.2	22.1	1.7	12.7
35		140	30	0	1	98.1	32.0	2.2	4.4
36		150	30	1	1	100.0	28.3	3.7	0.0

Note: T , temperature; C , catalyst loading (wt% based on glucose); I , coded value; X_G , conversion of glucose; Y_{HMF} , yield to 5-hydroxymethylfurfural; Y_{LA} , yield to levulinic acid; Y_{ANHG} , yield to anhydroglucose. Columns 3 and 4 represent the factor levels on a natural scale whereas columns 5 and 6 represent the 0 and ± 1 encoded factor levels on a dimensionless scale.

a confidence level of 95%. Thus, Eqs. (1)–(12) were obtained by multiple regression analysis using the Statgraphics software from the matrix generated by the experimental data (Table 3).

The analysis of the coefficients in Eqs. (1)–(12) allowed the identification of the most influential factors on each response

and reaction time. To facilitate the interpretation of the equations, Figs. 5–8 plot the response surfaces for glucose conversion and yields towards HMF and anhydroglucose at the three reaction times. In the case of glucose conversion (Fig. 5), the three variables, temperature, catalyst loading, and time, gave

Table 3

Predictive equations obtained by the response surface methodology.

Time (h)	Equation	R^2
1	$X_G = 70.20 + 8.01 I_T + 10.74 I_C + 1.84 I_T^2 - 0.65 I_T I_C - 0.88 I_C^2$	(1) 0.7078
6	$X_G = 90.48 + 1.99 I_T + 0.03 I_C - 0.18 I_T^2 - 0.83 I_T I_C - 0.93 I_C^2$	(2) 0.6009
24	$X_G = 95.79 + 4.53 I_T + 1.15 I_C - 0.49 I_T^2 + 0.49 I_T I_C - 0.50 I_C^2$	(3) 0.9019
1	$Y_{HMF} = 1.24 + 0.26 I_T + 2.59 I_C - 0.22 I_T^2 - 0.16 I_T I_C + 1.69 I_C^2$	(4) 0.9044
6	$Y_{HMF} = 7.28 + 6.45 I_T + 5.62 I_C + 3.44 I_T^2 + 2.29 I_T I_C - 0.34 I_C^2$	(5) 0.9558
24	$Y_{HMF} = 29.70 + 6.66 I_T + 5.43 I_C - 4.02 I_T^2 - 3.49 I_T I_C - 4.96 I_C^2$	(6) 0.9099
1	$Y_{LA} = 0.53 + 0.21 I_T + 0.26 I_C - 0.16 I_T^2 + 0.1 I_T I_C + 0.01 I_C^2$	(7) 0.7509
6	$Y_{LA} = 1.51 + 0.16 I_T + 0.07 I_C - 0.15 I_T^2 - 0.14 I_T I_C - 0.06 I_C^2$	(8) 0.9187
24	$Y_{LA} = 1.67 + 0.99 I_T + 0.13 I_C + 0.64 I_T^2 + 0.08 I_T I_C + 0.303 I_C^2$	(9) 0.9878
1	$Y_{ANHG} = 26.33 + 5.36 I_T + 6.90 I_C - 1.84 I_T^2 - 2.96 I_T I_C - 2.57 I_C^2$	(10) 0.8424
6	$Y_{ANHG} = 24.97 - 3.79 I_T - 3.99 I_C - 3.29 I_T^2 - 3.5 I_T I_C + 1.25 I_C^2$	(11) 0.9690
24	$Y_{ANHG} = 8.01 - 8.94 I_T - 5.34 I_C + 1.54 I_T^2 + 2.04 I_T I_C + 1.99 I_C^2$	(12) 0.9379

Note: The models include only the significant terms.

Fig. 5. Response surfaces for glucose conversion for models (1)–(3) at 1, 6, and 24 h reaction time. Reaction conditions: Amberlyst-70 as catalyst, glucose 0.38 g, DMSO 5.0 g.

an increase in conversion. The conversion was very high even at 1 h when the yields towards the identified products were still low. Therefore, there was a noticeable contribution of non-identified degradation products similar to the humins produced in an aqueous media. By analysing the coefficients in Eqs. (1)–(3), the most influential factors were the temperature and catalyst loading, while the contributions of interaction and quadratic terms remained low. Figure 6 shows the graphic representation of Models (4)–(6), corresponding to HMF yield. For each reaction time, there was a clear increase in Y_{HMF} as the temperature and the catalyst loading increased. More importantly, longer reaction time led to a higher production of HMF. Thus, significant yields of HMF over 30% can be obtained after 24 h. This indicated slow reaction rates and the need for long reaction time to achieve high yields. Eq. (6) revealed an important contribution of the quadratic terms T^2 , I_c^2 , and TI_c ,

resulting in a significant curvature of the model. As a result, the model predicted a maximum Y_{HMF} in the studied range. On the other hand, the predicted yield towards anhydroglucose is represented in Fig. 7, which includes the response surfaces corresponding to Eqs. (10)–(12). As shown, maximum values were obtained at short reaction times while Y_{ANGH} can reach values as low as 0% after 24 h (e.g., run 36 in Table 2). This was consistent with the blank reaction (Fig. 3) where the main product was anhydroglucose, confirming the dehydrating ability of the solvent, DMSO. The coefficients in Eqs. (10) and (11) revealed significant influences not only from the linear terms of the model, T and I_c , but also from each of the quadratic terms. Interestingly, the signs of the different coefficients changed from positive to negative (or *vice versa*) for the model at 1 h to the model at 24 h. This indicated the typical behavior of an intermediate compound with a fast rate of formation and a slow-

Fig. 6. Response surfaces for HMF yield for the models (4)–(6) at 1, 6, and 24 h reaction time. Reaction conditions: Amberlyst-70 as catalyst, glucose 0.38 g, DMSO 5.0 g.

Fig. 7. Response surfaces for anhydroglucose yield for the models (10)–(12) at 1, 6, and 24 h reaction time. Reaction conditions: Amberlyst-70 as catalyst, glucose 0.38 g, DMSO 5.0 g.

er rate of transformation/degradation. Furthermore, the evolution of Y_{ANHG} with time appeared to be the opposite to that of Y_{HMF} . So anhydroglucose was affecting the production of HMF from glucose in DMSO. Finally, the response surfaces of levulinic acid yield [Eqs. (7)–(9)] are shown in Fig. 8. Levulinic acid is produced from HMF by acid-catalyzed hydration. With DMSO as solvent, the presence of available water was very low, and thus rehydration was restricted. The models in Fig. 8 confirmed this, showing that Y_{LA} was very low even after 24 h and at the higher temperature (below 4%).

To have the maximum HMF yield, the selected reaction time was 24 h from the mathematical models in Table 3 for glucose conversion and product yields. An evaluation of the regression error was performed on these models to validate their use for making predictions. First, an F -test was performed to verify the significance of the second order models. The F values corre-

sponding to X_G , Y_{HMF} , Y_{LA} , and Y_{ANHG} were 11.03, 12.11, 97.16, and 18.12, respectively, and all of these were over the 5% F -value, 4.39. Hence, the four models were significant (at 95% confidence level). An additional indication of the goodness of the fit was that the regression coefficients were over 0.90 (Table 3). Figure 9 depicts the correlation between experimental results at 24 h (Table 2, runs 25–36) and the predicted values of the mathematical models, showing good agreement between experimental and predicted values for each of the responses. Finally, the arithmetical averages and standard deviations of all the responses were calculated from the central point replicas (Table 2, runs 25–27 and 32): glucose conversion ($96.0\% \pm 0.3\%$), HMF yield ($30.7\% \pm 0.2\%$), LA yield ($1.7\% \pm 0.1\%$), and ANHG yield ($7.0\% \pm 0.8\%$). Consequently, the standard deviations were low enough to show that experimental error was not significant.

Fig. 8. Response surfaces for levulinic acid yield for the models (7)–(9) at 1, 6, and 24 h reaction time. Reaction conditions: Amberlyst-70 as catalyst, glucose 0.38 g, DMSO, 5.0 g.

The mathematical model represented by Eq. (6) gave the maximal predicted value for the yield to HMF in the experimental region as 32.8 mol%. This optimal value corresponded to the following reaction conditions: 147 °C and 23 wt% catalyst ($I_T = +0.698$, $I_C = +0.302$, in coded values). At these conditions the model for 24 h predicted a glucose conversion of 99.2%, a yield to levulinic acid of 2.8%, and a yield to anhydroglucose of 2.8%. Noticeably, the maximum HMF yield was accompanied by minimum yields to levulinic acid and anhydroglucose. A catalytic experiment carried out under these reaction conditions provided the following results: X_G 100%, Y_{HMF} 33.7%, Y_{ANHG} 0.0%, and Y_{LA} 2.1%, in fair agreement with the model prediction.

In addition, to evaluate the reusability of the Amberlyst-70 catalyst, recycling tests were conducted at the optimized reaction conditions. Figure 10 displays the reaction results for the reutilization experiments. Catalyst recovery between consecu-

tive runs was carried out by simply filtering and washing with a mixture of *n*-hexane and methanol (to remove both polar and non-polar reactants and reaction products from the surface of the catalyst). Using this simple procedure, the catalyst can be reused once without appreciable loss of activity, but a second reutilization led to a gradual decrease, both in glucose conversion and yield to HMF. Furthermore, the yield to the undesired levulinic acid began to grow. This was probably due to the formation of deposits of organic matter on the catalytic centers of Amberlyst-70 that cannot be removed by the double washing with *n*-hexane and methanol, and which limit the accessibility of new reactant molecules to the sulfonic acid sites. These deposits would come primarily from the degradation of glucose to humins. In order to verify this hypothesis, spent catalysts were analysed by acid-base titration and elemental analysis to characterize the acid sites after reaction. The titrations revealed a pronounced loss of acid sites after each run. On the other hand,

Fig. 9. Experimental versus predicted values for glucose conversion (a), HMF yield (b), levulinic acid yield (c), and anhydroglucose yield (d). Reaction conditions: Amberlyst-70 as catalyst, glucose 0.38 g, DMSO 5.0 g, 24 h.

elemental analysis provided almost constant S content. This indicated an absence of the leaching of sulfonic species, but accompanied by a decay in the acidity, which was consistent with the proposed cumulative deposition of organic by-products on the catalyst surface.

In order to get a deeper perspective of the reaction system, additional experiments were performed using the optimized reaction conditions. Figure 11(a) shows the kinetic curves for glucose conversion and product yields at the optimal temperature and catalyst loading. The results are consistent with the above discussion for the experimental design, i.e., the conversion of glucose was very fast while the production of HMF was much slower. Interestingly, these differences in reaction rates indicated that the production of HMF was not due exclusively to unreacted glucose because Y_{HMF} kept growing even when glucose was almost depleted. On the other hand, anhydroglucose was formed very fast at the beginning and gradually dis-

appeared, which is the typical behavior of an intermediate compound. Furthermore, the maximum concentration of anhydroglucose was approximately equivalent to that of HMF at the end of the reaction. Therefore, we hypothesize that anhydroglucose was formed very fast from glucose in the presence of DMSO at high temperature. Once formed, anhydroglucose was much more stable against degradation side reactions than

Fig. 10. Reusability of Amberlyst-70 catalyst in the dehydration of glucose to HMF in DMSO under the optimized conditions: 147 °C, catalyst loading 23 wt% based on glucose, 24 h, glucose 0.38 g, DMSO 5.0 g.

Fig. 11. Effect of reaction time in the dehydration of glucose (a) and anhydroglucose (b) in DMSO over Amberlyst-70 under the optimized conditions: 147 °C, catalyst loading 23 wt%, glucose or anhydroglucose 0.38 g, DMSO 5.0 g.

the parent glucose, and at the same time it was slowly being reverted into glucose. The glucose so re-formed was rapidly transformed into HMF, probably by isomerization into fructose and consecutive dehydration into HMF. If this hypothesis is true, the formation of anhydroglucose would be beneficial for the minimization of undesired side reactions. To confirm this, the kinetic study was repeated under the same reaction conditions but with anhydroglucose as the starting substrate instead of glucose. The experimental results are depicted in Fig. 11(b).

As shown, anhydroglucose was also reactive in DMSO and gave HMF in high yields. In this case, the conversion of the substrate was slower than with glucose, and the formation of HMF was clearly enhanced. This showed that undesired side reactions leading to the formation of humins were strongly inhibited when the glucose is in anhydrous form. Furthermore, as expected, in this experiment the production of glucose from anhydroglucose was observed, indicating that the reaction of the dehydration of glucose to anhydroglucose in DMSO occurred through an equilibrium shifted towards the anhydrous form. Thus, the concentration of the more unstable glucose was kept very low, minimizing the extent of the undesired side reactions, and finally resulting in higher HMF yields.

4. Conclusions

The use of Brønsted solid acids and DMSO as solvent catalyzed the catalytic dehydration of C₆ monosaccharides into HMF. With fructose, the reaction proceeded fast with high yields. The sulfonic acid resin Amberlyst-70 gave 93 mol% yield to HMF with 100% fructose conversion after 1 h. However, with glucose, the reaction was more difficult and required longer reaction times, which promoted the undesired side reactions of glucose degradation. Amberlyst-70 gave the best

results because of its high surface concentration of sulfonic sites. Reaction conditions were optimized for Amberlyst-70 by the response surface methodology, which gave a maximum HMF yield of 33 mol% at 147 °C, 23 wt% catalyst loading (based on glucose), and 24 h. A study of catalyst reuse without regeneration showed a gradual decay in activity. In this system, DMSO promoted the dehydration of glucose into anhydroglucose and allowed the SO₃H sites on the solid acids to produce HMF. Anhydroglucose was an important intermediate in the production of HMF from glucose in DMSO because it reduces side reactions.

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Graphical Abstract

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Sulfonic acid heterogeneous catalysts for dehydration of C₆-monosaccharides to 5-hydroxymethylfurfural in dimethyl sulfoxide

Gabriel Morales*, Juan A. Melero, Marta Paniagua, Jose Iglesias, Blanca Hernández, María Sanz
Universidad Rey Juan Carlos, Spain

Sulfonic acid-functionalized Amberlyst-70 was used in dimethyl sulfoxide (DMSO) as solvent for the catalytic dehydration of C₆ monosaccharides into 5-hydroxymethylfurfural (HMF), a biomass-derived platform molecule.

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