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5-Hydroxymethylfurfural Synthesis from Hexoses Is Autocatalytic

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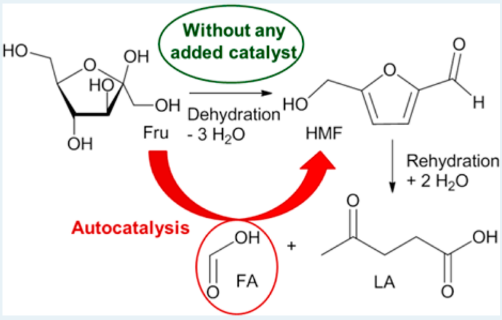
ABSTRACT: Many researchers and articles have reported the development of synthesis methods for 5-hydroxymethylfurfural, one of the top 12 biobased building blocks listed by the U.S. Department of Energy. The focus has especially been on the development of efficient catalytic systems for this synthesis. In contrast, we report here a process that does not require any added catalysts, yet leads to interesting yields and selectivities. Moreover, we demonstrate that the process is autocatalytic involving formic acid, the byproduct.



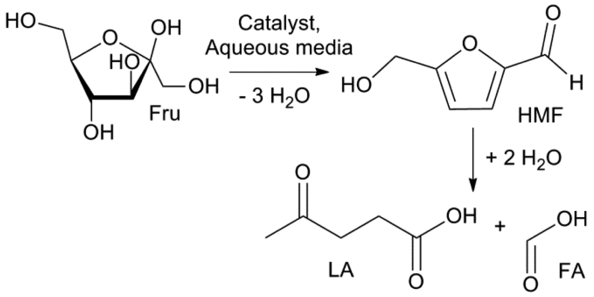
KEYWORDS: *HMF, 5-hydroxymethylfurfural, autocatalysis, aqueous media, water, fructose, glucose*

5-Hydroxymethylfurfural (HMF) is a biobased platform chemical with high potential.[1] It is formed through elimination of three molecules of water from hexoses, and therewith, it is a straightforward and easy way to upgrade sugars to molecules with a higher energy density. HMF serves as starting material for a wide variety of biobased chemical intermediates (e.g., levulinic acid, furandicarboxylic acid, dimethyl furan, γ-valerolactone, and dihydroxymethylfuran). Therefore, it is the key entrance to a whole range of products (solvents, polymers, biofuels) derived from all types of lignocellulosic biomass.[2]

The awareness that it will become necessary to produce materials from renewable resources rather than from fossil raw materials has led to an enormous increase in research efforts dedicated to the production and utilization of platform molecules, including HMF;[3] however, it is important to realize that the first report on the acid-catalyzed synthesis of HMF from sugars stems from 1895 by Düll.[4] The acid-catalyzed conversion of sugars (e.g., fructose, glucose, sucrose) into HMF has since then been implemented in many different media: aqueous,[5] organic, biphasic,[6] and ionic liquids.[7] Originally, oxalic acid-catalyzed reactions were described.[4,8] Since then, many different acidic catalysts have been reported, such as organic or inorganic acids[5d,6] and salts,[9] Lewis acidic metals,[10] zeolites,[11] and organic resins.[12] The proposed processes are generally complex and often involve toxic (such as chromium derivatives[13]) or corrosive (H_2SO_4, HCl) catalysts and harmful solvents (dichloromethane as the extracting solvent,[14] ionic liquids such as [BMIM]/[EMIM][Cl]/[Br][7a]); in the case of biphasic mixtures, especially when DMSO[6] is used as solvent (for complete review see[2a]), hard-to-handle separation procedures are required.

The development of a more sustainable process, especially in an aqueous medium, is highly desirable. It is, however, limited by the partial degradation of HMF by rehydration. In the presence of water, levulinic acid (LA) and formic acid (FA) are formed (Scheme 1). To our knowledge, no report of high conversion and selectivity has yet been published in purely aqueous media.

Scheme 1. Fructose Conversion into HMF and Its In Situ Rehydration/Degradation



Several articles have reported the synthesis of HMF without a catalyst in the presence of DMSO[12a,15] or ionic liquids.[16] In these systems, the solvent also plays the role of promoter, coordinating and activating intermediates. Older articles reported a possible autocatalysis of fructose in aqueous media with interesting yields when starting from a low concentration of the sugar (less than 5 wt %),[5a] or from sucrose, glucose, or sorbose with lower yields.[17]

In line with these early results, we report here high selectivities that can lead to the implementation of a highly improved and sustainable autocatalytic process for the synthesis of HMF in water. This process can be operated without any added catalyst and starts from a highly concentrated feed of sugar (30 wt %). In addition, experiments were carried out to

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study the mechanism and verify the potential of this autocatalytic reaction.

Systematic evaluation of the reaction parameters led us to identify temperature and reaction time as the most critical parameters. To obtain high yields, a compromise must be reached between conversion and selectivity. A too high temperature or too long reaction time leads to the degradation of the product and the formation of humins. The formation of the dehydration products LA and FA increases exponentially with time and temperature of the reaction, as shown in Table 1.

Table 1. HMF Synthesis from Fructose (30 wt %) in Water without Any Added Catalyst

sugar	concn wt %[a]	time (min)	temp (°C)	conv (%)[b]	selec (%)[b]	*Y* (FA) (%)[b]	*Y* (LA) (%)[b]
fructose	30	40	170	13	26	0.2	<0.1
fructose	30	60	170	25	41	0.65	0.15
fructose	30	120	170	47	56	2.2	1.05
fructose	30	180	170	84	51	5.9	6.85
fructose	30	20	200	19	44	0.3	<0.1
fructose	30	30	200	46	58	1.3	0.4
fructose	30	40	200	66	58	2.7	1.6
fructose	30	50	200	94	50	6.1	9.3
fructose	30	60	200	97	44	6.7	7.4
fructose	30	20	190	35	61	0.95	0.2
fructose	30	40	190	70	61	3.2	2.2

[a] 2 mL experiments, carried out in Ace pressure tubes. [b] Determined by HPLC analysis, in mol % (conv, conversion; selec, selectivity HMF; *Y*, yield calculated from HPLC analysis, not isolated).

With 30 wt % fructose, up to 70% conversion was obtained with a selectivity of 61% (Table 1). This result is one of the highest reported in a neutral, salt-free aqueous solution (compared, for example, with 52% conversion and 63% selectivity obtained at 200 °C from fructose at 27 wt % in the presence of HCl and under microwave irradiation[18]) and is comparable to the results obtained in many biphasic systems.[19] This result is exceptional, considering the high concentration of fructose used and the absence of a catalyst.

It should be noted that the literature on HMF synthesis reports only a few "blank" experiments (without catalyst).[5a,9,10b,17,20] For example, Wu et al. in their study on the effect of different salts on HMF formation and degradation[21] obtained up to 75% conversion of fructose with a selectivity of 42% after 60 min at 180 °C in their blank reaction.

We then extended our study to other sugars, such as glucose or sucrose. The formation of HMF from pyranoses as glucose is more challenging. Much lower conversions than in the case of fructose were achieved (Table 2). A catalyst is then indispensable to promote the required first step, the isomerization of the sugar (Scheme 2).

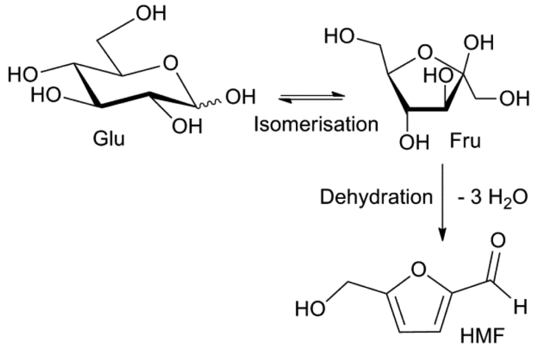
A mixture of glucose and fructose at a ratio 50/50, similar to the composition of a high fructose corn syrup (industrial product issued from the isomerization of glucose), was also tested. The fructose was then converted in the same proportion as described previously (around 40% yield), but the glucose remained unconverted (Table 2). This conversion of fructose in the absence of any catalyst or any possible promoter led to the question of the mechanism involved in HMF formation.

Table 2. HMF Synthesis from Sugars in Water without Any Added Catalyst

sugar	concn wt %[a]	time (min)	temp (°C)	conv (%)[b]	selec (%)[b]	*Y* (FA) (%)[b]	*Y* (LA) (%)[b]
fructose	30	40	190	70	61	3.2	2.2
glucose	10	80	195	19	38	0.4	<0.1
sucrose	20	40	200	39	56	4.85	1.0
Glu/Fru	20	40	195	40	51	2.2	0.4

[a] 2 mL experiments, carried out in Ace pressure tubes. [b] Determined by HPLC analysis, in mol % (conv, conversion; selec, selectivity HMF; *Y*, yield calculated from HPLC analysis, not isolated).

Scheme 2. Two-Step Glucose Conversion into HMF



Although no acid was added during this reaction, the final pH was unexpectedly low (around 3). This acidity can be explained by the formation of levulinic acid (LA) and formic acid (FA) as degradation products. One hypothesis is that these acidic byproducts are involved in the catalysis of HMF formation.

This autocatalysis was suggested for the first time in 1947[17] and again in 1977.[5a] To prove the involvement of the acidic byproducts, the reactions were first carried out in different organic and inorganic buffers (to eliminate any possible salt effect) at various concentrations (Table 3).

Using concentrated buffers, regardless of their type, the pH was maintained around 7, and no HMF formation occurred, whereas at a lower concentration of buffer, the formation of HMF was accompanied by a drop in pH. Obviously, neutralization of these acidic compounds leads to inhibition of the reaction. This result verifies our hypothesis by demonstrating that neutralization of the acidic byproducts, LA and FA, prohibits the formation of HMF. Large quantities of humins are then produced in these cases as a result of the degradation of the sugars. At low buffer concentrations, FA and LA catalyze and redirect the overall reaction away from humins.

To test the potential of LA and FA as catalysts of the reaction, experiments were carried out in their presence (Table 4). A net acceleration of the reaction when adding FA compared with the blank was demonstrated. After only 20 min, 45% yield was reached. LA has a much more limited effect. Only a slight increase in the conversion and yield could be observed. Thus, the reaction without added catalyst gives results essentially equally as good as with the FA catalyst.

The difference in acidities of LA (pK_a 4.59) and FA (pK_a 3.74) explains why the latter is a better catalyst for HMF synthesis. Thus, the observed formation of HMF in the absence of any added catalyst is mainly due to the "auto" catalysis mediated by FA.

It could also be noticed that the addition of FA at the beginning of the reaction dramatically increases the formation of degradation products, such as LA and humins. At 190 °C and 40 min, more than 8% of LA is formed in the presence of the initial FA. If no FA is initially added, only 2% of LA is detected.

Table 3. Buffered Media for the Synthesis of HMF

sugar	concn wt %^{a}	time (min)	temp (°C)	buffer	concn buff. (M)	pH beg.	pH end	conv (%)^b	*Y* (HMF) (%)^b	selec (%)^b	*Y* (FA) (%)^b	*Y* (LA) (%)^b
fructose	30	40	190	Tris/HCl	0.05	7.5	~3	79	48	61	4.05	4.7
fructose	30	40	190	Glygly	0.2	7.5	~4−5	69	23	33	1.4	1.3
fructose	30	40	190	phosphate	1	7.0	~7	98	4	4	10.4	0.8
fructose	30	40	190	Glygly	0.5	7.3	~5−6	98	5	5	1.4	0.2
fructose	30	40	190	phosphate	0.1	7.0	~4−5	92	28.5	31	2.8	0.45

[a] 2 mL experiments, carried out in Ace pressure tubes. [b] Determined by HPLC analysis, in mol % (conv, conversion; selec, selectivity HMF; *Y*, yield calculated from HPLC analysis, not isolated).

Table 4. HMF Synthesis from Sugars in Water with or without Added Catalyst[a]

sugar	concn wt %^{a}	time (min)	temp (°C)	catalyst	mol ratio %	conv (%)^b	*Y* (HMF) (%)^b	selec (%)^b¶	*Y* (FA) (%)^b	*Y* (LA) (%)^b
fructose	30	20	190			35	21	61	0.95	0.2
fructose	30	40	190			70	43	61	3.2	2.2
fructose	30	20	190	LA	50	44	27	61	1.1	+0.6^c
fructose	30	40	190	LA	50	93	49	53	3.4	+2.1^c
fructose	30	20	190	FA	50	70	45	64	+4.8^c	2.7
fructose	30	40	190	FA	50	96	47	49	+5.9^c	8.1

[a] 2 mL experiments, carried out in Ace pressure tubes. [b] Determined by HPLC analysis, in mol % (conv, conversion; selec, selectivity HMF; *Y*, yield calculated from HPLC analysis, not isolated). [c] Calculated in addition to the amount initially introduced.

The excellent selectivity results obtained for the reaction without any added catalyst can be thus explained by the slow formation of FA under these conditions (cf. Table 1). The small quantity of FA then present is enough to catalyze the HMF synthesis but also such that it limits HMF degradation. Therefore, it is logical to notice that the highest yield and selectivity results in the absence of any added catalyst are obtained for an "ideal" amount of FA between 2 and 4% (cf Table 1, 2, or 3). As for temperature and time, a compromise must be found between FA-catalyzed HMF formation and the equally FA-catalyzed HMF degradation. Furthermore, because FA formation depends mainly on time and temperature, these two parameters remain the two critical parameters for an efficient HMF synthesis.

In light of these findings on the effective autocatalyzed dehydration by release of FA in solution, we recommend the stringent evaluation of future potential catalysts for HMF formation in aqueous media against the blank reaction.

In conclusion, starting from a highly concentrated fructose solution containing only sugar and water, without any cosolvent, extracting phase, or coproduct (salts), good HMF yields can be achieved. This autocatalyzed reaction may facilitate the development of a very simple and sustainable process. Combined with an efficient isomerization step, it could also lead to a new HMF synthesis from glucose. To avoid the virtually impossible isolation of HMF,[22] the sugar and HMF-containing reaction mixture could be used as substrate. For instance, in the fermentative conversion of HMF to the stable and isolable 2,5-furandicarboxylic acid, FDCA.[23]

■ EXPERIMENTAL SECTION

Chemicals. Commercially available chemicals were used without further purifications.

General Procedure. A 600 mg portion of fructose was weighed and added to an Ace pressure 15 mL-glass tube. The solution was brought up to 2 mL by adding demiwater (pH 6.7) and placed in an oil bath at 190 °C. After 40 min, the tube was removed from the oil bath and allowed to cool to room temperature (~5 min). The aqueous phase was diluted 10 times by adding 8 mL of 5 mM H_2SO_4. Two milliliters of this diluted solution was placed in an Eppendorf tube and centrifuged, and the supernatant was analyzed by HPLC.

HPLC Analysis. The concentrations of HMF, fructose, glucose, sucrose and the degradation products in the aqueous phases were determined on a HPLC equipped with a CarboSep Coregel column, Shimadzu RI and UV detectors (210 nm), and a Perkin-Elmer series 200 autosampler. Samples were diluted by a factor of 10 or 20 with an aqueous solution of 5 mM H_2SO_4. Ten microliters of the diluted samples was measured by HPLC. The used eluent was an aqueous solution of 5 mM H_2SO_4. The method lasted 35 min with a flow rate of 0.8 mL/min. Both UV (for HMF and furaldehyde, Fal) and RI (for HMF, fructose, LA, FA, and Fal) detections were used. The column was maintained at 60 °C. A calibration was established by preparation of standard solutions of the different sugars, HMF, and organic acids, LA, and FA. Retention times (min), RI: glucose, 6.7; fructose, 7.3; sucrose, 6.7; FA, 10.3; LA, 11.5; HMF, 21.7; Fal, 32.6. UV (min): HMF, 21 min; Fal, 32 min.

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Notes

The authors declare no competing financial interest.

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