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Kinetic Study of 5-Hydroxymethylfurfural Synthesis from Fructose in High Pressure CO_2−Water Two-Phase System

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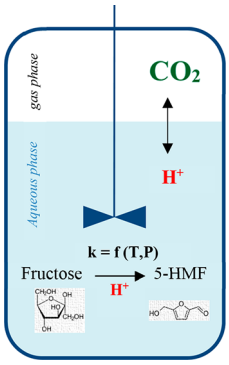
ABSTRACT: In this work, synthesis of 5-hydroxymethylfurfural (5-HMF) from lignocellulosic biomass derived hexoses, fructose in our case, was developed in two-phase supercritical CO_2−water systems. Conditions of reactions were above 10 MPa and 120 °C, i.e., the two-phase reacting mixture can be regarded as a subcritical water−supercritical CO_2 system. From kinetic experiments and their modeling, it was possible to assess the effect of CO_2 as a potential reversible acid catalyst. The kinetic model developed in this study considers also the catalytic contribution of acid byproducts, as proton providers, for the reaction of dehydration of fructose into 5-HMF. Selectivity toward 5-HMF was improved with increasing pressure to reach a maximum of 80 mol % after 3 h of reaction at 150 °C and under 25 MPa of CO_2, as only 60% was achieved without the use of pressurized CO_2.



INTRODUCTION

Biomass is nowadays the most attractive alternative feedstock to replace oil in the production of chemicals and energy for human beings. Biomass mainly consists of cellulose, hemicelluloses, and lignin, whose distribution depends on the type of vegetal. Hydrolysis of cellulose yields carbohydrates which show promise because of their natural carbon content and because they can provide biosourced chemical building blocks.

A typical interesting product obtained from the conversion of these sugars is 5-hydroxymethylfurfural (5-HMF), a promising platform chemical to produce fuels and renewably sourced polymers. For example, 5-HMF can be oxidized in 2,5-furandicarboxylic acid (2,5-FDCA), which is a green substitute to terephthalic acid in the production of plastics. Together with levulinic acid, another platform molecule derived from 5-HMF, 2,5-FDCA has been mentioned in the top 10 of biobased chemicals[1] by the U.S. Department of Energy in 2004.

5-HMF can be produced from the acid-catalyzed dehydration of fructose. It can also be synthesized from glucose after a first isomerization step of glucose to fructose (Scheme 1). Recent reviews report 5-HMF synthesis in different catalytic media.[2,3] A wide range of operating conditions, temperature (40−400 °C), catalysts (organic acids, mineral acids, salts, Lewis acids, solid acids), and solvents (water, organic solvents, ionic liquids) has been used, allowing 100% yield in some cases[4] (use of Amberlyst-15 powder resin as catalyst coupled with water removal). Nevertheless, the obtention of high yields of 5-HMF is strongly limited by its partial degradation into levulinic acid and formic acid. Insoluble byproducts, referred to as humins, are also formed from sugars and 5-HMF cross-polymerization. Besides, a few studies[5,6] have underlined the autocatalytic mechanism of the reaction in aqueous media which leads to interesting yields and selectivity (70% conversion of fructose in 40 min at 190 °C leading to 61% selectivity in 5-HMF[5]). This autocatalytic effect is due to the action of acidic byproducts, i.e., mainly formic acid and levulinic acid.

Current methods for 5-HMF synthesis suffer from non-reusable catalysts, short-term life regenerated heterogeneous catalysts, and use of toxic solvents or high boiling point solvents which make 5-HMF purification difficult. As a cheap, nontoxic, and easily recoverable molecule, CO_2 is ideally suited for use to build a two-phase system with water in this synthesis. Indeed, high pressure CO_2 in contact with water can act as a reversible catalyst by liberating carbonic acid in water which can promote carbohydrate dehydration. In 2015, the potential of high pressure CO_2−water biomass conversion technologies was reported in an extensive study by Morais et al.[7] Wu et al. were among the first authors in 2010 to demonstrate that CO_2 can be a catalyst for carbohydrate dehydration.[8] They showed that inulin, a polymer of fructose, was converted into 5-HMF with a yield up to 53% at 200 °C during 150 min under 6 MPa

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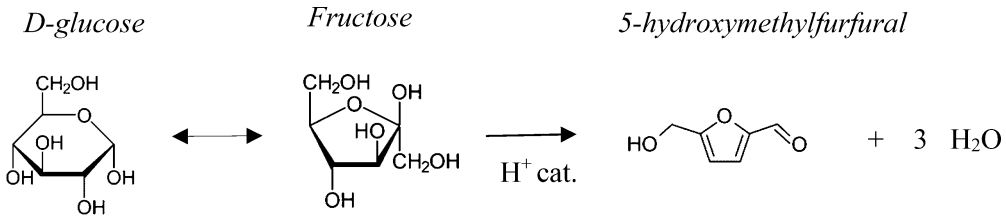
Scheme 1. Reaction Pathway for the Production of 5-Hydroxymethylfurfural from Hexoses



of CO_2. Six years later, three studies[9−11] showed the potential of a two-phase water−CO_2 system to dehydrate fructose and glucose in 5-HMF at temperatures ranging from 90 to 200 °C, and up to 7 MPa of CO_2. The best 5-HMF yield (92%) was obtained by Motokucho et al. in 2016 at 90 °C under 7 MPa of CO_2 after a 168 h[10] reaction.

Studies of kinetics of the conversion of fructose into 5-HMF, using strong homogeneous Brønsted acids (such as sulfuric acid and hydrochloric acid in water) have already been published. In 2014, Swift et al. published an extensive experimental study upon kinetics of fructose dehydration where distribution of fructose tautomers and a direct pathway of fructose conversion into formic acid were considered.[12] In 2015, Fachri et al. developed an effective model for the dehydration of fructose into 5-HMF and the subsequent degradation of 5-HMF into levulinic and formic acids, including the formation of humins.[13] Yet, to the best of our knowledge, kinetic studies on hexose dehydration, integrating the catalytic contributions of levulinic acid, formic acid, and dissolved high pressure CO_2, have not been reported.

Also, as an additional advantage, the solvent power of high pressure CO_2, in particular close to its critical point (T_c = 31 °C, P_c = 7.4 MPa), makes it possible to propose the simultaneous extraction of 5-HMF all along the duration of the reaction, yielding to an extractive reaction one-pot process with enhancement of reaction yield and selectivity. In 2010, Payne et al. published 5-HMF phase behavior in carbon dioxide,[14] showing that supercritical CO_2 would be a good choice for extraction. The solubility of 5-HMF in supercritical CO_2 was studied[15] 1 year later by Jing et al. and recently modeled with the group contribution with association equation of state (GCA-EoS) by González Prieto et al.[16] Jing et al. showed that 5-HMF solubility is greater at low temperature (40 °C) combined with high pressure CO_2 (18 MPa). Study of simultaneous 5-HMF extraction with high pressure CO_2 during the 5-HMF synthesis is out of the scope of this paper but is a very promising extension for this study.

We report here kinetics of the conversion of fructose into 5-HMF and byproducts in high pressure/high temperature CO_2−water two-phase medium. A broad range of process pressure conditions (10−25 MPa) was applied to the system in a batch setup, in the range 120−160 °C. Experimental evolution of concentrations of reagents and products along time enabled us to develop a kinetic model, including the contribution of levulinic acid, formic acid, and supercritical CO_2 as H^+ provider catalysts. Finally, best conditions for obtaining high 5-HMF selectivity have been estimated thanks to the kinetic model.

■ MATERIALS AND METHODS

Materials. D-(−)-Fructose (Sigma-Aldrich, >99% purity), D-(+)-glucose (Sigma-Aldrich, >99% purity), 5-HMF (Acros Organics, 98%), formic acid (Acros Organics, 99%), levulinic acid (Sigma-Aldrich, 99% purity), and sulfuric acid (PanReac, 0.01 M) were directly used without purification. Carbon dioxide was supplied by Air Liquid (99.98% purity).

General Procedure for the Synthesis of 5-HMF from Fructose. A mixture of 3.5 g of fructose and 60 mL of water was charged into a 90 mL high pressure reactor (Top Industrie, France). Then the mixture was heated at the desired temperature with electric heating collars. The temperature was reached after 15 min, and the reactor was charged with CO_2 using a syringe pump (Teledyne ISCO 260D). All the concentrations of reagents and products are known when high pressure CO_2 is injected into the reactor (time zero). The dehydration reaction was carried out under mechanical agitation (gas dispersing turbine) at 200 rpm rotation speed. Every hour, the progress of the reaction was monitored by analyzing the composition of the liquid phase using a high-pressure sampler (Top Industrie, France). Prior to analysis, 1 mL samples were filtered through a 0.45 μm syringe filter. At the end of the reaction, the reactor was cooled to room temperature and the pressure was released. The solution was collected from the reactor and filtered through a 0.45 μm filter (Millipore) before HPLC analysis. Each experiment was repeated twice.

Analysis. The liquid samples were analyzed with a Dionex Ultimate 3000 HPLC system equipped with a Shodex RI-101 refractive index detector and an Agilent Hi-Plex H column. H_2SO_4 solution (5 mmol/L) at a flow rate of 0.55 mL/min was used as the mobile phase. The column temperature was kept at 60 °C. Internal calibration of the products was performed using ethanol as internal standard to determine the concentrations of remaining reactants and synthesized products. The insoluble fraction of the final solution (insoluble humins) was filtered, washed with water, dried in an oven at 50 °C for 24 h, and weighted.

Determination of Product Conversion and Yield. Fructose conversion (X_F), 5-HMF, formic acid, and levulinic acid yields (Y_{HMF}, Y_{FA}, Y_{LA}), and 5-HMF selectivity (S_{HMF}) are calculated from eqs 1−5:

$$X_F = \frac{n_F^0 - n_F}{n_F^0} \tag{1}$$

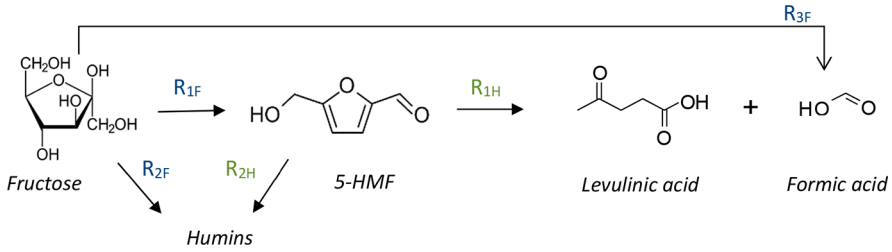
$$Y_{HMF} = \frac{n_{HMF}}{n_F^0} \tag{2}$$

$$Y_{LA} = \frac{n_{LA}}{n_F^0} \tag{3}$$

$$Y_{FA} = \frac{n_{FA}}{n_F^0} \tag{4}$$

$$S_{HMF} = \frac{n_{HMF}}{n_F^0 - n_F} \tag{5}$$

Scheme 2. Dehydration Scheme for Fructose Conversion into 5-HMF As Considered in This Study



with n_i the mole amount of product i and n_F^0 the mole amount of fructose at initial time.

Determination of Kinetic Parameters. The reaction network is given in Scheme 2. It describes the conventional reaction pathway for fructose transformation into 5-HMF and byproducts in five parallel and consecutive reactions which are all acid-catalyzed.[12,13] Fructose is dehydrated into 5-HMF (R_{1F}), which then rehydrates to form levulinic acid and formic acid (R_{1H}). Simultaneously, fructose and 5-HMF polymerize into solid humins (R_{2F} and R_{2H}). Formic acid formation from fructose was added to this scheme (R_{3F}), in accordance with literature reports[12] and experimental observation. According to literature review,[2] it was assumed here that levulinic and formic acids are the two main acids produced. Fachri's power-law modeling approach[13] was adopted here and adapted to the conversion of fructose into 5-HMF in the high pressure CO_2−water system. In this study, four acid−base equilibria were added to describe the liberation of H^+ ions in the aqueous phase: self-ionization of water, dissociation of levulinic acid, dissociation of formic acid, and dissociation of carbonic acid from the dissolution of CO_2 (eqs 6−9).

K_w:

$$H_2O \leftrightarrow HO^- + H^+ \tag{6}$$

K_{LA}:

$$LA \leftrightarrow LA^- + H^+ \tag{7}$$

K_{FA}:

$$FA \leftrightarrow FA^- + H^+ \tag{8}$$

K_{CO_2}:

$$H_2CO_3 \leftrightarrow HCO_3^- + H^+ \tag{9}$$

The evolution of concentrations of fructose (C_F), 5-HMF (C_{HMF}), formic acid (C_{FA}), and levulinic acid (C_{LA}) with respect to time was represented by four ordinary differential equations (eqs 10−13). The equations for the five reaction rates (R_{1F}, R_{2F}, R_{3F}, R_{1H}, R_{2H}) are given in the Supporting Information. Kinetic parameters were determined from minimization of errors between experimental data (total 44 experimental data points) and modeling using the Matlab software package (lsqnonlin Matlab function).

$$\frac{dC_F}{dt} = -R_{1F} - R_{2F} - R_{3F} \tag{10}$$

$$\frac{dC_{HMF}}{dt} = R_{1F} - R_{1H} - R_{2H} \tag{11}$$

$$\frac{dC_{FA}}{dt} = R_{3F} + R_{1H} \tag{12}$$

$$\frac{dC_{LA}}{dt} = R_{1H} \tag{13}$$

Determination of the Total H^+ Concentration. To better understand the effect of proton providers as catalysts in the dehydration of fructose, it was necessary to calculate the total H^+ concentration in solution. A system of eight equations was written to express the charge balance in solution (eq 14), the concentration of each acid, and the dissociation constants (see Supporting Information). The dependence on temperature of the dissociation constants (K_w, K_{CO_2}, K_{FA}, K_{LA}) was also considered (see the Supporting Information, Table S1) by using empirical equations for formic acid[17] and carbonic acid[18] or data available in the PhreeqC (llnl database) speciation software for water. As no data has been found for the pK_{LA} value for levulinic acid, its value at 25 °C (4.59) is applied at all temperatures. Also, the second dissociation reaction of carbonic acid is neglected here because its value is negligible compared to the first one under all our conditions of pressure (10−25 MPa) and temperature (120−160 °C). At this stage, eq 14 leads, upon rearrangement, to eq 15.

$$[H^+] = [HCO_3^-] + 2[CO_3^{2-}] + [FA^-] + [LA^-] + [OH^-] \tag{14}$$

$$[H^+]^2 - [H^+]\left(\frac{C_{FA}}{1 + \frac{[H^+]}{K_{FA}}} + \frac{C_{LA}}{1 + \frac{[H^+]}{K_{LA}}}\right) - K_{CO_2}C_{CO_2} - K_w = 0 \tag{15}$$

The predominance diagram for acid species in solution was used to simplify eq 15. Regarding the pH of the reactive medium (around 3), the concentrations of conjugated bases of levulinic and formic acids can be disregarded compared to the concentration of the corresponding acid. We performed comparisons of the calculated H^+ concentration with eqs 15 and 16, and the two methods yielded equivalent H^+ concentrations (Figure S1 in the Supporting Information). This justifies the use of eq 16 instead of eq 15. Indeed, eq 15, although more rigorous, is not convenient for computations because its solving requires iteration loops which slows down computations.

$$[H^+] = \sqrt{K_{CO_2}C_{CO_2} + K_{FA}C_{FA} + K_{LA}C_{LA} + K_w} \tag{16}$$

As formic acid and levulinic acid are products of the reaction, their concentrations depend on time: C_{FA} and C_{LA} are determined at each step thanks to the resolution of the system of differential equations of the model. On the other hand, the concentration of dissolved carbon dioxide in water (C_{CO_2}) was considered as a constant all along the reaction as it is in equilibrium with the high pressure CO_2 phase at constant

pressure and temperature. Therefore, this concentration of dissolved carbon dioxide in water has to be obtained from thermodynamic calculations at fixed temperature and pressure, considering water−CO_2 thermodynamic behavior.

Estimation of Dissolved Carbon Dioxide Concentration in Water. Literature data on the equilibrium concentration of carbon dioxide in water[19] was found for conditions similar to our reaction conditions of temperature and pressure (150 °C, 10 and 20 MPa). In a study which aims at demonstrating the feasibility of using CO_2−water mixtures as a reaction medium for acid catalysis,[20] Hunter and Savage have estimated the hydronium ion concentration in carbon dioxide enriched high pressure water using the well-known Henry's law.

We chose here to use conventional high pressure thermodynamic models to predict the mole fraction of carbon dioxide in the aqueous phase (x_{CO_2}). Moreover, thanks to data available on the density of the CO_2−water liquid phase,[21] the molar concentration of dissolved CO_2 (C_{CO_2}) is then calculated (eq 17). Thermodynamic behavior of the CO_2−water system under pressure was represented by the SRK−PSRK−UNIQUAC thermodynamic model, as validated in a previous study.[22] This model allows calculation of the mole fractions of CO_2 and water in each phase at thermodynamic equilibrium and at fixed temperature and pressure.

$$C_{CO_2} = \frac{\rho_m}{\frac{1 - x_{CO_2}}{x_{CO_2}} M_{H_2O} + M_{CO_2}} \tag{17}$$

where ρ_m is the density of the water and CO_2 mixture at (T, P) (in g/L), x_{CO_2} is the mole fraction of CO_2 in water at (T, P), M_{H_2O} is the water molecular mass (in g/mol), and M_{CO_2} is the CO_2 molecular mass (in g/mol).

RESULTS AND DISCUSSION

Autocatalytic Behavior. Before studying the effect of high pressure CO_2 on the conversion of fructose into 5-HMF, blank experiments were conducted to identify and quantify the autocatalytic behavior mentioned in the literature.[5,6] We observed that, without addition of any catalyst, 5-HMF was indeed produced from fructose in water with 17 mol % yield in 2 h at 150 °C and 40 mol % yield in 7 h at 150 °C. A typical concentration versus time profile is shown in Figure 1a. This result can be explained by two phenomena:[6] (i) the self-ionization of water at high temperature which releases protons that act as a Brønsted acid catalyst, also referred in the literature as hydrothermal conditions; (ii) the synthesis of acid coproducts during the reaction, such as formic acid and levulinic acid, whose dissociation liberates H^+ catalysts.

In the heated aqueous medium, rehydration of 5-HMF occurs as soon as H^+ ions are available to catalyze this reverse reaction. Levulinic acid and formic acid are thus expected to be formed in equimolar amount as shown in Scheme 2. However, our analyses revealed that formic acid and levulinic acid are indeed not produced in a 1 to 1 molar ratio, with the formic acid concentration detected in HPLC being higher than the levulinic acid concentration. The variation of the molar ratio formic acid/levulinic acid versus time at 150 °C is given in Figure 1b. After 1 h, the amount of formic acid is 10 times greater than that of levulinic acid and then this molar ratio diminishes to reach a plateau at the value 1.4. This clearly indicates another pathway for production of formic acid, and it

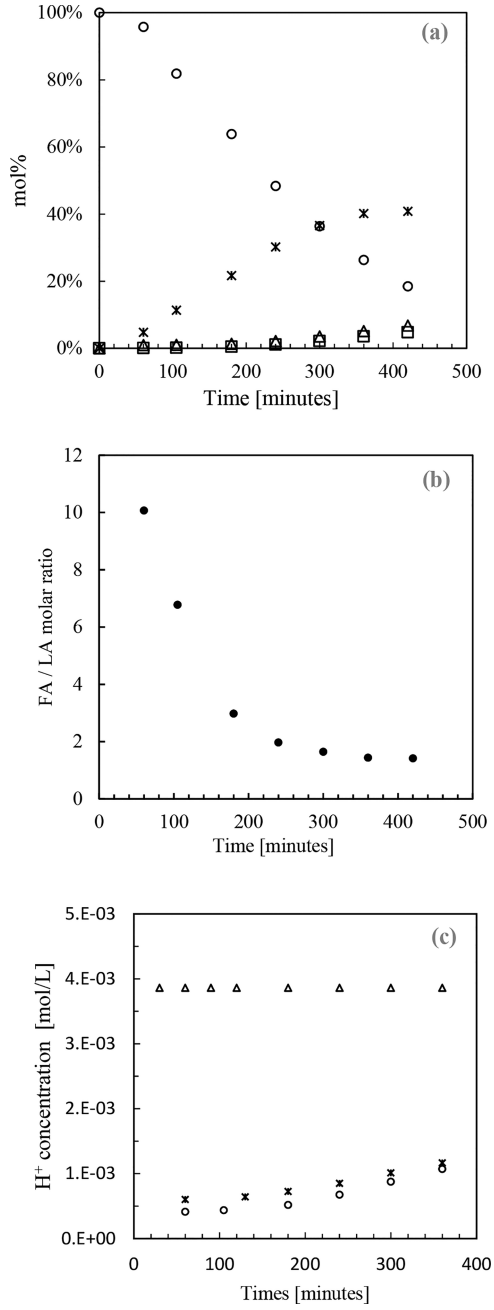


Figure 1. (a) Typical concentration profile for the conversion of fructose at 150 °C, water vapor pressure (no CO_2): fructose consumption (○), 5-HMF yield (∗), levulinic acid yield (□), and formic acid yield (△). (b) Formic acid (FA) to levulinic acid (LA) molar ratio versus time at 150 °C, water vapor pressure (no CO_2). (c) Calculated H^+ concentration as a function of time at 150 °C in three typical reactions: (○) water vapor pressure ((no CO_2), (∗) CO_2−water system at 25 MPa, (△) sulfuric acid as catalyst at pH 2.5 initial intake (water vapor pressure, no CO_2).

has already been suggested that formic acid may also be a degradation product of fructose.[12,23]

In blank experiments the production of acid byproducts is also evidenced by the increase of the total H^+ concentration (Figure 1c). During the reaction, the evolution of the total H^+ concentration shown in Figure 1c was calculated with eq 16, which takes into account the concentration of all H^+ sources in the medium. After 1 h at 150 °C, the production of levulinic

and formic acids in the medium contributed to form 4.1 × 10^{-4} mol/L H^+ in the aqueous phase, which is equivalent to a decrease in pH from 5.8 (initial value at 150 °C) to 3.4 (after 1 h at 150 °C). Then, the H^+ concentration increases slowly as carboxylic acids are produced.

As a comparison, the same reaction catalyzed by sulfuric acid as a strong acid (pH 2.5 initial intake) was carried out to compare the catalytic effect. In this experiment, 40 mol % 5-HMF yield was obtained in only 3 h, compared to 7 h in blank experiments. Moreover, as a strong acid, sulfuric acid has a clearly dominant contribution and sets the proton concentration to 3.9 × 10^{-3} mol/L (Figure 1c). This outcome shows that using sulfuric acid as a catalyst consists of buffering the aqueous medium and hiding the contributions of water, levulinic acid, and formic acid as proton providers and thus catalysts of the dehydration of fructose into 5-HMF.

These results indicate clearly that, to develop an efficient kinetic model of 5-HMF synthesis from fructose in aqueous medium without the addition of a strong acid catalyst, the contributions of water, levulinic acid, and formic acid as proton providers must be accounted for.

Effect of High Pressure CO_2 on the Synthesis. To evaluate the catalytic power of CO_2, the influence of CO_2 pressure and temperature upon the pH of high pressure CO_2-saturated water was preliminarily examined. In the CO_2−water two-phase system, CO_2 partially dissolves in water to form carbonic acid, H_2CO_3. Dissociation of H_2CO_3 in water leads to the liberation of H^+ ions (eq 9). The temperature dependence of H_2CO_3 dissociation constant as correlated by Ryzhenko et al. was adopted by van Walsum et al. to develop a model predicting the pH of the binary CO_2−water system. This model describes the influence of temperature and pressure in the range 100−250 °C and up to 15 MPa CO_2 partial pressure. At 150 °C, the pH decreases up to around 3.4 at 15 MPa. It is thus of interest to use high pressure CO_2 in our system to lower the initial pH of fructose aqueous solution and evaluate this effect on the kinetics. Experiments were carried out in a pressure range of 10−25 MPa.

The literature reports that selective synthesis of 5-HMF is dependent on the reaction temperature. Moreover, the acidic strength of the catalysts is another variable that governs 5-HMF selectivity, so the maximum 5-HMF yield could also be related to the strength of carbonic acid. Consequently, two studies were carried out here in order to uncouple these two effects: (i) the influence of pH on the 5-HMF yield at constant temperature; (ii) the influence of temperature on the 5-HMF yield at fixed initial pH. In this latter case, fixed initial pH was ensured by adjusting the CO_2 pressure because pressure directly influences the dissolved CO_2 amount, and thus the pH. As a matter of fact, at a given reaction temperature, a variation of pressure is equivalent to a variation of pH.

(i) Influence of pH. First of all, as seen in Figure 1c and in comparison to blank experiments, the addition of high pressure CO_2 contributed in increasing the total H^+ concentration in the aqueous phase all along the reaction time. At 150 °C, increasing the pressure from 10 MPa (equivalent pH 3.33) to 25 MPa (equivalent pH 3.22) resulted in a slight increase from 44 to 48 mol % for the 5-HMF yield after 7 h (Figure 2a) of reaction. In Figure 2b, it is seen that, compared to the blank experiment, high pressure CO_2 led to an enhanced selectivity all along the reaction: after 3 h, the selectivity at 25 MPa was still 80% whereas it was 60% without CO_2. Note that the initial pH of the blank experiment was 5.8 (Figure 1c).

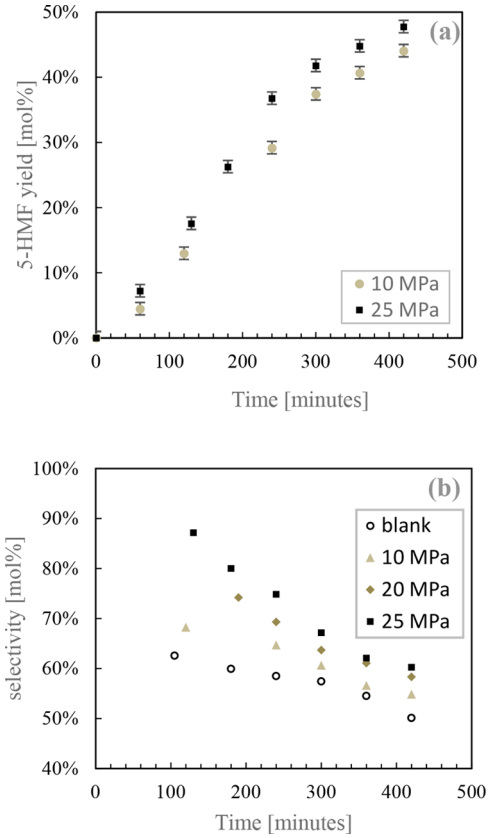


Figure 2. Dehydration of D-fructose at 150 °C in CO_2−water two-phase system. Effect of CO_2 pressure on (a) 5-HMF concentration profile and (b) 5-HMF selectivity.

Therefore, high pressure CO_2 in our system contributed to the enhancement of 5-HMF selectivity along time thanks to the acidifying power of CO_2 in the medium even if its action as a catalyst is masked by the autocatalytic character of the reaction in the conditions of our experiments.

(ii) Influence of the Reaction Temperature. Experiments were conducted at fixed initial pH 3.3. To obtain this value at different temperatures (120, 150, and 160 °C), the pressure was adjusted to 11, 20, and 25 MPa, respectively. The product concentration profiles are shown in Figure 3. As expected, dehydration of fructose is highly dependent on temperature: after 7 h at 120 °C, conversion of fructose and HMF yield are less than 5% whereas conversion reaches 80% and selectivity reaches 46% at 150 °C. At higher temperature (160 °C), the curve of 5-HMF production shows that HMF degradation accelerates after reaching a maximum yield of 48% after 4 h.

The effect of fructose initial concentration on the reaction kinetics was also studied. Varying the fructose initial concentration from 5 to 10 wt % slightly increased its conversion after 7 h of reaction. Starting from a 10 wt % fructose aqueous solution, fructose was 85 mol % converted in 7 h at 150 °C and 25 MPa of CO_2. In the same conditions of duration, temperature, and CO_2 pressure, starting from a 5 wt % fructose aqueous solution, fructose conversion reached 79 mol %. As suggested by the literature,[12,13] the dehydration into 5-HMF can be assumed as a first-order reaction with respect to fructose.

From these studies, it can be concluded that selective 5-HMF synthesis from fructose in high pressure CO_2−water two-phase system depends on two interconnected parameters:

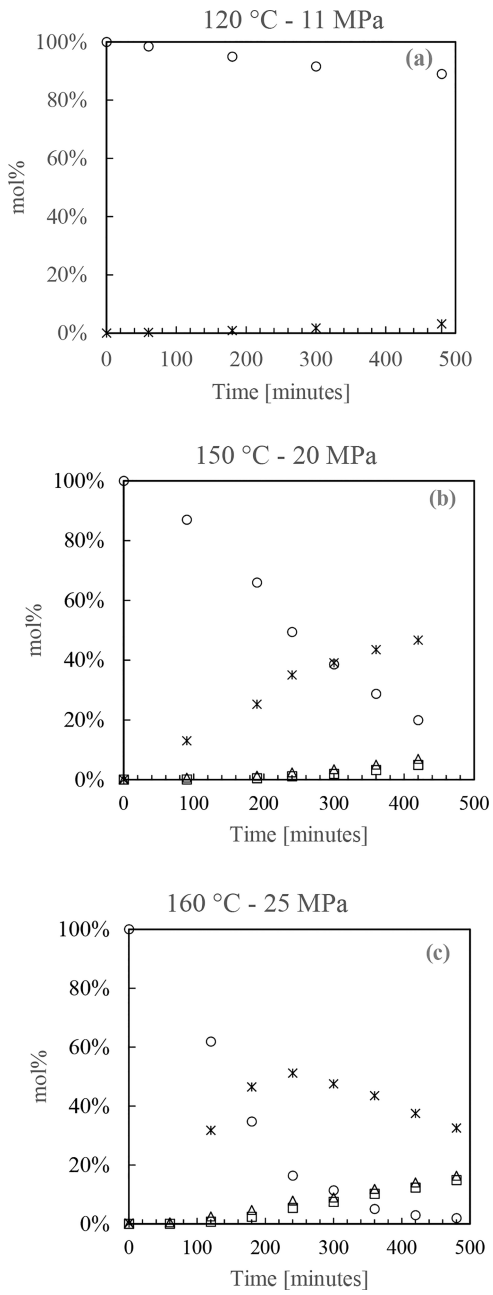


Figure 3. Effect of reaction temperature at initial fixed pH value (3.27) on remaining fructose (○), 5-HMF yield (∗), levulinic acid yield (□), and formic acid yield (△).

temperature and pH (and thus pressure). These coupled parameters justify establishing an adapted kinetic model to optimize the operating conditions with respect to selective transformation of fructose to 5-HMF. The results obtained from these experiments at various operating conditions (temperature, CO_2 pressure, fructose concentration) were thus used to develop the modeling of kinetics.

Modeling of Kinetics. Activation energy values were taken from previous studies in the literature and reaction orders for fructose and 5-HMF were set to 1 according to the kinetic scheme, experimental results on the influence of fructose initial concentration on the conversion, and the literature.[12,13] Ten parameters (kinetic constants and reaction orders for H^+) were identified by minimization of errors between experimental data and modeling. The reaction orders for H^+ were identified and values close to 1 were found, indicating a logically expected first-order dependence on the H^+ catalyst concentration (as already proposed in the literature[12]). Consequently, the reaction orders for H^+ were set to 1 and identification of the five kinetic constants with confidence interval was performed. Comparison of the results of the kinetic model and experiments is presented in Figure 4 and Table 1. As shown

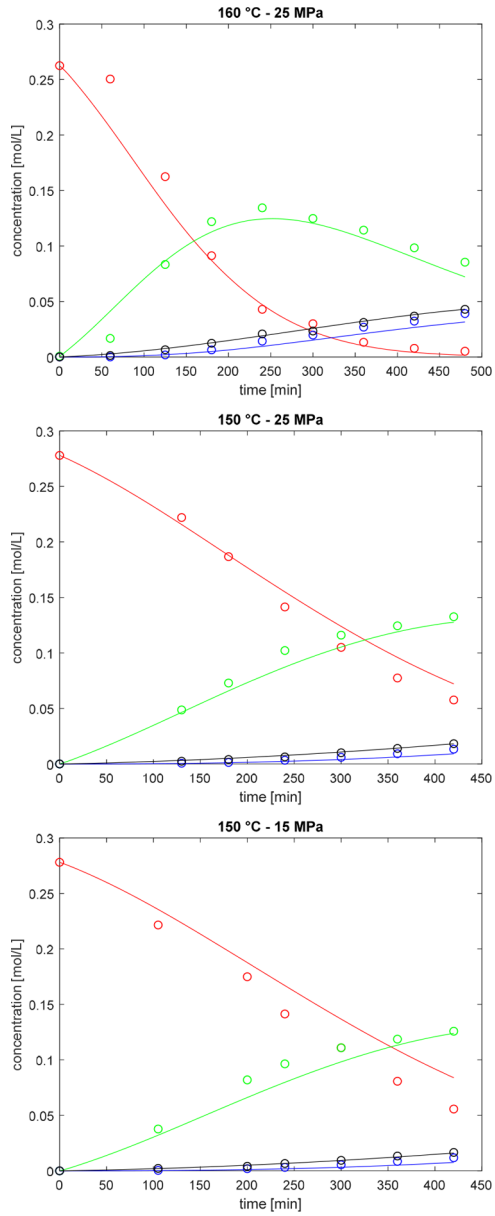


Figure 4. Comparison of experimental data (red circle, D-fructose; green circle, 5-HMF; blue circle, levulinic acid; black circle, formic acid) and kinetic model (solid line) for various reaction conditions.

in Figure 4, there is a good agreement between the model and experiments at the three different conditions presented here. The confidence intervals give a better awareness of the description of each reaction by the model. As mentioned by Swift et al. in their kinetic study,[12] higher concentrations (as for fructose and 5-HMF) are more closely matched than low concentrations (formic and levulinic acids) because only absolute values are used in the model. Further improvement of the parameter identification would consist of giving more

Table 1. Estimated Kinetic Parameters for the Conversion of D-Fructose into 5-HMF and Byproducts in CO_2−Water Two-Phase System

	reaction				
	R_{1F}	R_{2F}	R_{3F}	R_{1H}	R_{2H}
activation energy[a] (kJ mol^{-1})	123	148	130	92	119
kinetic constant (min^{-1})	1.28 ± 0.09	0.26 ± 0.09	0.06 ± 0.02	0.18 ± 0.03	0.33 ± 0.09

[a]Values taken from Swift et al.[12] and Fachri et al.[13] studies.

weight to these low concentration values to force the model to better fit them. Note that the kinetic constant values are in the same order of magnitude as those predicted by Fachri's model.[13] In the CO_2−water two-phase system, 5-HMF degradation into humins is faster than its hydration into acid byproducts, whereas it is the opposite in sulfuric acid medium.

Interpretation of Results Using a Simplified Model. A first important remark from the experimental results is that the value of the 5-HMF maximum yield R_{max} = 48 mol % could not be overpassed, whatever temperature or reactant concentrations. Also, this maximum yield was obtained at a given time t_{max} that depends on operating conditions, and the yield decreased significantly for times greater than t_{max}. Indeed, when successive reactions are involved, the bell-shaped curve (see Figure 4) for the yield of the intermediary product, as 5-HMF here, is a typical result. In this case, duration of the synthesis has to be carefully controlled and the value of t_{max} accurately identified.

The kinetic configuration of the synthesis is a combination of successive and parallel first-order reactions. Indeed, the originality of our modeling lies in the presence of equations allowing computation of the concentration of H^+ along time, accounting for its catalytic effect which affects the values of the kinetic constants of all reactions of the system. In Figure 1c is seen the computed time evolution of $[H^+]$ for a given set of operating conditions and it is shown that this value is not constant but increases rather slowly, as the pH of the aqueous phase is somewhat "buffered" by dissolved CO_2, levulinic acid, and formic acid all along the reaction. Therefore, we can propose as a simplification to assume an average value for $[H^+]$ that we consider as a constant in the set of differential equations. In this case, the set of differential equations for this simplified configuration can be analytically solved (see Supporting Information) and yields the expression of the maximum 5-HMF yield R_{max} and the corresponding time t_{max} (eqs 18 and 19).

$$R_{max} = \frac{K_{1F}}{K_F}\left(\frac{K_H}{K_F}\right)^{K_H/(K_F-K_H)} \tag{18}$$

$$t_{max} = \frac{\ln\left(\frac{K_H}{K_F}\right)}{K_H - K_F} \tag{19}$$

where K_{1F} is the global kinetic constant of fructose direct conversion to 5-HMF, i.e., the product of the H^+ concentration by the intrinsic kinetic constant k_{1F} and by the exponential term (see Supporting Information), K_F is the global kinetic constant of fructose transformation ($K_F = K_{1F} + K_{2F} + K_{3F}$), and similarly K_H represents the global kinetic constant of 5-HMF transformation ($K_H = K_{1H} + K_{2H}$).

Evaluation of the Maximum Yield. Equation 18 shows that R_{max} is a ratio of global kinetic constants. As suggested, factorizing the H^+ concentration term and simplifying it in the ratio of global kinetic constants in eq 18 shows that R_{max} is independent of the given H^+ concentration, as experimentally observed. Besides, if we assume that activation energies of the five reactions are similar, eq 18 also allows factorizing the exponential term and simplifying it in the fractions, yielding R_{max} as independent of reaction temperature, as experimentally observed. Therefore, R_{max} can be computed from the knowledge of the values of the intrinsic kinetic constant only (Table 1) and a value of 47.2% is found, very close to the experimental value of 48% and the one given by the complete model, which indicates that the proposed simplified modeling is relevant. These outcomes can also explain the results reported by Fachri et al. where they showed that 5-HMF yield reached a maximum value (56%), independently of the reaction temperature.

Therefore, this simplified model explains why, whatever the temperature and the pressure, the value of the yield is ineluctably fixed at 48% for our system. Also, the independence of the value of the maximum yield upon pressure (which indeed is equivalent to the independence upon $[H^+]$) was evidenced in the simplified model because $[H^+]$ is present in all global kinetic constants and therefore can be factorized in sums and simplified in fractions. This is indeed an indirect justification of the catalytic effect of H^+ on all reactions, as we assumed in our complete kinetic model.

Time at Maximum Yield. The expression of t_{max} (eq 19) can also be rewritten with the hypothesis of similar activation energy and constant H^+ concentration yielding eq 20, where E_a^{eff} represents a mean value of activation energies of all the reactions. In this case, the exponential term simplifies at the numerator and the factorized exponential term remains only at the denominator, indicating that t_{max} decreases when temperature increases, as experimentally observed.

Similarly, in the simplified eq 20, for t_{max} the $[H^+]$ term remains only at the denominator, indicating that t_{max} diminishes as H^+ concentration increases, as experimentally observed.

$$t_{max} = \frac{\ln\left(\frac{k_H}{k_F}\right)}{k_H - k_F}\frac{1}{[H^+]}\frac{1}{\exp\left(\frac{-E_a^{eff}}{R}\left(\frac{1}{T_R} - \frac{1}{T}\right)\right)} \tag{20}$$

Therefore, this simplified model proved to be very convenient to understand the influence of operating conditions and to give a rapid and accurate evaluation of the maximum yield. Actually, the 5-HMF reaction yield appears to be limited by the global kinetic configuration where degradation reactions limit the yield. This can be evidenced by artificially setting kinetic constants for the 5-HMF degradation reactions (R_{1H} and R_{2F}) to 0 in the model: a higher 5-HMF yield value (72 mol %) is thus obtained. A still higher value of this yield could be obtained by suppressing fructose degradation reactions as well (reactions R_{2F} and R_{3F}).

Increasing the 5-HMF yield could be experimentally attempted by adding specific catalysts[24] able to specifically increase the rate of the targeted synthesis reaction. Also, it was proposed to favor direct 5-HMF synthesis by modifying the reaction medium, through the addition of water miscible solvents or salts.[25]

Apart from the above proposed solutions based on the chemistry of the reaction, increasing 5-HMF yield could be done by a process-type solution which consists of extracting 5-HMF from the aqueous medium all along the reaction time to prevent its degradation. This leads to an extractive reaction one-pot process which would bring about enhancement of 5-HMF yield. The use of an extractive reaction one-pot process has already been done using organic solvents such as MIBK,[26] THF,[27] and 2-*sec*-butylphenol[28] and were successful to increase the yield. But these organic solvents suffer from environmentally unfriendly properties and conversely supercritical CO_2 extractive reaction would provide a fully sustainable process where 5-HMF is produced by selective fructose dehydration without addition of questionable solvents. Even though 5-HMF solubility in supercritical CO_2 is low (2×10^{-3} mole fraction of 5-HMF in CO_2 at 70 °C, 20 MPa[15]) because CO_2 is a nonpolar solvent, the application of CO_2 in the extraction of 5-HMF could be considered as an alternative to conventional organic solvents. No further purification step is needed with supercritical CO_2 extraction and fresh 5-HMF could be obtained after separation by pressure change.

■ CONCLUSION

The conversion of fructose into 5-HMF and its degradation products was performed in a two-phase CO_2−water system over a range of temperature (120−160 °C) and CO_2 pressure conditions up to 25 MPa. Thanks to a variation of pressure, the pH of the aqueous media where 5-HMF is produced can be tuned. It has been shown that fructose dehydration is catalyzed by H^+ ions generated from the dissociation of the different acidic reaction products (levulinic acid and formic acid) and also from CO_2 dissolution in water. Though rather weak due to the autocatalytic character of the reaction, the catalytic effect of high pressure CO_2 has been evidenced, allowing 5-HMF yield up to 48 mol % after 4 h of reaction at 160 °C under 25 MPa of CO_2. To be able to propose optimal conditions, a new complete modeling of kinetics, including CO_2 catalytic effect, has been developed in this study where the contributions of levulinic acid and formic acid as catalysts for the conversion of fructose to 5-HMF are also accounted for. The yield for the target molecule 5-HMF, which is the intermediate product of successive reactions, presented an expected bell-shaped curve. Knowledge of the maximum yield R_{max} and its corresponding reaction time t_{max} is of primary importance for this synthesis. Therefore, we proposed a simplification of the model which allows an easy and rapid evaluation of the maximum yield and gives a qualitative explanation of the evolution of t_{max} with respect to temperature and pressure.

As a perspective, as we mentioned in the Introduction, a relevant way to increase HMF yield by preventing its degradation in the aqueous phase would be to couple its simultaneous extraction by the supercritical CO_2 phase. This could be done by implementing a continuous CO_2 flow in the reactor. This operating mode would exploit all advantages of the use of CO_2 for such reactions. In this case, coupling the proposed kinetic modeling with the modeling of the extracting process by CO_2 (based on the thermodynamic equilibrium of the complete reactive mixture) will provide the theoretical tool allowing prediction of the best operating conditions for the extractive process, guiding the choice of the more suitable experiments for validation of this hybrid process of 5-HMF production from sugars issued from lignocellulosic biomass.

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Notes

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