

Efficient and Environmental-friendly Dehydration of Fructose to 5-Hydroxymethyl-2-furfural in Water under High Pressure of CO₂

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ABSTRACT

To develop reaction systems of chemical conversion of biomass, fructose was heated in an aqueous medium under pressurized CO₂, which caused *in situ* generation of carbonic acid. It gave 5-hydroxymethyl-2-furfural (HMF) as a dehydration product in good yields. The maximum yield of HMF was 92% in the reaction at 90 °C under 7.0 MPa of CO₂ for 168 h. The reaction proceeded in the absence of any other reagents such as non-volatile acids, organic solvents, inorganic and organic salts. It means green, environmental-friendly, and efficient process was achieved for production of HMF.

Keywords:

Biomass, Dehydration reaction, Carbonic acid, Fructose, CO₂

To realize sustainable society, utilization of natural sources instead of fossil chemicals and petroleum has been required. Therefore, efficient conversion of biomass to available chemicals such as polymerizable monomers for functional polymers has recently attracted considerable attentions.¹⁻³ Among them, monosaccharide is one of the promising renewable resources, and its base units are composed of 5 or 6 carbon atoms. Especially, fructose is abundant in nature and an easily available monosaccharide obtained from honey, fruit, and beet. Thus, fructose is an inherently versatile resource for functional chemicals. A typical chemical conversion of fructose is production of 5-hydroxymethyl-2-furfural (HMF).⁴ HMF can be also obtained from glucose through the isomerization to fructose.⁵

Recently, efficient synthetic methods of HMF production have been widely studied⁶⁻⁸ because HMF is an important platform as not only a precursor of biofuel dimethylfuran⁹ but also fine chemicals and bioactive ingredients.¹⁰⁻¹³ For the valuable chemicals, the further reactions such as oxidation or reduction of HMF afford furan-derived functional monomers, i.e., 2,5-furandicarboxylic acid (FDCA), 2,5-dihydroxymethylfuran, 2,5-diformylfuran, levulinic acid, and others.^{6-8,14-16} In particular, FDCA could be polymerized with ethylene glycol to produce a furan-based polyester, which is potentially usable as an alternative to poly(ethylene terephthalate).^{17,18}

The reaction from fructose to HMF proceeds *via* successive dehydration steps in the presence of acid catalysts (Scheme 1).

So far, there have been various kinds of mineral acids, organic acids, ammonium salts, ionic liquids and inorganic salts to promote the synthesis of HMF.⁶⁻⁸

Instead of Brønsted acid used in earlier studies,¹⁹⁻²² heterogeneous catalysts such as ion-exchange resins have been used.²³⁻²⁶ However, these reactions are usually carried out in polar organic solvents such as dimethylsulfoxide (DMSO) and *N,N*-dimethylformamide (DMF) exhibiting high boiling points. Separation of HMF from the reaction mixture sometimes requires a troublesome process. In many of these works, yields of HMF were measured by HPLC or GC analyses, and the yielded HMF was not isolated.^{6,7}

Recently, ionic liquids and metal salts have been used for HMF production.^{6,7} For the representative report, a chromium catalyst in an ionic liquid has been also reported.²⁷ However, Cr ion is toxic. Large amount of expensive ionic liquids are sometimes used.²⁸ Moreover, they are non-volatile, resulting in complicated separation of HMF from the reaction mixture.

Various kinds of acids, organic and inorganic salts, ionic liquids as well as organic solvents in biphased systems were used, and the reaction systems by using these additives often involve difficulty in the separation, high cost, toxicity, and requirement of large amounts.^{1-3,6-8} To date, HMF has been synthesized in relatively good yields in many previous studies. However, it is quite important and required that HMF is prepared efficiently and environmental-friendly free from organic solvents and additives in order to obtain and separate a large scale of HMF easily from the reaction mixture.^{6,7,29}

It is well-known that CO₂, especially under high pressure, effectively gives carbonic acid by reaction with water.^{30,31} This carbonic acid is expected to act as an acid catalyst. Therefore, saccharides in aqueous solution under high pressure CO₂ could be converted to dehydration products, HMF. In this work, dehydration of

fructose to give HMF was investigated in an aqueous solution under super- or sub-critical CO₂ conditions (below and above 7.3 MPa). It is noteworthy that our system is composed of three components, that is, only CO₂ gas, water, and fructose as starting material.

For industrial and large-scale production of HMF, this system is quite beneficial in many aspects:

- (1) CO₂ gas can be removed after depressurization.
- (2) water is removable below atmospheric pressure.
- (3) cheap, abundant and readily available chemicals.
- (4) nontoxic and non-flammable.
- (5) without any organic solvents such as DMSO and DMF.
- (6) without any additives such as metal salts and ion-exchange resins.
- (7) without any acids such as HCl and H₂SO₄, meaning that neutralization of the reaction mixture is not required after the reaction.

The CO₂ water system can enhance some organic reactions such as reduction³² and hydrolysis.^{33,34} In a previous study, Wu et al. reported that inulin was decomposed under pressured CO₂-water to produce HMF at relatively high temperature of 160-200 °C.³⁵ However, the yield was up to 53% (reaction condition: 180°C for 2h), and difference between under 0 MPa CO₂ and 4~9 MPa CO₂ was very small, i.e., 5-15% in the yields. In the literature, HMF was not isolated, and the yield was measured by HPLC. Similarly, Liu et al. have reported that 1-hydroxypentane-2,5-dione (HHD) from fructose through the formation of HMF was synthesized with Pd/C catalyst in CO₂-water.³⁶ In the literature, HMF *in situ* was produced in a 50% yield. However, the study focused on the synthesis of HHD, resulting in that HMF was not isolated and

the details such as optimized reaction conditions and relationships between the yield of HMF and reaction temperature/CO₂ pressure were not clear.

Therefore, the studies of (A) HMF isolation directly from monosaccharide fructose and (B) the optimized conditions giving a high yield of HMF production are required. In the previous studies,^{35, 36} these two points (A) and (B) were not fully achieved. On the other hand, it is novel that we here clarified both (A) and (B), and obtained HMF from fructose under more optimized conditions (especially, at 90°C) giving much higher yields. Our reaction conditions and starting material are different from the previous report.³⁵

In this study, we carried out dehydration of fructose to HMF in relatively high concentration of 21 wt% fructose in water (see the section of general procedure). Under pressured CO₂, the heating of fructose in the aqueous solution gave HMF with consumption of fructose even at 90 °C, which is a relatively mild condition. The reaction temperature is lower than that reported by Wu et al.³⁵ The product HMF in water could be obtained by only depressurization of CO₂ without filtration and neutralization. Therefore, this process is very efficient. On the other hand, without CO₂ at 90 °C for 24 h, fructose did not give HMF. This indicates that fructose was converted to HMF by pressurizing the reaction vessel with CO₂. Moreover, these results with and without CO₂ differ from the study with inulin under CO₂ water system.³⁵

Figure 1 shows the reaction time dependence of the isolated yields of HMF at 90 and 120 °C under 7.0 MPa CO₂. At 90 °C, the yield increased with increasing reaction time. After 24 and 48 h, it reached 29 and 50 %, respectively. Surprisingly, after a reaction time of 168 h, the yield gave up to 92%. Although there remains a

requirement of a longer time of 168 h, this yield is of quite a higher value in many reports.⁶⁻⁸ It suggests that the dehydration of fructose smoothly proceeded, and is hardly accompanied by side reactions such as formation of levulinic acid, fumin and polymers.³⁵ On the other hand, at 120 °C, yields of HMF increased with increasing reaction time until 36 h. At that time, the yield reached 79%. However, when the reaction time was elongated to 50, 72 h, the yields were decreased. Under these conditions, fumin precipitated from the reaction mixture. It is reported that HMF was polymerized to produce fumin.³⁷ Indeed, after the reaction for 72 h, insoluble black precipitates were observed in the reaction mixture. Judging from these results at two reaction temperatures, it was concluded that HMF could be synthesized most efficiently at 90 °C. In the previous study, longer reaction times resulted in decrease of the yields.³⁵ This behavior is similar to our results at 120°C.

Figure 2 shows typical HPLC profiles of soluble component of the reaction mixture (Reaction conditions: 90 °C, 7.0 MPa of CO₂). Two peaks were observed at 7.8 and 14.3 min, respectively. These peaks were assigned to HMF and fructose, respectively, with the help of reference samples. It is obvious that, when reaction time passed from 48 h to 168 h, the peak for HMF was increased and accompanied by a decrease of the peak for fructose. No other peaks for by-product such as levulinic acid were observed in the HPLC profiles. These results mean that the dehydration of fructose proceeded with high selectivity, that is, efficient conversion to HMF was achieved. They also agreed well with the reaction behavior in Figure 1, in which it gave high yields of HMF.

Figure 3 shows CO₂ pressure dependence of conversion of fructose and yields of HMF at 90 °C for 24 h. The conversion of fructose was calculated based on the integral ratio of chemical shifts in ¹H-NMR spectrum of the reaction mixture by the

internal standard (anisole) method. Both the conversion of fructose and the yield of HMF showed maximum values at 7.0 MPa. These results indicate that the applied CO₂ pressure accelerates the dehydration of fructose to form HMF below 7.0 MPa, but suppressed the reaction over this pressure. At CO₂ pressures below 7.0 MPa, the formation of carbonic acid possibly increased with increasing pressure to accelerate the dehydration. However, high pressures in excess of 7.0 MPa suppressed conversion of fructose. Since the phase change of CO₂ to a supercritical fluid occur around 7.3 MPa, the decrease of the conversion under high CO₂ pressures is probably due to the reduced solubility of fructose in the solution, and/or reduction of polarity and permittivity of water with increasing pressure of hydrophobic CO₂ to suppress dissociation of carbonic acid.³¹

In summary, we developed an efficient conversion of fructose into HMF in aqueous solution under applied CO₂ pressure. Dehydration of fructose at 90 °C was accelerated by CO₂ pressurization in aqueous solution at pressures lower than 7.0 MPa without side reactions. However, when performing the reaction at 120 °C, the formation of fumin as by-product was observed. Although further investigation is in progress to precisely settle the mechanism, by using CO₂-water system, we have provided a green, environmental-friendly, and easily separable method of HMF production from fructose with in a high yield of 92%.

General Procedure

In an autoclave of 200 mL, fructose 5.0 g (27.7 mmol) was dissolved in water (18.0 g, 1.0 mol) with stirring by using magnetic stirring bar. Then, predetermined weights of liquid CO₂ was introduced into the autoclave. The mixture in the autoclave was stirred

and heated at 90 °C under 7.0 MPa CO₂. After the reaction for 168 h, the autoclave was cooled, depressured, and the aqueous reaction mixture was evaporated to give the crude products. By using the aliquot, HPLC was measured. The crude product was purified by short column chromatography on silica gel with CHCl₃ eluent to obtain HMF as a slightly yellowish liquid (92% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.59 (s, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 6.52 (d, *J* = 8.7 Hz, 1H), 4.72 (s, 2H). The same reactions were individually carried out for predetermined times at 90 or 120°C under 0 ~ 9 MPa CO₂. After the reaction, in the same procedure aforementioned, conversion of fructose was measured, and HMF was isolated to estimate the yield.

Acknowledgments

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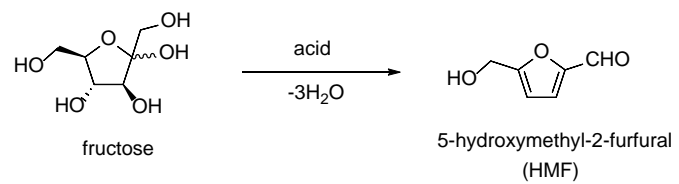
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Scheme 1. Dehydration reaction of fructose to HMF.

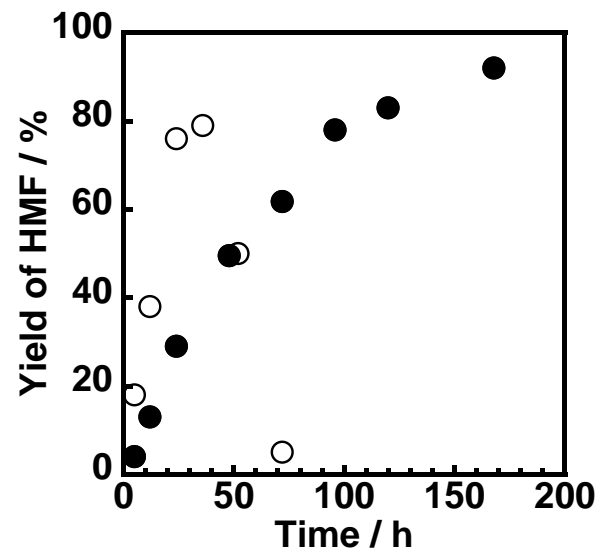


Figure 1. Time dependence of yields of HMF at 90 (●) and 120 °C (○) under 7.0 MPa CO₂.

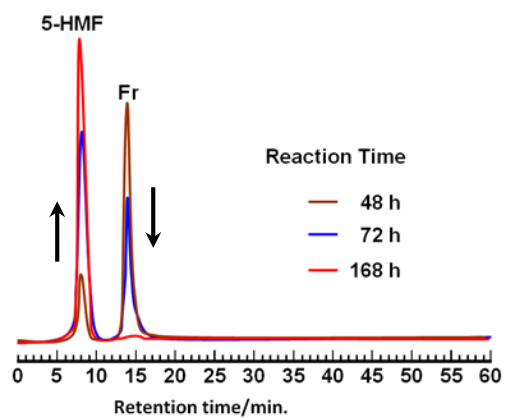


Figure 2. HPLC profiles of soluble components of reaction mixture using a Cosmosil-sugar-D column (Nakaraitesque) (Experimental conditions: eluent; $\text{CH}_3\text{CN}:\text{H}_2\text{O} = 3:1$, RI detector; RI-2031(JASCO), column temperature; 30°C , flow rate; 0.5 mL/min.).

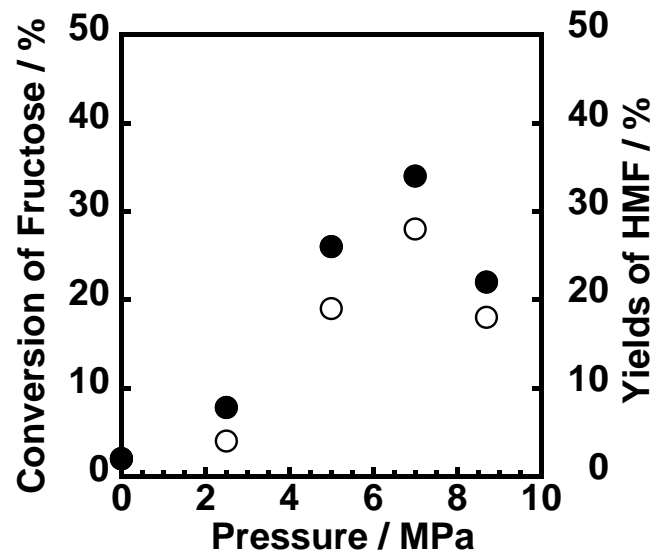


Figure 3. CO₂ Pressure dependence of conversion of fructose (●) and yields of HMF (○) at 90 °C for 24 h.