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Continuous 5-Hydroxymethylfurfural Production from Saccharides in a Microreactor

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ABSTRACT

5-Hydroxymethylfurfural (HMF) was effectively produced from saccharides in a microreactor. A biphasic reaction system was employed to achieve the immediate extraction of produced HMF and suppress the overreaction. A microreactor was utilized to ensure that the reaction occurred under segmented flow to enhance the extraction efficiency. Through many attempts using phosphate buffer saline (PBS) as the reaction phase and 2-sec butyl phenol (2BP) as the extraction phase, the favorable conditions were determined. By using PBS with pH of 2.0 and 2BP at a volume ratio of 3 to PBS, 80.9 mol% of fructose and 75.7 mol% of glucose were converted into HMF, respectively, at 180 °C. By comparing the results obtained through monophasic reactions, it was confirmed that the biphasic system successfully suppressed both the overreaction and byproducts. The system employed only a simple experimental apparatus and the acid solution and organic solvent reagents without any complex expensive catalyst.

1. Introduction

Biomass is one of the most attractive alternatives to fossil resources for producing fuels and many other important chemicals and has therefore been studied intensely in recent years.[1-4] In countries with large forested areas, such as Japan, lignocellulosic biomass is expected to be an abundant natural resource; thus, its utilization has gradually increased. Its potential as an alternative to fossil resources is not the only reason why the utilization of biomass is important. For example, Oosawa et al. reported that deliberate deforestation is required to maintain forests and must be started as soon as possible.[5] This fact results in the utilization of cut woods, which are known as lignocellulosic biomass. The most practical refinery process for converting lignocellulosic biomass into chemicals involves lignin removal,[6-9] followed by cellulose and hemicellulose hydration to saccharides[10-14] and then saccharide conversion to various chemicals.[15-19] This study focused on converting glucose and fructose, which are lignocellulosic biomass-derived saccharides, to 5-hydroxymethylfurfural (HMF). HMF is one of the most valuable chemicals in applications such as bioplastics and medical supplies. Glucose conversion to HMF proceeds under acidic conditions. However, HMF is hydrated to levulinic acid (LA) and formic acid (FA) under these conditions. Although LA is also a very valuable chemical, HMF is more valuable because it can be used in more applications, including LA production. Therefore, many researchers have attempted to produce HMF from saccharides using, e.g., organic solvent, ionic liquid, and metal catalyst to prevent its further conversion.[20-24] In particular, many metal chloride catalysts have been studied. Several reports indicated that chromium chloride is a promising catalyst, converting glucose to HMF in yields of up to approximately 50 – 70 %.[25,26] Saccharide conversion over a chromium catalyst in an ionic liquid resulted in HMF yields of 60

– 80 %,[27-29] and a yield of 90 % was achieved in a microwave-assisted reaction.[30] However, chromium is a very toxic metal to many different organisms, and ionic liquids are expensive. Thus, the use of chromium or ionic liquid requires the complete recovery of these reagents, which makes the process difficult to realize. In 2006, a remarkable production method was proposed by Román-Leshkov et al.: the "biphasic reaction system".[31] In this system, an organic solvent was employed in addition to an acidic aqueous reaction solution. Because HMF has a high affinity for some organic solvents, the HMF product was extracted to the organic phase before further conversion. The key to a successful biphasic system is the immediate extraction of the HMF product, which can be achieved by increasing the interfacial surface area between the two phases or the HMF mass transfer rate, and selecting an efficient organic solvent. A microreactor could provide a significant contribution to increasing the specific surface area and mass transfer rate. Furthermore, a unique flow state known as "segmented flow" or "slug flow" can be achieved in a microreactor. Scheme 1 shows a conceptual illustration of segmented flow in a biphasic reaction system and the glucose reaction pathways to HMF. A segmented flow consists of at least two immiscible fluids flowing through a channel alternately in slug-like segments. In each segment, internal circulation occurs, which decreases the boundary film thicknesses of the phases and thus promotes mass transfer between them. Internal circulation also promotes mass transfer by decreasing the concentration gradient in each segment, thus preventing the accumulation of targeted substances near the boundaries. Therefore, microreactors have great potential for achieving more efficient biphasic HMF production. In addition, the introduction of a microreactor has another advantage. It is usually noted that the main hurdle of biomass utilization is the high collecting cost due to the regional dispersity of biomass. A microreactor is a compact and mobile apparatus and can thus realize the onsite treatment of

dispersed biomass resources. Furthermore, its large specific wall area for fluids enables the rapid and accurate reaction temperature control, and the reactor wall thickness is considerably larger than the channel thickness, thus ensuring safe operation, even at high pressures. Due to these many advantages of microreactors, continuous HMF production from saccharides in a biphasic microreactor was investigated.

Scheme 1. Conceptual Illustration of Segmented Flow in a Biphasic Reaction System and Glucose Reaction Pathways to HMF
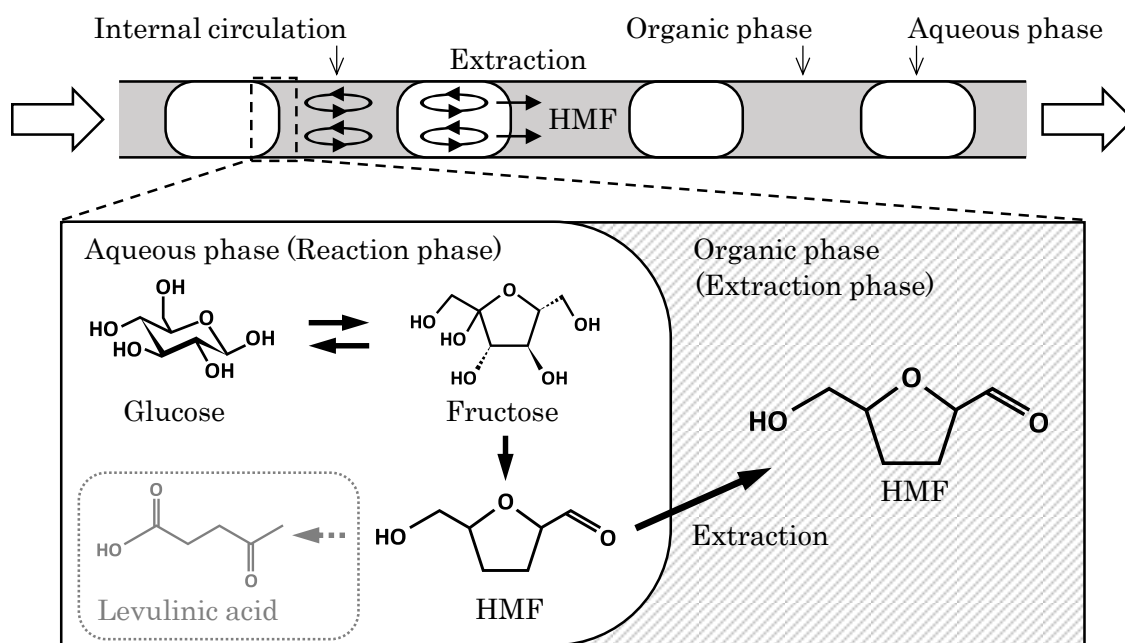
2. Experimental Section

2.1. Samples and Reagents

HMF and the saccharides glucose and fructose were purchased from Wako Pure Chemical Industries, Ltd. (Japan). Phosphate buffer saline (PBS), which was used as the acidic reaction

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solution, was prepared by mixing phosphoric acid (85.0 %, Wako), sodium phosphate dihydrate (Nacalai Tesque, Inc., Japan), and deionized water in the amounts listed in Table 1. 2-Sec butyl phenol (2BP) (98.0 %, Alfa Aesar, U.K.) was used as the extraction organic phase.

Table 1. Recipe (in 250 mL) and pH of Prepared PBS

Name	pH	85 wt% H_3PO_4 [mL]	NaH_2PO_4-$2H_2O$ [g]
PBS-1.5	1.5	11.78	16.167
PBS-2.0	2.0	6.72	25.981
PBS-2.5	2.5	2.62	33.916
PBS-3.0	3.0	0.86	37.335

2.2. Continuous HMF Production from Glucose and Fructose

An aqueous solution of 1 wt% glucose or 1 wt% fructose in PBS was fed using a high performance liquid chromatography (HPLC) pump (LC-20AD, Shimadzu Corporation, Japan), and an organic solvent of 2BP was fed using the HPLC pump. The solutions were mixed in a stainless steel SUS 316 union tee with an internal diameter of 1.3 mm (I.D. = 1.3 mm), which was connected in sequence to a 1/16" PTFE tube (I.D. = 1 mm) and 1/16" SUS 316 tube (I.D. = 1 mm). To construct the reactor, 9 m of the stainless steel tube were coiled and placed in an oil bath, which was used to maintain the reaction temperature at 170 – 190 °C. At the reactor outlet, 1 m of the coiled stainless steel tube was placed in an ice bath to quench the reaction. The quenching section was followed sequentially by a filtration section, PTFE tube, pressure sensor

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(AP-14S, KEYENCE, Japan), back pressure regulator (FC-BPV-250, DFC, Japan), and ambient sampling section. The entire channel (except the sampling section) was pressurized to 2.0 MPa by the back pressure regulator to prevent fluid evaporation in the reactor. In addition to the biphasic reaction, the corresponding monophasic reaction was conducted. For the monophasic reaction, the experimental setup was essentially the same as the biphasic setup, except the 2BP union tee inlet was sealed with a plug. The residence time (space time) was changed by varying the flow rate, and the ratio of the organic and aqueous phase flow rates (O/A ratio) was varied over the range of 0 – 4. The PTFE parts were prepared for the observation of the fluid states, and all of the biphasic experiments were guaranteed to be conducted under segmented flow.

2.3. HMF Behaviour in Different Solutions

To study the HMF behaviour in different solutions, several tests were performed. First, the decomposition profile of extracted HMF was obtained by treating 1 wt% HMF in 2BP according to the procedure used for the monophasic reaction (described in Section 2.2). Next, the HMF extraction ability of 2BP was investigated by following the experimental procedure used for the biphasic reaction (described in Section 2.2), except the sample consisted of 1 wt% HMF in deionized water or a 1 wt% HMF aqueous solution in PBS.

2.4. Biphasic Batch Reaction System

As the batch reaction apparatus, Personal Organic Synthesizer CCX-3200 (Tokyo Rikakikai Co, Ltd., Japan) was used. First, 5 mL of 1 wt% glucose or 1 wt% fructose in PBS was poured into a batch reactor, and 15 mL of 2BP was added (O/A = 3). Before adding these solutions, a magnetic stirrer was placed in the reactor. The reactor vessel was then sealed and placed in a preheated

oven. The reaction was performed under stirring for 10 – 60 min. After the reaction, samples were collected and analyzed by HPLC to determine the product concentrations.

2.5. Product Analysis

All the reactants and products (glucose, fructose, HMF, LA, FA) in the solutions were quantified by HPLC. To analyze the aqueous phase, 2.5 mM of sulfuric acid was flowed through a polystyrene-divinylbenzene column (Aminex HPX-87H, Bio-Rad Laboratories, Inc., U.S.A.) at a rate of 0.6 mL/min, and a refractive index detector (RID-20A, Shimadzu) was employed. To analyze the organic phase, a 1:4 (w/w) methanol:5 mM sulfuric acid mixture was flowed through a silane column (ZORBAX SB-C18, Agilent Technologies, U.S.A.) at a rate of 0.7 mL/min, and a UV/VIS detector (SPD-20A, Shimadzu) was employed. The dilute sulfuric acid was prepared by mixing sulfuric acid (97.0 %, Wako) with deionized water.

3. Results and Discussion

3.1. Continuous HMF Production from Fructose in a Microreactor

Based on the conversion pathways shown in Scheme 1, continuous HMF production from fructose was studied first. Figure 1 shows the fructose conversion and HMF, LA, and FA yields obtained at 180 °C using PBS-2.0 and O/A = 1 (biphasic) or 0 (monophasic). A higher HMF yield was achieved in the biphasic reaction than in the monophasic reaction. The highest HMF yields were 66.4 mol% and 62.5 mol% for the biphasic and monophasic reactions, respectively. However, the longer reaction time for the monophasic reaction resulted in a decrease in the HMF yield and an increase in the LA and FA yields. This was obviously because of the overreaction.

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In contrast, the HMF yield did not decrease with increasing reaction times in the biphasic reaction, because HMF conversion was suppressed by extracting it from the reaction phase to the extraction phase. The suppression of HMF conversion in the extraction phase was confirmed by performing an experiment in an organic monophasic system. When 1 wt% HMF in 2BP was fed into the reactor at 180 °C for 25 min, 100 % of the HMF was recovered, indicating that it did not decompose in the extraction phase. In addition, the monophasic reaction produced a residue, whereas the biphasic reaction did not. Generally, a large obstacle to HMF production is the formation of a residual humin component, which consists of inert HMF and HMF/saccharide condensates. Immediate extraction of the HMF product from the reaction phase in the biphasic system ensured that the contact time between HMF and HMF/saccharides was short. Thus, humin production was suppressed, and the HMF yield increased. Furthermore, when the collected solution samples were stored at room temperature for one week, additional residue was produced only from the monophasic reaction products, not the biphasic reaction products. This result also supported the conclusion that humin was not formed in 2BP. It should be noted that the LA and FA yields were different, as shown in Figure 1. Based on the stoichiometry of the conversion pathways shown in Scheme 1, the LA and FA molar yields from fructose should be the same. However, the FA yield was higher than the LA yield in all the experiments. It might be speculated that the produced humin adsorbed LA and decreased the yield; however, the result was the same for the biphasic reaction that did not produce humin. This fact implied that although the fructose conversion pathway to FA in Scheme 1 was the dominant pathway, other fructose conversion pathways might have occurred. Traditionally, researchers have achieved good HMF or LA yields by suppressing humin formation. To achieve an even higher yield in the future, the other pathways in HMF production must be identified and suppressed.
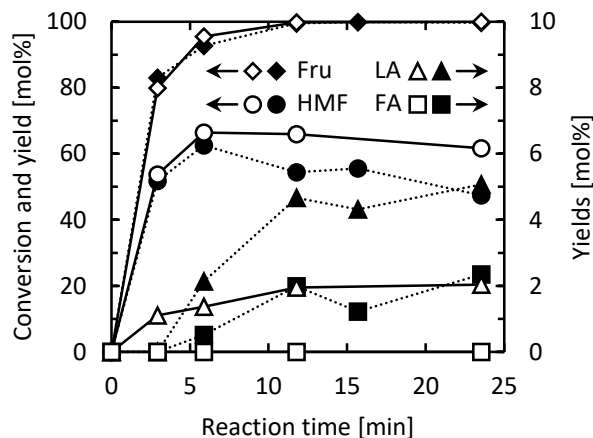
Figure 1. Fructose conversion and HMF, LA, and FA yields (180 °C, PBS-2.0). Solid line: O/A = 1 (biphasic); dotted line: O/A = 0 (monophasic).

Next, the effects of the PBS pH, O/A ratio, and reaction temperature on the fructose conversion and HMF yield were examined. Figure 2(a) shows the fructose conversion and HMF yield obtained using PBS with different pH values at 180 °C and O/A = 1. Previous reports concluded that saccharides were efficiently converted to HMF or LA in the pH range of 1.5 – 3.5.[32,33] As shown in Figure 2(a), the HMF yield and reaction rate increased with decreasing pH within the tested pH range. The yields obtained with PBS-1.5 and PBS-2.0 were very similar; however, the colors of the product solutions were considerably different. Figure 3 shows the product solutions obtained using PBS-1.5 and PBS-2.0 after 6 min of reaction. The PBS-1.5 product solution was bright green, indicating the dissolution of Fe, Ni, or Cr ions, i.e., the corrosion of the stainless steel tubing. Based on these results, the optimal PBS pH for this reaction system was 2.0. The highest HMF yield achieved using PBS-2.0 was 66.4 mol% after 3 min of reaction. The HMF yield also increased with increasing O/A ratio (Figure 2(b)). When the O/A ratio was high, the HMF concentration in the extraction phase remained relatively low, preventing a decrease in the

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extraction rate. To verify this conclusion, the HMF extraction ability of 2BP was studied using 1 wt% HMF in deionized water. Whereas the O/A ratio affected the results, the effects of the reaction temperature (< 180 °C) and time (2 – 10 min) on the extraction ability were negligible. The distributions of the recovered HMF between the organic and aqueous phases were 8:2 and 10:0 for O/A = 1 and O/A = 3, respectively. Therefore, HMF could not be completely extracted by the amount of 2BP in the system at O/A = 1. The HMF extraction ability of 2BP was also examined using 1 wt% HMF in PBS-2.0. The results were the same, except the HMF distribution between the organic and aqueous phases was 80:5 when O/A = 1 at 180 °C (regardless of the reaction time); i.e., 15 % of the HMF was lost. In contrast, when O/A = 3, 100 % of the HMF was extracted to 2BP, indicating that HMF extraction by 2BP proceeded more rapidly than HMF conversion in PBS-2.0. Because the results obtained with O/A = 3 and O/A = 4 were very similar (see Figure 2(b)), the optimal O/A ratio for this reaction system was determined to be 3. The reaction temperature is also a significant factor. The highest HMF yields from saccharides reported in the literature were obtained in the temperature range of 160 – 200 °C. Figure 2(c) shows the fructose conversion and HMF yield obtained at different temperatures using PBS-2.0 and O/A = 3. The highest HMF yield was observed after 5 – 10 min of reaction at 170 °C and 180 °C, and the yield stayed approximately the same thereafter. In contrast, at 190 °C, the yield reached a maximum at 3 min and then decreased as the reaction proceeded, indicating that HMF conversion occurred at this temperature. Therefore, the reaction should be performed at a lower temperature, i.e., 180 °C. In summary, the optimal reaction conditions for fructose conversion to HMF in this system were a pH of 2.0, O/A ratio of 3, and temperature of 180 °C. Under these conditions, the highest HMF yield achieved was 80.9 mol% after 12 min of reaction.
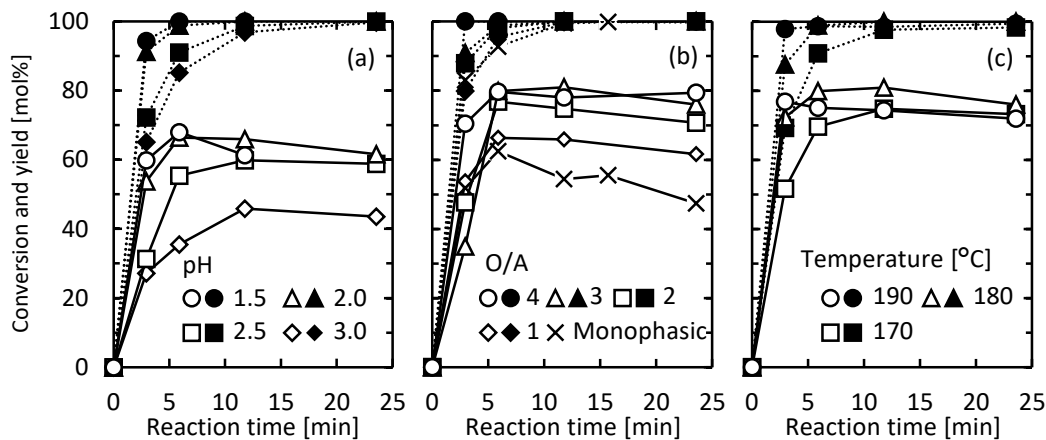
Figure 2. Effects of the (a) pH (180 °C, O/A = 1) (b) O/A ratio (180 °C, PBS-2.0), and (c) reaction temperature (PBS-2.0, O/A = 3) on the fructose conversion and HMF yield. Solid line: HMF; dotted line: fructose.

Figure 3. Colors of the product solutions obtained using PBS-1.5 (left) and PBS-2.0 (right).

3.2. Continuous HMF Production from Glucose in a Microreactor

Experiments were also conducted using glucose as the reactant. The effects of the PBS pH, O/A ratio, and reaction temperature on the glucose conversion and HMF and fructose yields were studied. Figure 4 shows the glucose conversion and HMF and fructose yields. In all cases, the highest HMF yield was observed at a longer reaction time during glucose conversion (approximately 20 – 50 min) than during fructose conversion (approximately 3 – 10 min). These

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results indicated that fructose conversion to HMF was faster than glucose isomerization to fructose under the tested reaction conditions. The effects of the pH, O/A ratio, and temperature on the glucose conversion reaction were the same as those on the fructose conversion reaction: the reaction rate and HMF yield increased with decreasing pH (Figure 4(a)), the HMF yield increased with increasing O/A ratio (Figure 4(b)), and the reaction rate increased with increasing temperature, although the HMF yield decreased at longer reaction times at 190 °C (Figure 4(c)). The results for LA, FA and residue tended to be the same, as little FA was produced during the biphasic reaction (< 2 mol%), whereas residue, LA (approximately 5 mol%), and FA (approximately 10 mol%) were produced during the monophasic reaction. A comparison of the results shown in Figures 2(b) and 4(b) revealed that the difference in the HMF yields of the monophasic and biphasic systems was larger when glucose was the starting material. This result indicated that glucose reacted more readily with HMF to produce undesirable humins than fructose; therefore, the yield increased remarkably when humin formation was suppressed by the biphasic reaction. The highest HMF yield from glucose was 75.7 mol%, which was obtained at a pH of 2.0, O/A ratio of 3, and temperature of 180 °C after 47 min of reaction. This result is remarkable, considering the simplicity of the reaction system and the absence of a complex, expensive catalyst.
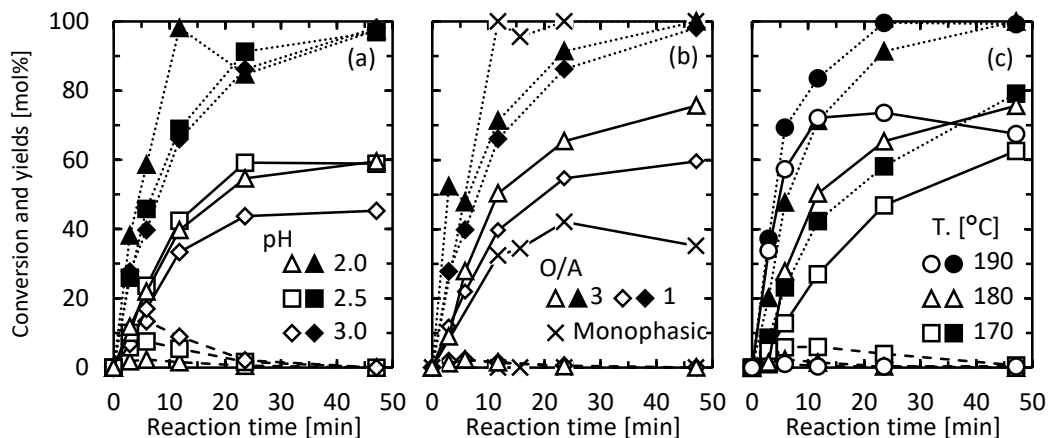
Figure 4. Effects of the (a) pH (180 °C, O/A = 1), (b) O/A ratio (180 °C, PBS-2.0), and (c) reaction temperature (PBS-2.0, O/A = 3) on the glucose conversion and HMF and fructose yields. Solid line: HMF; dashed line: fructose; dotted line: glucose.

3.3. Comparison of the Microreactor and Batch Reactor Results

For comparison, the biphasic fructose and glucose conversion reactions were conducted in a batch reactor at a pH of 2.0, reaction temperature of 180 °C, and O/A ratio of 3. The HMF yields obtained in the batch and flow reactors are compared in Figure 5. In the batch reactor, the HMF yield from glucose was low, whereas a high yield of 81.0 mol% was achieved from fructose. However, the amount of time required to obtain 80 mol% of HMF from fructose was significantly longer in the batch reactor than in the flow reactor. This result was partially due to the slow heating rate in the batch reactor. The microreactor enabled the rapid heating to the desired temperature due to the large specific surface area where the reaction solutions met the reactor wall. The batch reaction, in contrast, required approximately 5 min before reaching the desired temperature. Another important reason was the difference in extraction efficiency

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between the systems. In the microreactor, the internal circulation in each flow segment enabled the HMF product to be instantly extracted, which resulted in faster HMF production due to the suppression of the reverse reaction. In contrast, rapid extraction was not possible in the batch reactor, and therefore, some of the HMF was converted back to fructose, resulting in slower HMF production. Glucose conversion in the batch system resulted in little HMF production within the reaction time, confirming that glucose isomerization to fructose is the rate-determining step in this reaction. Glucose conversion in the batch reactor also resulted in humin formation. This result supported the assumption that glucose is more likely to react with HMF to form humins than fructose. Because HMF was not rapidly extracted in the batch reactor, the contact time between glucose and HMF was longer, which led to undesirable humin production. The use of the microreactor solved this problem by controlling the flow state and thus the extraction efficiency. Thus, the significantly higher yield and shorter reaction time achieved with the microreactor were enabled by the rapid heating and extraction in this system.
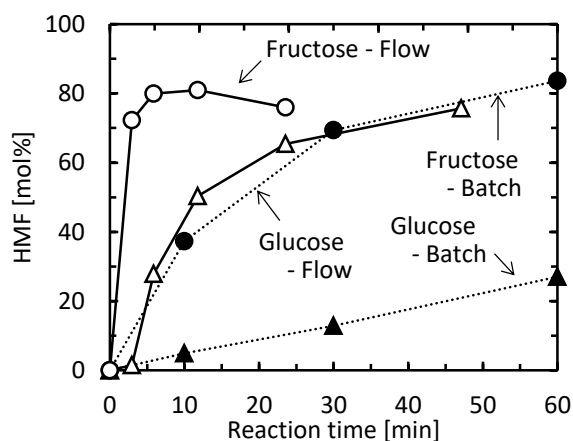

Figure 5. Comparison of the HMF yields obtained in a batch reactor and microreactor.

4. Conclusions

HMF was effectively produced from saccharides in a microreactor. The biphasic reaction was conducted under segmented flow, and the HMF product was immediately extracted from the reaction phase to suppress its conversion. A comparison of the results obtained for the monophasic and biphasic reaction systems confirmed that HMF conversion and humin by-product formation were successfully suppressed in the biphasic system. The effects of the reaction conditions, namely, the reaction phase pH, organic phase/aqueous phase ratio, and reaction temperature, on HMF production were investigated. The optimal reaction conditions were determined to be a pH of 2.0, O/A ratio of 3, and temperature of 180 °C for both the fructose and glucose starting materials. Under these conditions, fructose and glucose were converted to HMF in high yields of 80.9 mol% (12 min) and 75.7 mol% (47 min), respectively. Notably, these high yields were achieved without the use of a complex or expensive catalyst in a simple experimental system with acid and organic reagents.

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ABBREVIATIONS

HMF, 5-hydroxymethylfurfural; LA, levulinic acid; FA, formic acid; PBS, phosphate buffer saline; 2BP, 2-sec butyl phenol; HPLC, high performance liquid chromatography.

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