

Fast Synthesis of Hydroxymethylfurfural from Levoglucosenone by Mixing with Sulphuric Acid and Heating in a Microtube Reactor

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Abstract Hydroxymethylfurfural (HMF) is a promising platform chemical in future bio-based chemical industry for synthesis of a variety of furan derivatives. Studies on the HMF synthesis have focused mainly on saccharides as the feedstock. Recently, levoglucosenone (LGO), anhydrosugar available from cellulose pyrolysis, has been identified as an alternative feedstock, which can be converted to HMF under milder conditions only with acid and water as catalyst and solvent, respectively. To further explore the potential of this reaction, in this study, we demonstrated the HMF synthesis below 100°C within a few minutes at high yields. The employment of microtube reactor and high concentration sulfuric acid as catalyst was effective, leading to the highest HMF yield of 61.5%-C with the reaction selectivity over 80%. Kinetic analysis revealed that rapid heating after mixing LGO with the catalytic aqueous solution was essential to suppress side reaction that generates degradation products from LGO. The reaction with glucose or fructose as feedstock under same conditions resulted in poor HMF yield.

1 Introduction

Hydroxymethylfurfural (HMF) has vast potential to be an important building block in future bio-based chemical industry, and, therefore, often referred to as “sleeping giant” (Mukherjee *et al.*, 2015). As evidenced by many studies, HMF can be converted to chemicals used in a wide range of markets/applications such as fuels, solvents, polymers, and pharmaceuticals (van Putten *et al.*, 2013). The industrial scale production has already been started by some companies. On the other hand, the price is still high as a platform chemical to be competitive with petroleum derived chemicals (E4tech, RE-CORD, and WUR, 2015). Although there are many factors affecting the price, most importantly, it is necessary to reduce the cost of chemicals needed to convert the feedstock into HMF. In other words, development of more efficient process is required.

Saccharides are generally employed as feedstock for HMF in researches and industries. Fructose is the best option for achieving higher yields. Glucose is also converted to HMF basically after isomerization to glucose. Polysaccharides including cellulose or lignocellulosic biomass can be used as the feedstock but need depolymerisation that causes lower yields in general. As summarised in recent review studies (van Putten *et al.*, 2013; Qi *et al.*, 2014; Mukherjee *et al.*, 2015), much effort has been made for achieving the high HMF yield through development of catalytic and solvent systems. However, even for fructose and using costly catalyst and solvent, it

is hard to achieve near-complete conversion of the feedstock to HMF. This is due to the occurrence of side-reactions in the course of multi-step removing of three water molecules from saccharides. The complexity of reaction thus has been a drawback of HMF production from conventional resources.

Levoglucosenone (LGO) is a compound available from cellulose. Pyrolysis of cellulose under acid catalysis selectively produces LGO (Kawamoto *et al.*, 2007; Cao *et al.*, 2015; Kudo *et al.*, 2017; Ye *et al.*, 2017; Huang *et al.*, 2019a). Although it is still expensive, recently, a commercial scale production has been started in Australia, and the production method is intensively studied by researchers for making it more accessible. The target product from LGO in current market is limited mainly to dihydrolevoglucosenone, which is used as solvent (Sherwood *et al.*, 2014), but extensive studies have revealed the potential to be a type of platform chemical similarly to HMF (Krishna *et al.*, 2018). Recent studies (Krishna *et al.*, 2016; He *et al.*, 2017; Huang *et al.*, 2019b) have identified LGO as an alternative feedstock for HMF. LGO is readily isomerises to HMF under acid catalysis even in water. Because of simplicity in chemistry, the reaction is relatively selective and occurs at milder conditions compared to saccharide conversion to HMF.

With the purpose of contribution to development of more efficient process, in the present study, we investigated HMF production at atmospheric pressure in a short reaction time using LGO as feedstock. A

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microtube was employed as the reactor, which was important to achieve high HMF yields.

2 Experimental

2.1 Materials

LGO was purchased from Circa Group, Australia. Sulphuric acid, HMF, levulinic acid (LA), and formic acid (FA) were purchased from Wako Pure Chemical Industries and used as catalyst or standard reagent for quantification of reaction products.

2.2 Reaction

Experiments of aqueous phase LGO conversion were performed with the setup schematically shown in Figure 1. H₂SO₄ aqueous solution (1.0–4.9 mol/L) was fed into PEEK tube with inner diameter of 0.5 mm. The solution passed through T-mixer, heater (60–90°C), cooler, and then flowed out as the reaction product. After confirming steady flow at the outlet, feeding of pure LGO was started. LGO was readily dissolved in H₂SO₄ aqueous solution at the mixer without forming separated phases and then heated up. The reaction time was controlled by the flow rate and length of tube in oil bath (10 m). The flow ratio between two solutions was adjusted to achieve LGO concentration of 0.1 mol/L. The LGO conversion experiment was also carried out with a batch system. LGO was added to 5 mL of H₂SO₄ aqueous solution (4.9 mol/L) in a pressure tube with stirring bar. The tube was immersed in a water bath for temperature control immediately after the LGO addition. The reaction was quenched with an iced water.

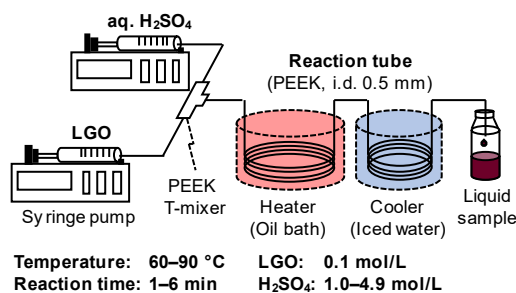


Figure 1. Experimental setup used for aqueous phase conversion of LGO in microtube reactor

2.3 Product analysis

The product liquid was diluted with water and subjected to composition analysis with high-performance liquid chromatography (HPLC, Shimadzu LC-20 prominence series). The molecules were separated by a BioRad Aminex 87H column and detected by refractive index detector and photo diode array detector. Details about the analytical conditions can be found elsewhere (Huang *et al.*, 2019b). LGO forms dehydrated product (DH) when dissolved in water. The conversion between LGO and DH is fast and determined thermodynamically to the equilibrium. In accordance with previous studies (Krishna

et al., 2016; Huang *et al.*, 2019b), the conversion of LGO (X_{LGO}) was calculated from concentrations of DH as well as LGO before and after the reaction. Degradation products (DPs) were defined as compounds other than LGO, DH, HMF, LA and FA. Since those were basically only compounds detected in HPLC analysis, DPs were apparently large molecules such as humins. The yield of DPs was calculated from the carbon balance.

3 Results and Discussion

3.1 LGO conversion with high concentration sulphuric acid in microtube reactor

The effect of H₂SO₄ concentration on the reaction was investigated at 90°C, and the result is presented in Figure 2. The formation of HMF under atmospheric pressure was confirmed. The rates of LGO conversion and HMF formation were improved with the H₂SO₄ concentration. Krishna *et al.* (2016) first demonstrated the formation of HMF from LGO in the aqueous phase reaction. They used 0.05 mol/L of H₂SO₄ and needed more than 1 h to achieve a high HMF yield at 125°C. Their kinetic analysis (available only for the reaction with 0.05 mol/L of H₂SO₄) indicated that higher temperature was preferred for HMF yield. At low temperature such as 100°C the HMF yield was much below 20% even with 100 min reaction, and further extension of reaction time was less effective. Our previous study (Huang *et al.*, 2019b) using a solid acid catalyst needed harsher conditions.

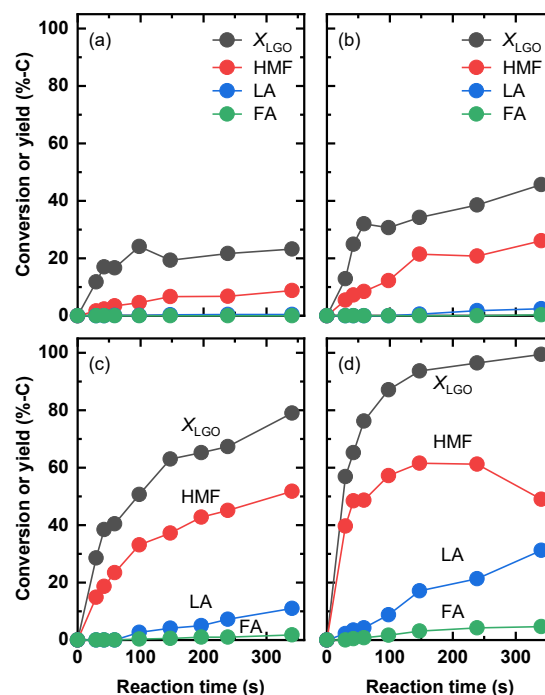


Figure 2. LGO conversion in microtube reactor. Conditions: LGO 0.1 mol/L, 90°C, H₂SO₄ (a) 1.0 mol/L, (b) 2.2 mol/L, (c) 3.5 mol/L, and (d) 4.9 mol/L

The present results revealed the possibility of HMF production with the substantial yield even below 100°C if the H₂SO₄ concentration was sufficiently high. The highest LGO yield on a carbon basis was 61.5 %-C. The

total yield of HMF, LA, and FA, indicating the reaction selectivity, was over 80% at 147–340 s with 4.9 mol/L H₂SO₄. The formation of LA and FA was clearly observed in the reaction with H₂SO₄ ≥ 3.5 mol/L. This is a type of side-reaction for the HMF production, but LA is also considered as a promising building block (Rackemann *et al.*, 2011).

The experiment was carried out with conventional feedstock such as glucose and fructose under the same conditions with LGO conversion using 4.9 mol/L H₂SO₄ (Figure 3). The yield of HMF was very low. For glucose, the yield was below 1 %-C even at 340 s. As mentioned above, they are essentially good feedstock for HMF. Shimanouchi *et al.* (2016) and Muranaka *et al.* (2017) showed high yields of HMF in aqueous phase conversion of fructose or glucose in a microtube reactor. When applied biphasic system with water-insoluble organic solvent, the HMF yield was well above 70% at 180°C because HMF formed in aqueous phase was extracted to the organic solvent before converted to LA. However, the present result demonstrates that LGO is better as feedstock for achieving high HMF yield under atmospheric pressure with short reaction time. This is likely due to the simplicity of reaction, which involves only ring-opening and closing via acyclic intermediate with no loss of atoms from the molecule (Krishna *et al.*, 2016) and therefore has low activation energy. On the other hand, HMF formation from saccharides consists of multi-step reactions. Fructose dehydration is initiated by protonation, followed by a number of protonation–dehydration–deprotonation, resulting in HMF (Yang *et al.*, 2012). Dehydration of glucose needs one more step, isomerization to fructose, although HMF forms directly from glucose in parallel under catalysis of Brønsted acid (Saha and Abu-Omar, 2014). Intermediates rich in active functional groups are precursor to undesired humins.

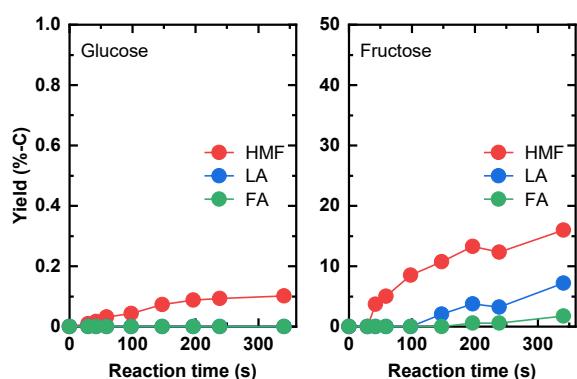


Figure 3. Glucose or fructose conversion in microtube reactor. Conditions: glucose or fructose 0.1 mol/L, 90°C, and H₂SO₄ 4.9 mol/L.

3.2 Kinetic analysis

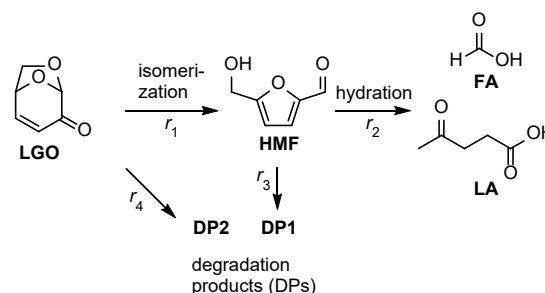
For better understanding of the LGO conversion with high concentration H₂SO₄ (4.9 mol/L), the experiment was carried out at different temperatures. The result is shown in Figure 4 as data points. The formation of HMF was confirmed in all the experiments at 60–90°C. The HMF

yield profile had a maximum above 80°C mainly due to the conversion to LA and FA.

The experimental data was kinetically analysed according to the reaction scheme 1. LGO is sequentially converted to HMF and then LA + FA. LGO and HMF also form DPs. The scheme is similar to that in our previous study (Huang *et al.*, 2019b), which effectively represented the LGO conversion under acid catalysis, but lacks in the pathways of furfural formation and degradation since it was not observed in this study. The analysis assumed first order reaction with respect to the reactant as represented by eq. (1):

$$r_i = k_{0,i} \exp(-E_i/RT) C_j \quad (1)$$

where $k_{0,i}$ and E_i are frequency factor and activation energy of reaction i ($i = 1-4$), respectively. R , T , and C_j are gas constant, temperature, and concentration of j (= LGO, HMF, FA, and LA), respectively. To focus on the reaction under catalysis of high concentration H₂SO₄, the influence of its concentration was not considered in the calculation. Kinetic parameters ($k_{0,i}$ and E_i) were optimized by regression analysis to the best fit between experimental and calculated yields.



Scheme 1. Reaction pathways used for kinetic analysis from LGO to HMF, LA, FA, and DPs

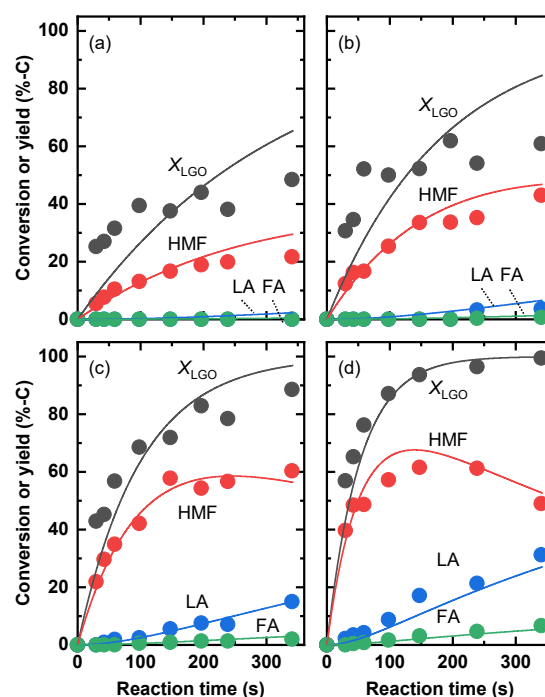


Figure 4. LGO conversion in microtube reactor. Conditions: LGO 0.1 mol/L, H₂SO₄ 4.9 mol/L, (a) 60°C, (b)

70°C, (c) 80°C, and (d) 90°C. Data points represent the experimentally obtained results. Lines represent the conversion and yields calculated with kinetic parameters.

Table 1 lists kinetic parameters obtained from the analysis. The magnitude relation among the parameters is in line with reported one (Huang *et al.*, 2019b). Figure 5 shows HMF yield calculated with the parameters as functions of temperature and reaction time. The yield maximum was observed at high temperature and short reaction time area. Apparently, the yield could be over 80 %-C, although this was not examined experimentally since high pressure reaction was outside the scope of this research. At any temperature, the HMF yield first increased and then decreased with reaction time. This was due to consumption of HMF by r_2 and r_3 . However, the contribution of r_3 was far smaller than that of r_2 . The ratio of rate constants, k_2/k_3 , was at the order of 10^4 even at 140°C. The formation of DP1 was thus negligible, and therefore HMF was selectively converted to LA and FA. An important observation was difference in the maximum HMF yield by reaction temperature. This is explained by the formation of DP2. As shown in Figure 6 and indicated by the low value of E_4 , DP2 yield was higher at lower temperature. The ratio of k_1/k_4 , at 60, 70, 80, and 90°C was 0.98, 1.8, 3.3, and 5.8, respectively. DP2 is thus major product rather than HMF at low temperatures. The similar DP2 yields at short reaction time (Figure 6) regardless of the difference in k_1/k_4 are resulted from increase in r_4 with temperature.

Table 1. Kinetic parameters calculated with experimental data in Figure 4, assuming Scheme 1 and eq. (1) under conditions of LGO 0.1 mol/L and H₂SO₄ 4.9 mol/L

| | $k_{0,i}$ (L/mol/min, $\times 10^{-10}$) | | E_i (kJ/mol) |
|-----------|----------------------------------------------|-------|-------------------|
| $k_{0,1}$ | 2.60×10 | E_1 | 79.4 |
| $k_{0,2}$ | 1.99×10^{-5} | E_2 | 43.8 |
| $k_{0,3}$ | 1.28×10^6 | E_3 | 176 |
| $k_{0,4}$ | 1.17×10^{-8} | E_4 | 20.0 |

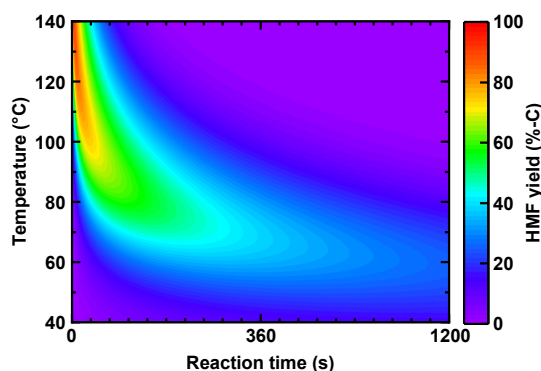


Figure 5. HMF yield map calculated with kinetic parameters, assuming validity of the parameters at extended range of temperature (40–140°C)

3.3 Comparison with batch system

Overall trend found in the kinetic analysis indicated importance of precise control of temperature and reaction time for achieving high selectivity toward the target reaction. The reaction at low temperature is in particular unfavourable because it causes loss of LGO. This problem can be apparent in the reaction with batch system, which needs long time for heating the solution to desired temperature, depending on conditions. The reaction in a batch reactor was simulated by calculation with kinetic parameters. Before heating, the temperature (room temperature; 20°C) was kept constant for 0–10 min, which assumed time for reactor setup, and then increased to 90°C at slow heating rate of 1–10 °C/min (Figure 7 (a)).

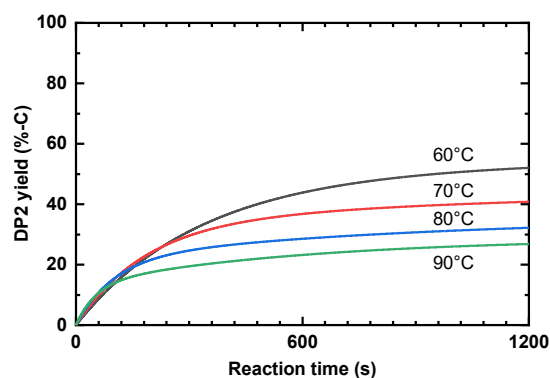


Figure 6. DP2 yield calculated with kinetic parameters .

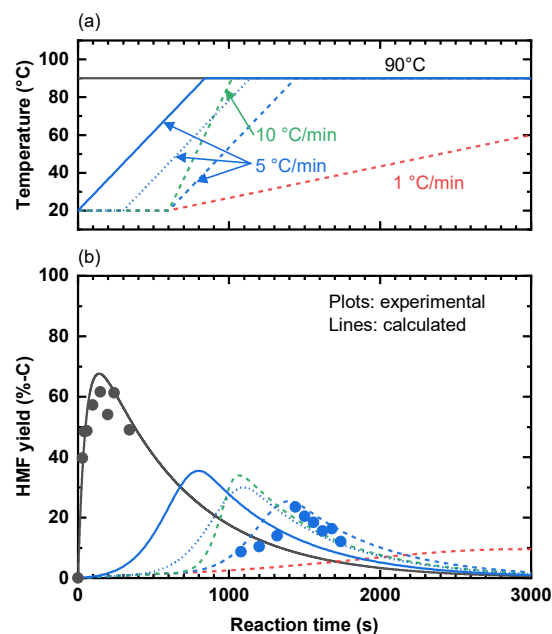


Figure 7. LGO conversion in a batch reactor: (a) temperature profile and (b) HMF yield. Black plots and line show the results in experiment and calculation with microtube reactor. The batch experiment was carried out with 10 min holding time at 20°C and 5 °C/min heating rate. Conditions: LGO 0.1 mol/L, H₂SO₄ 4.9 mol/L

The result is presented in Figure 7 (b). All the yield profiles showed the maximum in the calculated time range. In spite of the same final temperature (90°C), the maximum HMF yield varied over a wide range of 9.5–67.6 %-C. Holding time even at 20°C had a substantial influence. The maximum yield of 35.5 %-C decreased to

25.4 %-C by the difference of holding time from zero to 10 min with 5 °C/min heating rate. To ensure the calculation results, experiments were carried out with 10 min holding time at 20°C and 5 °C/min heating rate. The experimental and calculation results agreed well as shown in Figure 7 (b). The formation of DP2 at low temperature thus significantly influences the available maximum HMF yield. To suppress the influence, rapid heating soon after dissolving LGO into the H₂SO₄ aqueous solution is effective for this reaction system.

4 Conclusions

In this study, aqueous phase conversion of LGO into HMF was investigated using microtube reactor and high concentration H₂SO₄ as catalyst. The HMF yield reached 61.5 %-C with the reaction selectivity over 80% in a few minutes of reaction when used 4.9 mol/L H₂SO₄ at 90°C. The experiment with glucose and fructose under the same experiment failed to achieve such high yield, indicating suitability of LGO as HMF feedstock for achieving the high yield under atmospheric pressure with short reaction time. Kinetic analysis of the experimental results revealed that rapid heating after mixing LGO with the acidic solution was essential to suppress side reaction that formed undesired degradation products directly generated from LGO.

Acknowledgements

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