

Catalytic Conversion of Fructose, Glucose, and Sucrose to 5-(Hydroxymethyl)furfural and Levulinic and Formic Acids in γ -Valerolactone As a Green Solvent

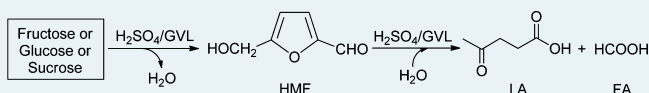
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S Supporting Information

ABSTRACT: The conversion of fructose, glucose, and sucrose to 5-(hydroxymethyl)furfural (HMF) and levulinic acid (LA)/formic acid (FA) was investigated in detail using sulfuric acid as the catalyst and γ -valerolactone (GVL) as a green solvent. The $\text{H}_2\text{SO}_4/\text{GVL}/\text{H}_2\text{O}$ system can be tuned to produce either HMF or LA/FA by changing the acid concentration and thus allowing selective switching between the products. Although the best yields of HMF were around 75%, the LA/FA yields ranged from 50% to 70%, depending on the structure of the carbohydrates and the reaction parameters, including temperature, acid, and carbohydrate concentrations. While the conversion of fructose is much faster than glucose, sucrose behaves like a 1:1 mixture of fructose and glucose, indicating facile hydrolysis of the glycosidic bond in sucrose. The mechanism of the conversion of glucose to HMF or LA/FA in GVL involves three intermediates: 1,6-anhydro- β -D-glucofuranose, 1,6-anhydro- β -D-glucopyranose, and levoglucosenone.

KEYWORDS: carbohydrates, 5-(hydroxymethyl)furfural, levulinic acid, formic acid, γ -valerolactone, sulfuric acid, isotopic labeling



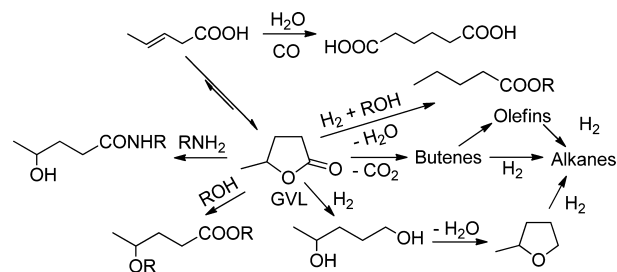
INTRODUCTION

The gradual replacement of all fossil resources with biomass in the production of carbon-based consumer products should greatly reduce carbon dioxide emission, a key issue of sustainability.^{1–4} The rapidly expanding field of biomass conversion has resulted in the identification of several platform chemicals,⁵ which could either replace the currently used commodity and fine chemicals or serve as the renewable feedstock for their production. γ -Valerolactone (GVL) has been previously suggested as a sustainable liquid for the production of transportation fuels and carbon-based chemicals.⁶ GVL is naturally occurring and nontoxic and is also currently used by the food industry as food additive. It is miscible with water but, unlike ethanol, does not form an azeotrope with water. GVL has desirable properties as a sustainable liquid, including a remarkably low vapor pressure,^{6a} and does not form hazardous peroxides under air.⁷

GVL has been used successfully as an additive in gasoline as well as an illuminating and lighter fluid.^{6a,c} The addition of GVL to a diesel and biodiesel mixture resulted in the significant reduction of carbon monoxide and smoke emission,⁸ a key issue of sustainability in large cities. GVL can be also used as a platform chemical for the synthesis of 1,4-pentanediols,^{9,10} 2-MeTHF,^{9–12} alkyl 4-alkoxy and tetraalkyl ammonium 4-hydroxyvalerates,^{13,14} isomers of butenes,^{15,16} mixtures of alkanes,⁹ alkyl valerates,¹⁷ 4-hydroxypentane alkylamides,¹⁸ and adipic acid via pentenoic acids (Scheme 1).¹⁹

Large-scale production of GVL requires the development of an economical production technology starting from carbohydrate-based biomass. The process occurs via four consecutive reactions,^{9,20} including the acid-catalyzed dehydration of

Scheme 1. Conversion of GVL to Chemicals



carbohydrates to 5-(hydroxymethyl)furfural (HMF),²¹ the acid-catalyzed hydration of HMF to levulinic acid (LA) and formic acid (FA),²² and the catalytic hydrogenation of LA to 4-hydroxyvaleric acid (4-HVA) followed by ring closure via dehydration to GVL (Scheme 2).²³

It should be noted that the one-pot conversion of carbohydrates to LA and FA has been a very attractive, step-skipping approach.²⁴ Although HMF and LA/FA are key intermediates, they are also high value-added platform molecules in their own right and could be the desired product(s).

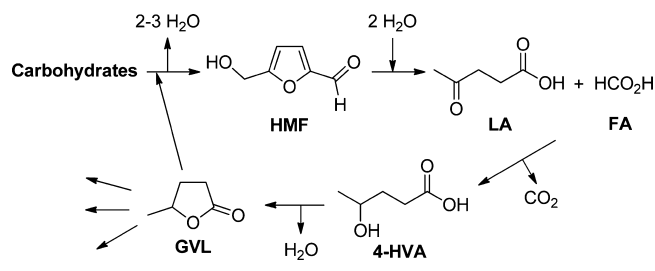
In light of the beneficial use of solvents for the conversion of carbohydrates, a key element of our strategy has been the use of GVL as the solvent for each step (Scheme 2).²⁵ This embodies an important principle of green chemistry in limiting the use of solvents and auxiliaries.²⁶ The use of the product GVL could

Received: December 7, 2013

Revised: March 25, 2014

Published: March 28, 2014

Scheme 2. Conversion of Carbohydrates to GVL in GVL



eliminate all solvent-related separation and environmental issues, which is an enormous challenge for solvents such as water, DMF, DMSO, and even ionic liquids, if its performance is comparable to these solvents. We have recently demonstrated that ^{13}C -labeled fructose can be converted to ^{13}C -labeled GVL in GVL via the intermediacy of HMF and then FA and LA.^{20b} The first biphasic separation system using GVL, water, and supercritical carbon dioxide as green solvents in continuous mode was reported by Poliakoff in 2007.^{23c} Dumesic and co-workers have reported the use of similar biphasic systems, using GVL, water, phase modifiers,²⁷ and supercritical carbon dioxide^{27b} to enhance phase separation. GVL was also able to largely suppress the formation of side products humins, although no mechanistic proofs were provided.²⁸

We report here the continuation of our preliminary study^{20b} on the use of GVL as a green solvent for the catalytic conversion of fructose, glucose, and sucrose to HMF or LA and FA. Several intermediates were identified, which shine light on the mechanism of the conversion of glucose to HMF in the presence of sulfuric acid catalyst.

EXPERIMENTAL SECTION

D-(−)-Fructose ($\geq 99.9\%$, Sigma), D-(+)-glucose (ACS Reagent, Sigma-Aldrich), 2- ^{13}C -D-fructose (99%, Cambridge Isotope Laboratories), 2- ^{13}C -D-glucose (99%, Cambridge Isotope Laboratories), sucrose (ACS Reagent, Sigma-Aldrich), levoglucosenone (LGN, 95%, Carbosynth), H_2SO_4 (95–97%, Sigma-Aldrich), conc HCl (37%, Sigma-Aldrich), 5-(hydroxymethyl)furfural ($\geq 99\%$, Aldrich), levulinic acid (98%, Aldrich), formic acid (98%–100%, Merck), biphenyl (99.5%, Sigma-Aldrich), *p*-anisaldehyde (98%, Aldrich), dimethyl carbonate (DMC, 99%, Sigma-Aldrich), acetone (99.99%, Fisher), acetonitrile (MeCN, 99.9% RCI LabScan), sulfolane (99.9%, Aldrich), dimethyl sulfoxide (DMSO, 99.9%, Sigma-Aldrich), dimethyl sulfoxide- d_6 (DMSO- d_6 , $>99.5\%$ atom % D, Sigma-Aldrich), and deuterium oxide (>99.8 atom % D, Armar) were all used as received. γ -Valerolactone (GVL, 98%, Aldrich) and tetrahydrofuran (THF, 99.8%, 250 ppm BHT, RCI LabScan) were distilled before used.

NMR spectra were collected using a Bruker AV III 400 instrument at 20 °C. Quantitative ^1H NMR was carried out using 90° flip angles with a recycle delay of 80 s. Quantitative ^{13}C NMR data was collected by using inverse-gated decoupling with a recycle delay of 50 s. Yields were measured using ^1H NMR of the reaction mixture, as calculated from the addition of known amounts of either biphenyl or *p*-anisaldehyde as an internal standard. Since the solubility of the monosaccharides in GVL is low, the reaction vessel could have contained both solid and dissolved monosaccharides at room temperature just before samples are taken for analysis. Therefore, the measurements of the conversion of the monosaccharides could have been limited

until their total amount in the reactor reached the solubility in the reaction mixture at room temperature. In addition, the solvent properties of the reaction mixture are changing with time and the methine-peak of 4-HVA (formed from GVL in the presence of acids) is overlapping with the middle of the region of the peaks of the monosaccharides between 2.9 and 5.3 ppm. We marked in the Tables of the Supporting Information all the samples in which the monosaccharides were not observable by ^1H NMR, indicating that their conversion reached 100% and the selectivity of the products was equal with the reported yields.

Solvent Screening for the Conversion of Fructose.

Solvent screening experiments were performed by using a CEM Discover S microwave synthesizer. A sample of 1.88 g (10 mmol) fructose, 1.67 mL 0.5 mol/L HCl, and 10 mL of the desired solvent (DMSO, THF, MeCN, acetone, GVL, or DMC) were placed in a 35 mL glass vessel and heated at 130 °C for 10 min, during which the conversion of fructose was complete in all solvents.

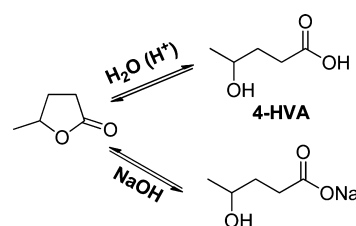
Conversion of Carbohydrates in GVL. The conversion of various carbohydrates in GVL was performed in a 15 mL Ace pressure tube (bushing type, front seal, $L \times \text{O.D.} = 10.2 \text{ cm} \times 25.4 \text{ mm}$). The reactions were performed by heating the mixture of carbohydrate(s), biphenyl, 1.5 mL aqueous H_2SO_4 , and 10 mL GVL in an oil bath at the required temperature (± 1 °C). The tube was cooled to room temperature at certain time intervals to take liquid samples (0.3 mL) to monitor the progress of the reactions. These experiments were repeated three times.

Conversion of 2- ^{13}C -D-Fructose or 2- ^{13}C -D-Glucose or LGN in GVL. Experiments were carried out in NMR tubes by adding 2- ^{13}C -labeled fructose (18.1 mg, 0.1 mmol) or 2- ^{13}C -labeled glucose (18.1 mg, 0.1 mmol) or LGN (14.2 mg, 0.1 mmol) to the solution of 75 μL of H_2SO_4 (1 or 5 mol/L) and 0.5 mL of GVL. The NMR tubes were heated to 130 °C for the required time and then cooled to room temperature in an ambient temperature water bath. The NMR measurements were performed with a coaxial insert tube containing D_2O for locking. Between NMR experiments or heating cycles in the oil bath, the samples were stored at 4 °C.

RESULTS AND DISCUSSION

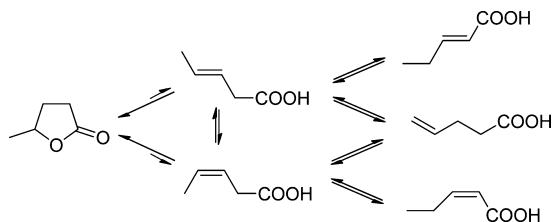
The application of GVL as a solvent in any acid catalyzed reaction at higher temperatures requires the investigation of its stability under acidic conditions. It has been shown previously using H_2^{18}O that GVL does not react with water to form 4-HVA at neutral pH.^{6a} On the other hand, GVL undergoes reversible ring-opening to form 4-HVA under acidic conditions, which was confirmed by NMR measurements. Under basic conditions, for example in the presence of NaOH, GVL is in equilibrium with the sodium salt of 4-HVA (Scheme 3).

Scheme 3. Reaction of GVL with Water or NaOH



The thermal stability of GVL is largely limited by its ring-opening to *cis*- and *trans*-3-pentenoic acids,^{17,19} which can undergo further isomerization (Scheme 4) and other reactions.

Scheme 4. Ring-Opening of GVL to *cis*- and *trans*-3-Pentenoic Acids and Their Subsequent Conversion to *cis*- and *trans*-2- and 4-Pentenoic Acids



The solubility of fructose in GVL is significantly lower (0.01 g/100 g of GVL) than in water (400 g/100 g of H₂O at 25 °C),²⁹ which can be increased modestly by the addition of water and sulfuric acid. For example, 2.8 g of fructose can be dissolved in a mixture of 82.3 g of GVL, 9.2 g of H₂O, and 5.7 g of H₂SO₄ at room temperature, resulting in a colorless solution after stirring for 15–30 min, depending on the size of the fructose crystals. ¹³C NMR of the solution revealed the presence of the four cyclic isomers, the α - and β -D-fructopyranoses and the α - and β -D-fructofuranoses, reaching their equilibrium concentrations after 2 h at room temperature.^{20b}

Solvent Effects on the Dehydration of Fructose to HMF. Although the solvent dependence of the acid catalyzed dehydration of fructose to HMF has been observed,^{21k,n} no comparative study has been reported for GVL under the same conditions. Thus, 1.88 g of fructose, 1.67 mL of aqueous HCl (0.5 mol/L), and 10 mL of solvent was placed in a 35 mL sealed glass reaction vessel and heated at 130 °C in a microwave reactor. After 10 min, all the fructose was converted to HMF and small amounts of LA (Figure 1) and FA (Supporting Information Table SI1).

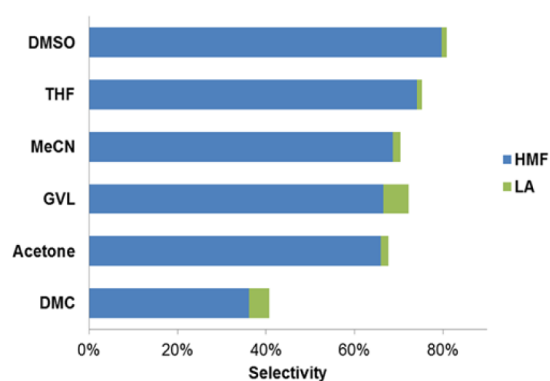


Figure 1. Complete conversion of fructose to HMF and LA by microwave heating of a mixture of 1.88 g (10.4 mmol) of fructose, 1.67 mL of 0.5 mol/L HCl, and 10 mL of solvent at 130 °C for 10 min.

Although DMSO and THF were the best solvents for producing HMF, GVL was comparable to MeCN and acetone, with about a 70% selectivity of HMF. In the case of THF, in addition to the well-known issues of formation of peroxides during storage under air, the formation of 0.2% side product 4-chlorobutan-1-ol was observed under the reaction conditions,

which raised an unexpected environmental concern. Because the formation of chlorine-containing organics could lead to serious environmental issues, we have decided to use sulfuric acid only in all future studies.

The effect of the concentration of the sulfuric acid on the formation of HMF or LA in GVL was investigated by using microwave irradiation (Figure 2). When the acid concentration

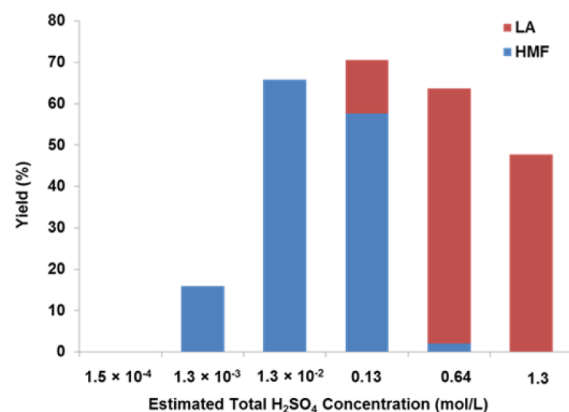


Figure 2. Heating a mixture of 2 mmol of fructose, 1.5 mL of H₂SO₄ (0.001, 0.01, 0.1, 1, 5, and 10 mol/L, respectively), and 10 mL of GVL by microwave at 130 °C for 10 min.

was below 10⁻⁴ mol/L, no HMF or LA could be detected. The maximum yield (58% HMF and 13% LA) was achieved when the acid concentration was 0.1 mol/L after 10 min at 130 °C. When the acid concentration was increased to 0.6 mol/L, the yield of HMF decreased to 2%, and that of LA increased to 62%. Thus, the reaction product distribution in GVL was very sensitive to the acid concentrations, and GVL is a tunable solvent for the conversion of carbohydrates to either HMF or LA and FA, allowing selective switching between the products. Compared with DMSO as the solvent, the required acid concentrations that gave the highest yields of HMF were similar.

Dehydration of Fructose to HMF in GVL. All reactions were performed in pressure tubes with thermal heating in an oil bath. After the reactions were completed, the tubes were cooled in ice water immediately. Samples were taken periodically, and the yields were quantified against internal standards using NMR spectroscopy. It was confirmed that the sulfuric acid catalyzed dehydration of fructose to HMF in GVL was strongly dependent on the concentration of H₂SO₄, as expected.^{21k} Over a broad range of acid concentrations, the rapid formation of HMF was followed by its fast disappearance (Figure 3). At lower acid concentrations, the maximum yields of HMF were higher and its subsequent conversion was slower. These results showed that further reaction of HMF was also acid-catalyzed and required a higher acid strength. When changing the catalyst to 1.5 mL phosphoric acid (3.33 mol/L), similar yields of HMF (70%) could be established in 1 h; however, the subsequent conversion of HMF to LA/FA did not take place, showing that the acidity of phosphoric acid was not high enough for the desired transformation.

Concerning formation of side products, it should be noted that immediately after the addition of sulfuric acids, GVL undergoes a reversible ring-opening reaction to form trace amounts of 4-HVA (Scheme 3). In addition, the formation of *cis* and *trans* isomers of various pentenoic acids (Scheme 4)

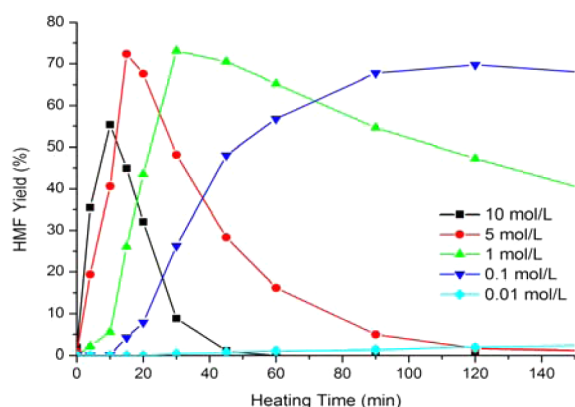


Figure 3. Acid concentration dependence of the yields of HMF during the heating of a mixture of 2.0 mmol of fructose, 1.5 mL of H_2SO_4 , and 10 mL of GVL at 130 °C. The concentration of added sulfuric acid is indicated in the legend.

was also observed at the highest sulfuric acid concentration (10 mol/L). The observation of these side products could lead to additional side reactions with the starting carbohydrates or formed intermediates and products.

The formation of HMF and the side products is highly dependent on the reaction temperature (Figure 4). The

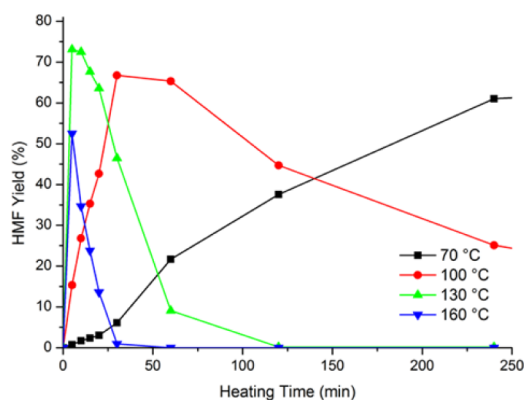


Figure 4. Temperature dependence of the yield of HMF during the heating of a mixture of 2.0 mmol of fructose, 1.5 mL of 5 mol/L H_2SO_4 , and 10 mL of GVL.

maximum yield of HMF (73%, 1.46 mmol) was achieved at 130 °C in only 5 min. The use of either higher or lower temperatures resulted in lower HMF yields. The disappearance of HMF was also faster at higher temperatures. Only a trace amount of cis and trans isomers of pentenoic acids was observed at 150 °C, and their concentrations increased at higher temperatures.

Varying the initial concentration of fructose between 0.053 and 0.53 mol/L resulted in only a small effect on HMF yields, typically ~73% (Figure 5). When the fructose concentration was higher than this, the HMF yield was lower as a result of more side reactions; the maximum HMF yield was reduced to 60% at 1.7 mol/L fructose concentration. This increased loading also resulted in incomplete dissolution of fructose at ambient conditions, although the reaction mixture did become homogeneous at higher temperatures.

Dehydration of Glucose and Sucrose to HMF. The conversion of glucose and sucrose to HMF in GVL was also investigated (Figure 6). The maximum yield of HMF from

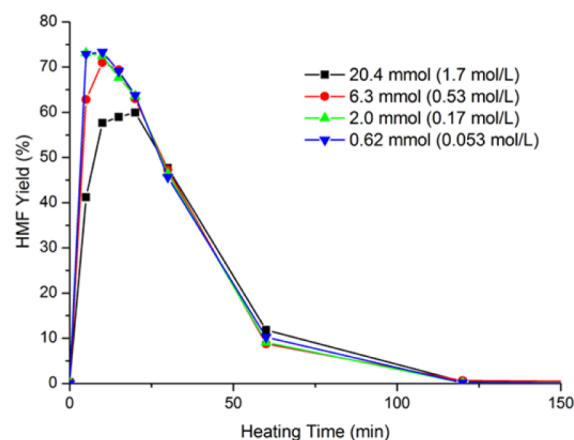


Figure 5. Fructose concentration dependence of the yield of HMF during the heating of a mixture of fructose, 1.5 mL of 5 mol/L H_2SO_4 , and 10 mL of GVL at 130 °C.

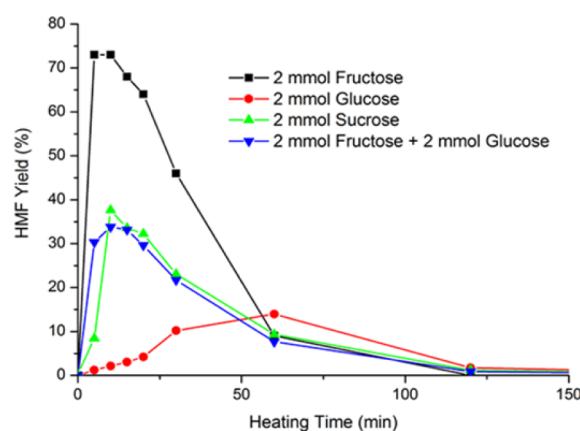


Figure 6. Yield of HMF after heating different carbohydrates in 1.5 mL 5 mol/L H_2SO_4 and 10 mL GVL at 130 °C.

glucose was 13% after 1 h, which was much lower than that from fructose (73% after a few minutes), suggesting a different reaction mechanism (vide infra).

The somewhat slower formation of HMF from sucrose suggested that its conversion went through hydrolysis of its glycosidic bond first. Indeed, sucrose or the 1:1 molar mixture of fructose and glucose gave the same maximum HMF yields under the same reaction conditions. The slower decrease in the HMF yield in the case of sucrose is presumably the result of a slower conversion of glucose compared with fructose. HMF was fully converted after 2 h in both cases. In other words, sucrose behaved similarly to the 1:1 mixture of fructose and glucose under the same reaction condition.

Hydration of HMF to LA and FA in GVL. The dependence of the conversion of HMF on the acid concentration was investigated with HMF as the starting materials (Figure 7). Three equivalents of water was also added to simulate the reaction mixture from monosaccharides. The HMF conversion to LA and FA became faster and faster as the concentration of sulfuric acid was increased. In addition, the reaction mixture rapidly turned to black at the beginning of the reaction due to the formation of humins. We estimated that ~20% of HMF was converted to humins because the yield of LA remained practically constant once all HMF was converted.

Conversion of Fructose to LA and FA in GVL. The one-pot conversion of monomers, oligomers, and polymers of C_6 -

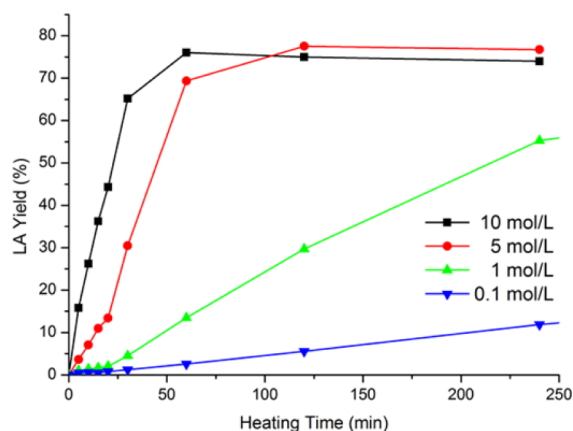


Figure 7. Hydration of HMF at different acid concentrations during the heating of 2.0 mmol of HMF, 1.5 mL of H₂SO₄, 6.0 mmol of distilled H₂O, and 10 mL of distilled GVL at 130 °C. The concentration of added sulfuric acid is shown in the legend.

carbohydrates to LA and FA in GVL would significantly simplify the overall process.^{6d,24} The steady-state concentration of HMF would also be expected to be lower when converting polysaccharides, leading to less humins from HMF; therefore, the overall selectivity to LA and FA could be higher.

It is well-known that the hydration of HMF to LA is acid catalyzed and that the higher the acid concentrations, the faster the reaction,^{22c} with which our data is consistent (Figure 8). After the maximum LA yield was reached, it did not decrease, indicating the high stability of LA under the reaction conditions. When the concentration of H₂SO₄ was as low as 0.01 mol/L, the reaction was very slow and stalled after 8 h. The LA yield was only 10% (0.2 mmol) after 32 h. The best yield of LA from fructose was 70% (1.4 mmol), obtained with the addition of 5 mol/L H₂SO₄ after 2 h of reaction time.

The corresponding yield of FA was practically the same as that of LA below 5 mol/L H₂SO₄ concentrations. In the presence of high concentrations of acids, formic acid will decompose.³⁰ Indeed, our studies showed that in the presence of 10 mol/L H₂SO₄ at 130 °C, more than half of the FA decomposed after 8 h of heating. The slightly higher yield of FA compared to LA was observed in many cases. Heating ¹³C-labeled fructose or glucose resulted in ¹³C-FA with extra nonlabeled FA in small amount, which showed that the decomposition of humins or even a carbohydrate itself will also produce formic acid.

Although an increase in the reaction temperature resulted in faster formation of LA, its final yield was the same at 100, 130, and 160 °C after 16, 2, and 0.5 h, respectively (Figure 9), indicating that the side reactions are not sensitive to temperature changes.

The initial fructose concentration showed no effect on the yields of LA below 0.17 mol/L (Figure 10). At higher fructose concentrations, the yields of LA decreased because of the side reactions involving fructose and HMF (e.g., formation of difructose anhydrides and humins, etc.).

Conversion of Glucose, Fructose, and Sucrose to LA and FA in GVL. The one-pot conversion of glucose, fructose, sucrose, and the 1:1 mixture of fructose and glucose to LA and FA using GVL as the solvent was investigated under the same conditions (Figure 11). After heating glucose at 130 °C for 4 h, the yields of LA and FA were 51% and 56%, respectively. These yields were ~20% lower than from fructose. The maximum

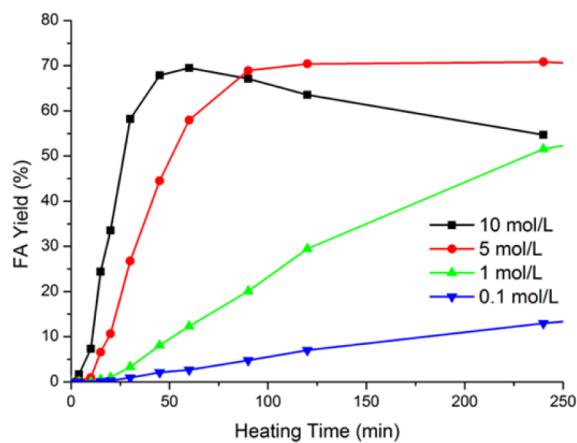
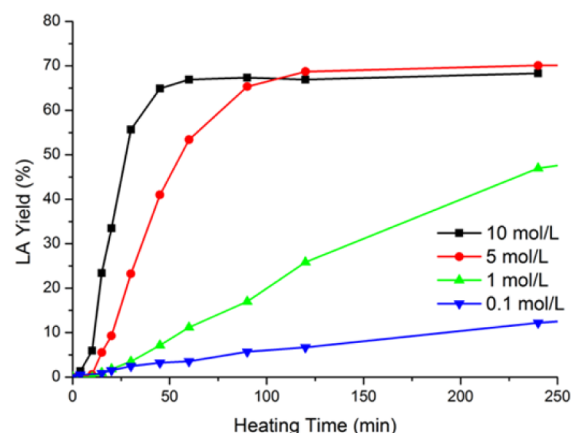


Figure 8. Acid concentration dependence of the yield of LA (top) and FA (bottom) during the heating of 2.0 mmol of fructose, 1.5 mL of H₂SO₄, and 10 mL of GVL at 130 °C. The concentration of sulfuric acid added is shown in the legend.

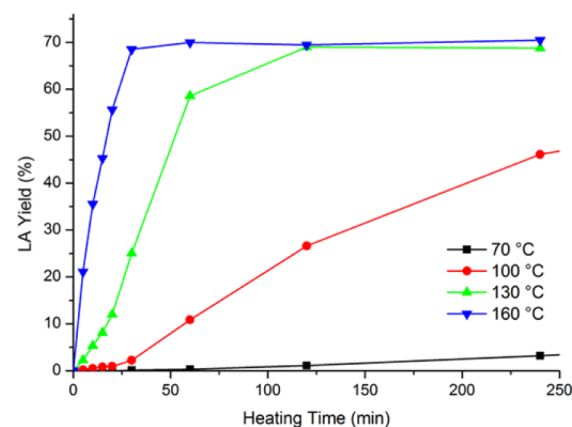


Figure 9. Temperature dependence of the yield of LA during the heating of 2.0 mmol of fructose, 1.5 mL of 5 mol/L H₂SO₄, and 10 mL of GVL at 130 °C.

yields from sucrose reached 52% LA and 57% FA, which were similar to those from the 1:1 mixture of fructose and glucose (53% LA and 58% FA). The latter results show that the acid catalyzed hydrolysis of the glycosidic bond in sucrose is fast and “sucrose” behaves as the 1:1 mixture of fructose and glucose.

Mechanistic Studies of the Conversion of Fructose and Glucose in GVL. The mechanism of the acid-catalyzed dehydration of fructose has been previously studied in

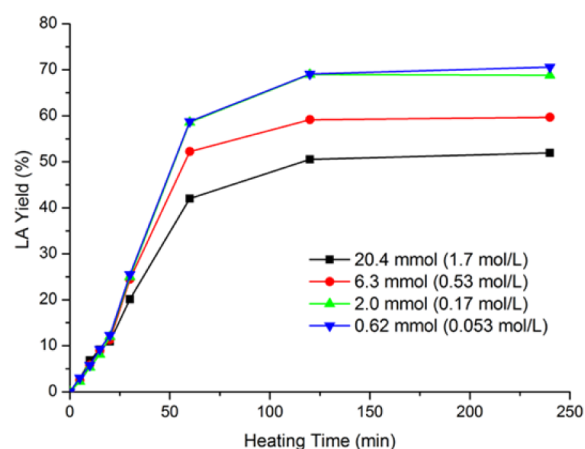


Figure 10. Initial fructose concentration dependence of the yield of LA during the heating of 2.0 mmol of fructose, 1.5 mL of H₂SO₄, and 10 mL of GVL at 130 °C.

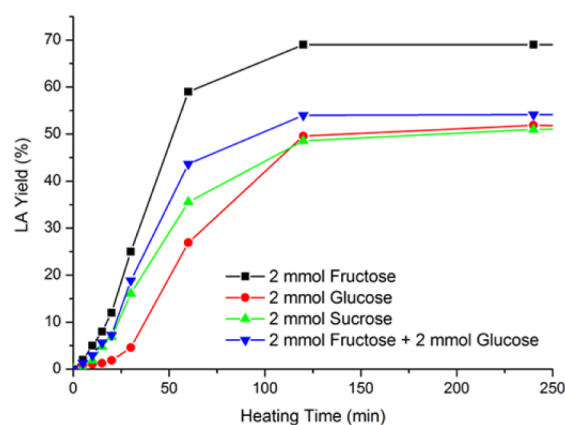
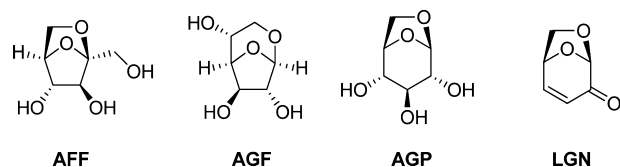


Figure 11. Comparisons of the yield of LA in GVL from fructose, glucose, and sucrose as starting materials with 1.5 mL of 5 mol/L H₂SO₄ in 10 mL of GVL at 130 °C.

DMSO,^{21k} with the reaction paths via the two fructofuranose isomers being established by observing the transient formation of intermediates. The role of another species, the 2,6-anhydro- β -D-fructofuranose (AFF) (Scheme 5) was established: reversibly connecting the fructofuranose path leading to HMF and the fructopyranose path leading to side products.^{21k}

Scheme 5. Structures of 2,6-Anhydro- β -D-fructofuranose (AFF), 1,6-Anhydro- β -D-glucopyranose (AGF), 1,6-Anhydro- β -D-glucopyranose (AGP), and Levoglucosenone (LGN)



We have now investigated the mechanism of the dehydration of fructose and glucose in GVL in the presence of sulfuric acid by NMR spectroscopy. First, 0.1 mmol 2-¹³C-fructose and 1 or 5 mol/L of H₂SO₄ were mixed with 0.5 mL GVL. After the tautomerization reached equilibrium within 2 h at room temperature, only the four cyclic isomers of fructose could be identified, and the noncyclic isomer (either in the form of a

ketose or a hydrate) was below the detection limit. After 1 min of heating at 130 °C, AFF was detected in small quantities only in the case of 1 mol/L H₂SO₄ and reached a maximum (~0.6%) after 15 min; it completely disappeared in 30 min simultaneously with the cyclic isomers, indicating full conversion of fructose. This suggests that AFF was in equilibrium with the cyclic isomers and, interestingly, also demonstrated its relatively high stability, even in the acidic reaction media containing substantial amounts of water. The highest HMF yield was 0.072 mmol (72%) in the presence of 1 mol/L H₂SO₄ (overall 0.13 mol/L) at 15 min, after which the HMF was converted to LA (0.071 mmol, 71%) within 960 min. When the concentration of the added H₂SO₄ was increased to 5 mol/L (overall 0.64 mol/L), the maximum amount of HMF (68%) was reached after 1 min, and it was converted to LA (64%) in about an hour. These results suggest that the mechanism^{21k} confirmed for fructose in DMSO is also operational in GVL in the presence of aqueous sulfuric acid.

A similar experiment was performed using 0.1 mmol 2-¹³C-glucose with the addition of 5 mol/L H₂SO₄ at 130 °C, with a maximum yield of 0.013 mmol HMF (13%) being achieved after 20 min (Figure 12). The HMF disappeared after 2 h to

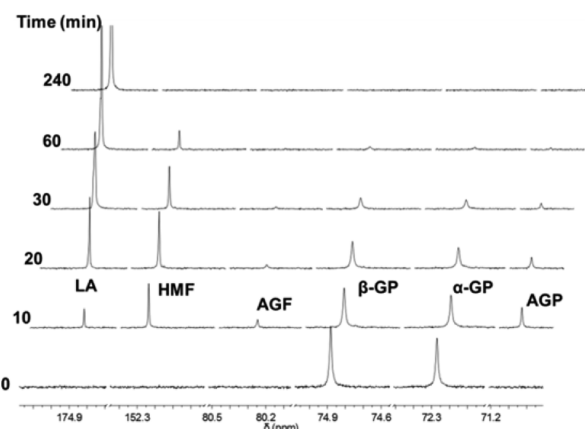


Figure 12. Conversion of 18.0 mg (0.1 mmol) 2-¹³C-glucose in 0.075 mL of 5 mol/L H₂SO₄ and 0.5 mL of GVL at 130 °C.

yield 0.052 mmol of LA (52%) and 0.050 mmol of FA (50%). It should be noted that glucose has a lower solubility in GVL than fructose at room temperature. On the basis of quantitative ¹³C NMR, 40% of the glucose was dissolved at room temperature, and only the α - and β -D-glucopyranoses (α -GP and β -GP) were observable.

After 1 min of heating at 130 °C, 1,6-anhydro- β -D-glucopyranose, (AGF),^{31,32} and 1,6-anhydro- β -D-glucopyranose (AGP)³³ (Scheme 5) were observable; their maximum yields were 3% and 10%, respectively. After 2 min, a very small amount (<0.07%) of levoglucosenone (LGN) was also detected, which is one of the typical decomposition products of AGP.³⁴ The concentration of the anhydroglucose remained the same after 10 min heating while the concentration of the two glucopyranose isomers approximately halved. The complete disappearance of AGF and AGP was also accompanied by the complete disappearance of glucose. Similar experiments with AGP as the starting material showed that both α -GP and β -GP were generated immediately after heating. This suggests that AGF and AGP were in equilibrium with glucose. Moreover, the formation of AGF and AGP as “side-equilibria” analogous to the formation of AFF from fructose is

also possibly the case, which also explains why glucofuranoses are not favored glucose isomers but AGF is still relatively abundant in solution in comparison to AGP. The dehydration of AGP in liquid phase has not been well studied; however, it has been suggested that the hydration of AGP to glucose is the first step in the reactions leading to HMF.^{34,35} However, the presence of AGF and AGP suggests that the conversion of glucose to HMF may also proceed through AGF and AGP.³⁶ We have also confirmed that LGN can be converted to HMF with added 5 mol/L H₂SO₄ at 130 °C in up to 65% yield in only 4 min and reaching almost 80% LA and FA by further heating. The numerous pathways available for acid-catalyzed conversion of glucose to HMF makes determining which pathways are the most dominant challenging, and this will be the subject of a future publication.³⁷

CONCLUSIONS

The conversion of fructose, glucose, and sucrose to HMF or LA/FA using sulfuric acid as the catalyst and GVL as a green solvent was investigated in detail. The H₂SO₄/GVL/H₂O system can be tuned to produce either HMF or LA/FA by changing the acid concentration. The overall performance of GVL was similar to DMSO, THF, acetonitrile, and acetone. Although the best yields for HMF were around 75%, the LA/FA yields ranged from 50% to 70%, depending on the structures of the carbohydrates and reaction parameters, including temperature, acid, and carbohydrate concentration. While the conversion of fructose was much faster and gave higher yields than glucose, sucrose behaved like the 1:1 mixture of fructose and glucose, as expected. The mechanism of the conversion of glucose to HMF or LA/FA in GVL involves three intermediates: 1,6-anhydro- β -D-glucopyranose, 1,6-anhydro- β -D-glucopyranose, and levoglucosenone.

ASSOCIATED CONTENT

Supporting Information

The yields of HMF and/or LA/FA at different reaction conditions are reported. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was funded by the City University of Hong Kong, Project No. 9380047.

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