

Sustainable Solvent Systems for Use in Tandem Carbohydrate Dehydration Hydrogenation

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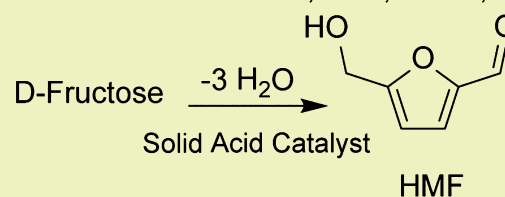
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S Supporting Information

ABSTRACT: Monophasic separation-friendly solvent systems were investigated for the sustainable acid-catalyzed dehydration of fructose to 5-hydroxymethylfurfural (HMF). The HMF selectivity depends on both fructose conversion, temperature, and the amount of cosolvent present in the aqueous solvent mixture. Use of HMF-derived 2,5-(dihydroxymethyl)-tetrahydrofuran (DHMTHF) or low-boiling tetrahydrofuran (THF) as co-solvents results in increased selectivity (>70%) to HMF at fructose conversions of ca. 80%. Analysis of the fructose tautomer distribution in each solvent system by ¹³C NMR revealed higher furanose fractions in the presence of these and other protic (tetrahydrofurfuryl alcohol) and polar aprotic co-solvents (DMSO) relative to water alone. Formation of fructosides and/or difructose anhydrides in the presence of the co-solvents causes lower selectivity at early reaction times, but reversion to fructose and dehydration to HMF at longer reaction times results in increasing HMF selectivity with fructose conversion. In 9:1 DHMTHF:water, a 7.5-fold increase in the initial rate of HMF production was observed relative to water alone. This mixed solvent system is proposed for use in a tandem catalytic approach to continuous DHMTHF production from fructose, namely, acid-catalyzed dehydration of fructose to HMF, followed by its catalytic hydrogenation to DHMTHF.

KEYWORDS: Sustainable solvents, Biomass, Fructose, 5-Hydroxymethylfurfural, ¹³C NMR spectroscopy, Tandem catalysis

Phase Modifiers: DHMTHF, THF, THFA, DMSO



Conversion > 80%

Selectivity > 70%

INTRODUCTION

Concerns regarding the depletion of fossil fuels and their negative environmental impact are driving a search for methods to efficiently utilize renewable carbon resources, such as biomass, in the production of chemicals and fuels. The United States alone produces 1.3 billion dry tons of cellulosic biomass annually, which could potentially replace as much as half of the transportation fuels we consume.^{1,2} The development of a sustainable large-scale chemical processing of biomass is critical to its efficient utilization. In addition to the feedstock, the other components (e.g., reaction solvent) within the system must be renewable and energy efficient (e.g., low boiling point) for an economical and environmentally sustainable process.

5-Hydroxymethylfurfural (HMF) is a platform chemical that can be derived from carbohydrates for the production of petrochemical alternatives such as biofuels and high value chemicals.^{3–6} Biomass-derived HMF is most commonly obtained by the dehydration of fructose. The overall efficiency of HMF production is hindered by multiple side reactions, including rehydration of HMF to levulinic and formic acid, and condensation of HMF and fructose to form polymeric humins.^{3,6,7} Some solvents are effective in suppressing these undesired reactions. For example, polar aprotic solvents such as

DMSO cause both an increase in the rate of HMF production and the selectivity to HMF. However, separating HMF from DMSO is energy intensive due to its high-boiling point, and consequentially, the overall efficiency and economics of the process decreases.^{3,4,8,9} The use of a Brønsted acid catalyst with DMSO as the solvent results in high selectivities and yields of HMF from fructose, making the intrinsic comparison of different acid catalysts in DMSO difficult as most catalysts demonstrate high yields at similar conditions. High yields of HMF from biomass have also been reported using ionic liquids as solvents,^{10,11} although the subsequent separation is also complex. Thus, there is a need for sustainable solvent systems that enable a high HMF selectivity at high conversion required for its large-scale production, while facilitating product separation to minimize energy use.¹²

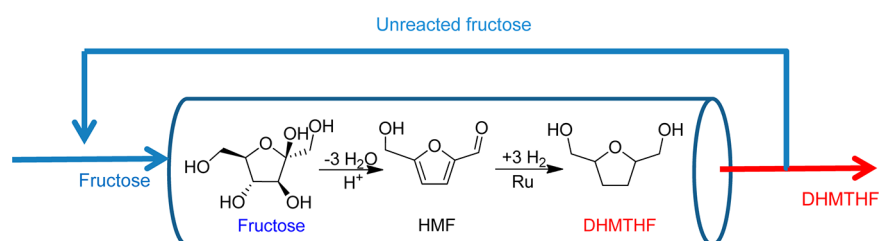
We have previously reported on the use of biphasic systems, consisting of a reactive aqueous phase and an extracting organic phase, to produce HMF from fructose by protecting the HMF from further degradation, thereby increasing the overall yield.

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Scheme 1. Proposed Tandem Catalytic Sequence in Which Fructose Is First Dehydrated to HMF, and Then HMF Is Hydrogenated to DHMTHF^a



^a A certain amount of DHMTHF is recovered as product, while the remainder is recycled to serve as the co-solvent in the dehydration reaction.

The partitioning of HMF into the organic layer was promoted by the addition of NaCl, resulting in high HMF yields (80–90%) in a separation-friendly solvent such as 1-butanol.⁴ However, NaCl in combination with the mineral acid catalyst (HCl) is corrosive, and the presence of NaCl precludes the use of solid acid catalysts due to ion-exchange (which generates mineral acids in situ).

In the present paper, we explore various single-phase solvent systems, including 2,5-(dihydroxymethyl)tetrahydrofuran, (DHMTHF, the product of complete HMF hydrogenation), for their use in acid-catalyzed fructose dehydration to HMF. Scheme 1 shows a sustainable continuous process for the conversion of fructose to DHMTHF, using DHMTHF as a co-solvent with water to increase the overall efficiency of carbohydrate conversion to high value products. In the first step, fructose is dehydrated to HMF in the presence of DHMTHF, using a solid acid catalyst. In the second step, HMF is hydrogenated to DHMTHF over a metal catalyst. Both reactions have been investigated using heterogeneous catalysts in single-phase solvent systems under similar conditions. In this respect, we reported previously an acid-functionalized SBA-15-type periodic mesoporous organosilicas that can be used in conjunction with a single-phase solvent system in the production of HMF from fructose.¹³ We also reported high yields (above 90%) in the production of DHMTHF from HMF using 1 wt % Ru dispersed on a support with a high isoelectric point (e.g., ceria or magnesia-zirconia) under conditions similar to those used in the dehydration reaction.¹⁴ Scheme 1 shows that a fraction of the reactor effluent can be recycled as solvent to convert unreacted fructose and to take advantage of the promoting effect of DHMTHF on fructose dehydration. This tandem reaction system shows how linking two reactions can result in a more efficient and sustainable process.

In the present paper, we have also studied tetrahydrofurfuryl alcohol (THFA), ethanol, tetrahydrofuran (THF), and DMSO as phase modifiers in the exploration of sustainable single solvent systems for fructose dehydration. These co-solvents were chosen as examples of alcoholic or aprotic solvents to explore the nature and importance of side reactions between fructose and the solvent. In addition, THF may be of practical importance due to its low boiling point, allowing for efficient separation from HMF and/or DHMTHF. Fructose tautomer distributions were evaluated in each solvent system using ¹³C NMR, to shed light on the observed trends in HMF selectivity.

EXPERIMENTAL METHODS

Reaction Studies. Fructose dehydration experiments were carried out in thick-walled glass batch reactors (10 mL, Alltech). Dimethylsulfoxide (DMSO, Sigma) tetrahydrofuran (THF, Fisher), tetrahydrofurfural alcohol (THFA, Aldrich), ethanol (Aldrich), and

DFA III (Wako Chemicals) were used as received. Except where specified, the catalyst was crushed Amberlyst 70 (A-70, The DOW Chemical Company), a phenylsulfonic acid-derivatized polystyrene resin containing 2.55 mmol H⁺/g. It was washed with Milli-Q water, dried overnight at 393 K, and crushed before use. Decreasing the particle size of a resin increases the rate of HMF production by increasing the rate of water removal by improving the rates of mass transfer and product desorption.¹⁵ Each reactor was loaded with the catalyst (50 mg) and 1.5 g aqueous fructose (2 wt %) along with a triangular magnetic stirring bar. The reactors were then sealed using Teflon liners (Alltech) inserted into the plastic caps. The reactions were initiated by inserting the reactors into a 16-well oil-filled aluminum block. The temperature in the block was maintained at 403 K using a Fisher Scientific Isotemp digital stirring hot plate equipped with a temperature probe. The contents of each reactor were stirred at 500 rpm, and after reaction, they were cooled in a slurry of dry ice and ethylene glycol.

Batch reactions were carried out in water modified with various amounts of co-solvent at 403 K under autonomous pressure. Amberlyst 70 (A-70) was chosen as the catalyst because our previous work showed that its sulfonic acid sites are active for HMF production.¹⁶ Also, the catalyst was stable for at least 100 h on-stream in a packed-bed reactor at this temperature. Thus, we can focus here on solvent effects, without having to consider catalyst deactivation. For each solvent mixture, reaction times were also varied to assess selectivity at different conversions.

Fructose conversion is defined as moles fructose reacted per mole fructose fed, eq 1, where $N_{F,0}$ and $N_{F,t}$ are the number of moles fructose present before and after reaction, respectively, as determined by HPLC. HMF selectivity is defined as moles HMF produced per mole fructose reacted, eq 2.

$$\text{Conversion} = \left(\frac{N_{i,0} - N_{i,t}}{N_{i,0}} \right) \times 100\% \quad (1)$$

$$\text{Selectivity} = \left(\frac{N_{j,t}}{N_{i,0} - N_{i,t}} \right) \times 100\% \quad (2)$$

Product Analysis by HPLC. High pressure liquid chromatography (HPLC) analyses were carried out using a Waters e2695 HPLC system equipped with a 2998 UV-vis photodiode array detector and a 2414 refractive index detector. In a typical experiment, fructose and HMF were separated on an Aminex HPX-87P column (Biorad) at 358 K, using Milli-Q water as the mobile phase at a flow rate of 0.6 mL min⁻¹. HMF concentration was determined using the UV detector (320 nm), while all other species were monitored using the refractive index detector (maintained at 323 K). When ethanol was present, the fructose and ethanol peaks eluting from the Aminex HPX-87P column overlapped. In this case, fructose concentrations were measured using an Aminex HPX-87H column (Biorad) at 353 K instead, with 5 mM aqueous H₂SO₄ as the mobile phase at a flow rate of 0.6 mL min⁻¹.

Product Analysis by LC/MS. Analysis by liquid chromatography/mass spectrometry (LC/MS) was carried out using an Agilent 1200 series HPLC system connected to an Agilent 6320 ion trap MS, using atmospheric pressure chemical ionization (APCI) in the negative

mode. Two different columns were used: a Zorbax Eclipse XDB-C18 column (4.6 mm × 250 mm, 5 μm; Agilent) and an Ascentis Express HILIC column (4.6 mm × 150 mm, 2.7 μm; Agilent). The Zorbax column was operated at 303 K and a flow rate of 1.0 mL min⁻¹. The mobile phases were 0.02 M ammonium acetate (Aldrich) in Milli-Q water (A) and LC-MS grade methanol (B, Aldrich). The gradient started at 95:5 A:B, switching to and holding at 20:80 A:B after 20 min. The following instrument parameters were used for the APCI-MS analysis in the negative mode: capillary voltage, 1 kV; corona current, -15 μA; vaporization temperature, 623 K. The Ascentis column was used at 318 K with a flow rate of 0.4 mL min⁻¹. The mobile phase was an isocratic mixture of 98% acetonitrile and 2% Milli-Q water. The following instrument parameters were used for APCI-MS analysis in the negative mode: capillary voltage, 1 kV; corona current, 10 μA; vaporization temperature, 623 K.

Synthesis of DHMTHF. In a typical synthesis, 28.45 g deionized water (saturated with 1-butanol), 60 g 1-butanol (Aldrich, saturated with DI water), 1.55 g HMF (Aldrich, Kosher grade), and 0.87 g Pd/C (10 wt %, Aldrich) were added to a 300 mL Parr reactor. The Pd/C catalyst was reduced ex-situ in H₂ using a 4 h ramp and a 4 h hold at 533 K and passivated using a stream of 2% O₂ in He before it was loaded into the reactor. The reactor was purged three times with He and four times with H₂, and then charged with 400 psi H₂. It was heated to 403 K, and then held at the same temperature for 8 h. The selectivity for DHMTHF from HMF was 90% after complete HMF conversion, as determined by HPLC. The main impurity was identified as 1,2,5,6-hexanetetrol, in agreement with previous reports.¹⁴ After cooling, the reactor contents were filtered to remove humins and the solvent was removed using rotary evaporator. The tetrol was quantified to be less than 0.5 wt % in the final product using HPLC analysis.

NMR Study of D-Fructose Tautomer Distribution. Solutions of 0.10 M labeled D-fructose (2-¹³C, Cambridge Isotopes Laboratories) were prepared in the following solvent mixtures: DHMTHF:D₂O (9:1), THFA:D₂O (9:1), THF-*d*8:D₂O (4:1), EtOH:D₂O (9:1) and DMSO-*d*6: D₂O (9:1). ¹³C-labeled dimethylformamide (Cambridge Isotopes, 0.10 M) was added as an internal analytical standard. The fructose tautomer composition was analyzed by ¹³C NMR (pulse sequence: zgig30, relaxation delay: 10 s, 128 scans), within 10 h of sample preparation. Spectra were collected using a Bruker AVANCE DMX500 spectrometer equipped with a variable temperature probe. After data collection at 303 K, the probe temperature was re-equilibrated at 333 K. Each sample was heated inside the magnet for 25 min, and then the spectrum was reacquired at 333 K.

RESULTS AND DISCUSSION

DHMTHF as Co-Solvent in the Single-Phase Dehydration of Fructose. The selectivity for the conversion of fructose to HMF in water as a solvent decreases monotonically with increasing conversion (Figure 1). This behavior indicates that HMF degradation reactions, for example, to form humins and formic acid, take place in series with fructose dehydration. Addition of DHMTHF as a co-solvent in an equal weight amount with water resulted in the same trend. Importantly, however, the HMF selectivity increased by 20–30% at all conversions. In contrast, a 3:1 (by weight) mixture of DHMTHF:water showed a maximum in selectivity at intermediate conversion. The maximum was displaced to higher conversion when the DHMTHF:water ratio was increased further, to 9:1.

At the highest concentration of DHMTHF, we observed formation of a glycoside (carbohydrate-acetals or ketals) using LC/MS (Supporting Information). A reversible glycosidic bond is formed between the anomeric carbon of fructose and the alcohol solvent to yield the glycoside, DHMTHF-fructoside (Scheme 2, where R = DHMTHF). At short reaction times, some fructose is converted rapidly to fructosides, leading to the low observed HMF selectivity at low fructose conversions.

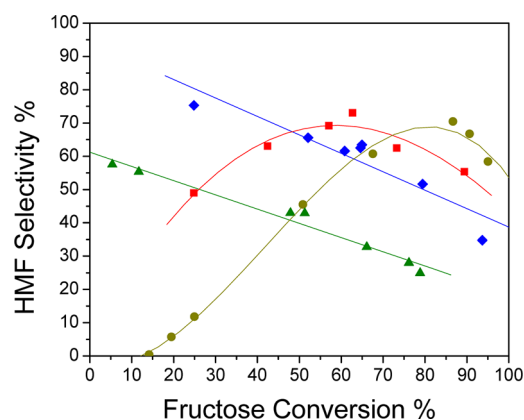
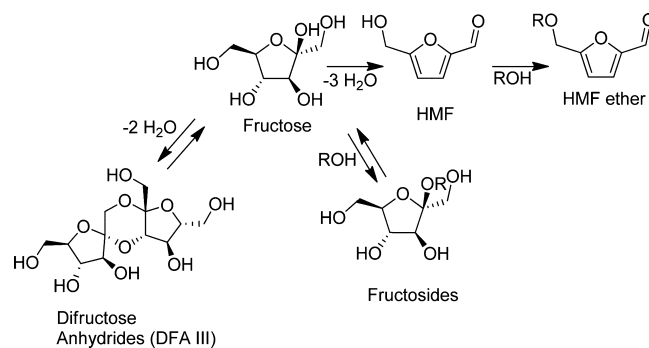


Figure 1. HMF selectivity as a function of fructose conversion in monophasic dehydration experiments with Amberlyst 70 as the catalyst in a mixed solvent consisting of DHMTHF:water in molar ratios of 0:1 (triangles), 1:1 (diamonds), 3:1 (squares), and 9:1 (circles).

Scheme 2. Reaction Pathways Observed for the Dehydration of Fructose in Alcohol and Non-Alcohol Solvents



However, these fructosides hydrolyze back to fructose as the reaction proceeds, accounting for the increased selectivity with conversion. At high conversion in 9:1 DHMTHF:water, the selectivity begins to decrease due to formation of the HMF-DHMTHF ether (Scheme 2), which was also observed by LC/MS (Supporting Information). When 0.1 M HCl was used as a homogeneous acid catalyst instead of Amberlyst 70, a high HMF selectivity (64%) was also observed at high fructose conversion (99%) in 9:1 DHMTHF:water. For comparison, the HMF selectivity in water was only 36% at 86% fructose conversion.

In addition to enhancing the selectivity to HMF, using DHMTHF as a co-solvent enhances the initial rate of HMF formation (Figure 2 and Table 1). Higher rates at lower water concentrations have been previously reported, and a variety of explanations have been proposed. For example, higher HMF production rates in DMSO compared to water have been attributed to (i) the effect of water on the position of the equilibrium for reversible removal of the first water molecule (assumed to be the rate-determining step) and/or (ii) formation of a fructosyl cation intermediate that reverts back to fructose by reaction with water.¹⁷ The lower rate in water was also suggested to be caused by solvation of the proton catalyst.^{3,18} Another possibility for the effect of water involves the fructose tautomer equilibrium (Figure 3), which shifts toward the furanose forms in nonaqueous solvents.^{19,20} It has been suggested that this shift is responsible for higher rates of

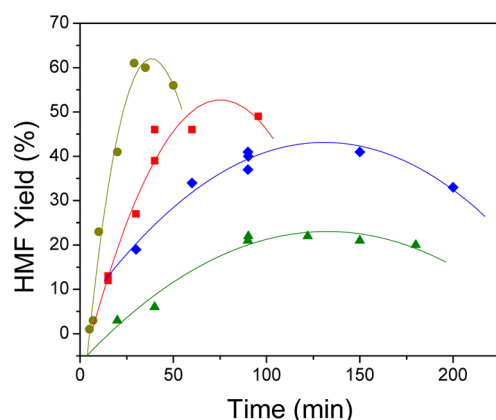


Figure 2. Solvent effects on the time-dependent yield of HMF by dehydration of fructose using an Amberlyst 70 catalyst in DHMTHF:water ratios with molar ratios of: 0:1 (triangles), 1:1 (diamonds), 3:1 (squares), and 9:1 (circles).

Table 1. Initial Rates of HMF Production in DHMTHF:H₂O

| solvent ratio | initial TOF (h ⁻¹) |
|---------------|--------------------------------|
| 9:1 | 1.5 |
| 3:1 | 0.67 |
| 1:1 | 0.42 |
| 0:1 | 0.22 |

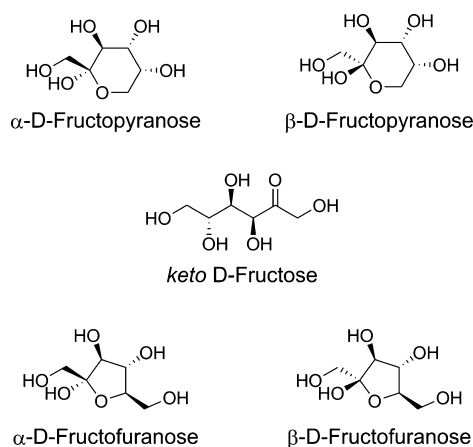


Figure 3. Structures of the various fructose tautomers in solution.

HMF formation in DMSO compared to water because the fructo–furanose tautomers are proposed to be intermediates in the reaction pathway to HMF from fructose.⁹ Finally, a quantum mechanics/molecular mechanics study of a closed-ring mechanism for the acid-catalyzed dehydration of fructose predicted an increase in rate with decreasing water concentration. In particular, the authors showed that one of the proton transfer steps in the overall mechanism was inhibited by high concentrations of water.²¹ Accordingly, the single-phase co-solvents used in the present study could displace excessive water and thus lead to increased rates of HMF formation.

Fructose dehydration is first-order with respect to fructose concentration.⁶ The rate of fructose tautomerization in 9:1 ethanol:water was estimated to be 250 times faster than the rate of fructose dehydration in 9:1 DHMTHF:water, and it is estimated that the various fructose tautomers are quasi-equilibrated at 403 K.²² A first-order rate constant can be estimated for a particular solvent system using the measured

rate constant in water if the tautomer distribution in the solvent system of interest is known by assuming that the dehydration rate is proportional to the fructo–furanose fraction. The fraction of fructose present in the furanose form in water at 333 K is 40% (Table S2, Supporting Information). However, this underestimates the value at the reaction temperature of 403 K because the fraction of fructose in the furanose form increases with temperature.²³ The first-order rate constant for dehydration of the furanose tautomer in water is therefore ca. 0.45 h⁻¹ based on the TOF for fructose dehydration in water (Table 1) and an estimated furanose fraction of 50%. Next, the initial concentrations of fructo–furanose in the 1:1, 3:1, and 9:1 DHMTHF:water solvent systems were estimated to be 0.094, 0.15, and 0.34 mol L⁻¹, respectively, based on their observed first order rate constants (0.45 h⁻¹) and their respective TOF (Table 1). The acid loading of the catalyst in these systems was 2.55 mmol H⁺/g. However, the latter two concentration values estimated exceed by far the total concentration of fructose in these solvent mixtures (0.125 and 0.130 mol L⁻¹, respectively). Therefore, the increased rate with decreasing water concentration is not caused solely by shifts in tautomer equilibria, although this effect is a contributing factor, as discussed below.

Fructose Dehydration with Other Co-Solvents. To further explore the effect of solvent on the fructose dehydration rate, ethanol and tetrahydrofurfuryl alcohol (THFA) were also studied as co-solvents with water. Using A70 as the catalyst, trends similar to those observed for DHMTHF:H₂O were found for both of these alcohol co-solvents: selectivity initially increased, and then decreased with conversion, although the trends were less pronounced with ethanol and THFA (Figure 4). As with DHMTHF, the corresponding fructosides and

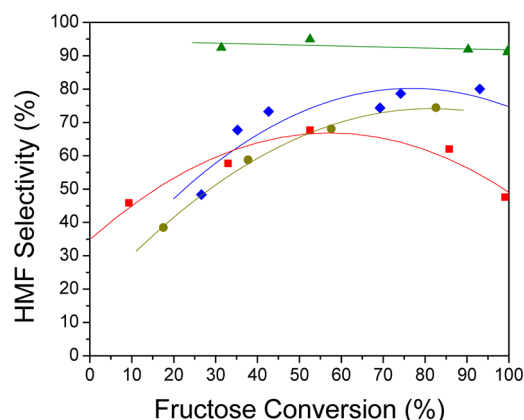


Figure 4. Comparison of HMF selectivity as a function of fructose conversion for over an Amberlyst 70 catalyst in mixed solvents consisting of 9:1 DMSO:water (triangles), 4:1 THF:water (diamonds), 9:1 ethanol:water (squares), and 9:1 THFA:water (circles).

HMF–solvent ethers were observed by LC/MS (Supporting Information). In addition, difructose anhydrides (DFAs) were observed. The same reactivity trends were observed when A70 was replaced by a homogeneous catalyst, 0.1 M HCl.

In 9:1 THFA:water, high selectivity (78%) to HMF was achieved at high fructose conversion (95%) when the feed concentration was 2 wt %. The trend of increasing selectivity with conversion was also observed with a 10 wt % fructose feed (Figure 5). However, at the higher fructose concentration, HMF selectivity was consistently lower, and rehydration of HMF to levulinic acid and formic acid was observed as well as

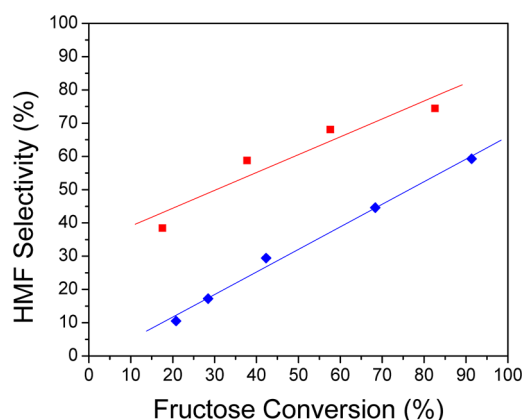


Figure 5. Comparison of HMF selectivity as a function of fructose conversion over an Amberlyst 70 catalyst in 9:1 THFA:water for fructose feeds at 2 wt % (squares) and 10 wt % (diamonds).

formation of humins. Previous reports have suggested that these humins are derived mainly from HMF rather than from either levulinic or formic acid. This expectation is consistent with the large decrease in HMF selectivity at the higher fructose concentration. It has also been suggested that 2,5-dioxo-6-hydroxyhexanal, a proposed intermediate in the mechanism of HMF formation, plays an important role in humin formation via aldol addition/condensation with HMF.²⁴

Difructose anhydrides (DFAs, an example of which is shown in Scheme 2) are formed by loss of two water molecules in a reaction analogous to the formation of fructosides (in which a fructose molecule forms a glycosidic bond by reacting with a hydroxyl group of another fructose molecule). A variety of DFAs can be formed because of the many tautomers of fructose and the variety of hydroxyl groups that can react.^{3,25} To establish the importance of these side reactions, fructose dehydration was studied in two polar aprotic co-solvents: DMSO and THF. Their lack of hydroxyl groups limits the number of possible side reactions, resulting in higher selectivity for HMF (as reported previously for DMSO).²⁶ This behavior is confirmed by the results in Figure 4. The HMF selectivity does not change significantly with conversion in 9:1 DMSO:water. The stability of HMF in this solvent mixture is confirmed by the high selectivity even when fructose had been completely converted. For THF:water, a 4:1 ratio was used because 9:1 THF:water undergoes phase separation in the presence of 2 wt % fructose. In 4:1 THF:water, high selectivity to HMF was also observed, and a slight increase in selectivity with increasing conversion was observed. This trend for THF can be explained by the formation of DFAs, which was observed in the reaction mixture by LC/MS.

To explore whether DFA formation is reversible, a 2 wt % solution of DFA III was heated at 403 K in 4:1 THF:water using the same catalysts in previous reactions. After 35 min, all of the DFA had been converted. The major products were HMF (78%) and fructose (7%). The presence of fructose indicates that its dimerization to DFA III is reversible. The high HMF yield suggests that the DFA has a positive effect on selectivity. This phenomenon has been observed previously, and it was proposed that DFA formation protects the reactive anomeric hydroxyl groups from polymerization.³

Solvent Effects on D-Fructose Tautomer Distribution.

In solution, fructose adopts five structural conformations: α -pyranose, β -pyranose, α -furanose, β -furanose, and a keto form,

as shown in Figure 3.²⁷ The relative amounts of each tautomer depend on both solvent and temperature. In fructose dehydration, the tautomer distribution can have a significant effect on product selectivity. Because HMF is derived from the α -furanose and β -furanose tautomers, increasing their concentrations through solvent effects leads to higher HMF yields by minimizing side reactions with water. In water at 303 K, ca. 30% of fructose exists in these furanose forms, while in DMSO, the corresponding fraction is increased to 53%. At 333 K, the furanose fractions increase to ca. 40% and 70% in water and DMSO, respectively.

At 80% fructose conversion in water, we observed an HMF selectivity of ca. 30%. However, in neat DMSO, near-quantitative yields (>90%) have been reported.^{3,5,28,29} Although the lower HMF selectivity in water relative to DMSO is not solely due to the lower concentration of the furanose tautomers, it is a factor. The effect of various co-solvents on the fructose tautomer distributions was assessed by analyzing the ¹³C NMR spectra of isotopically labeled fructose (¹³C₂).³⁰

Like DMSO, DHMTHF alters the relative amounts of the various fructose tautomers in favor of the furanose forms. At 303 K in 9:1 DHMTHF:D₂O, 38% of the fructose exists in the furanose form. At 333 K, the furanose concentration increases further to 48%. At both temperatures, these values represent a 10% increase in the α,β -furanose fraction for the mixed solvent relative to water alone. The higher concentrations of the α,β -furanoses contribute to the observed higher HMF selectivities in fructose dehydration.

The effects of THFA, THF, EtOH, and DMSO as co-solvents (mixed either 5:1 or 4:1 with D₂O) on fructose tautomer distributions are similar to those found for neat DMSO and DHMTHF. Interestingly, the tautomer distributions in 9:1 DMSO:D₂O rapidly attained the values reported for fructose at equilibrium in pure DMSO, despite published reports that several weeks are required.³¹ At 303 K, the furanose tautomers represent 52%, 51%, 40%, 38%, 33%, and 29% of the total fructose concentrations in DMSO, THFA, DHMTHF, THF, and water, respectively (Figure 6 and Table S2, Supporting Information). Upon increasing the temperature to 333 K, the fractions increased further in favor of the furanose tautomers (Figure 6). We observed a nearly 20% increase in the furanose concentrations in both aprotic solvents (THF and DMSO) at 333 K, while the protic solvents (with the exception of 9:1 EtOH:D₂O) showed an increase of ca. 10%. Similar to a

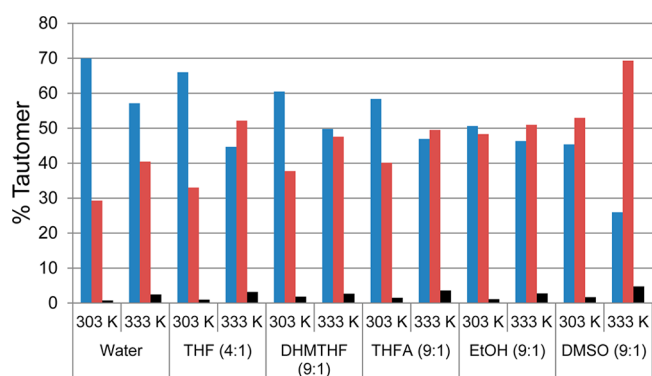


Figure 6. Tautomer distributions for D-fructose in various solvents at 303 K and 333 K. Values for the α and β forms of the pyranose (blue) and furanose (red) tautomers have been combined. Keto is shown in black.

previous report,³² we observed that the tautomer distribution in EtOH remains roughly constant despite the increase in temperature. For a variety of EtOD:D₂O ratios and temperatures, the pyranose and furanose concentrations remain approximately constant.

CONCLUSION

The use of DHMTHF as a co-solvent has a beneficial effect on both the rate of fructose dehydration and on the selectivity to HMF over a heterogeneous catalyst (Amberlyst 70) compared to water alone. Fructose tautomerization favors the furanose form in the mixed solvent relative to water alone, explaining at least part of the rate enhancement. The HMF selectivity depends on both the fructose conversion and the amount of DHMTHF present. With high levels of the co-solvent in water (e.g., ratios of 3:1 and 9:1), the HMF selectivity increases with fructose conversion. Thus, a tandem approach may be feasible in the production of DHMTHF based on the use of an inexpensive, easily separable, non-corrosive solvent system. Other alcoholic co-solvents, including ethanol and THFA, showed similar, but less pronounced, selectivity enhancements.

The use of polar aprotic THF as the co-solvent also leads to the selective production of HMF. Because of its high volatility, this solvent facilitates isolation of HMF by simple evaporation, which is an advantage relative to high-boiling DMSO. Side reactions involving the anomeric hydroxyl groups of fructose give rise to fructosides and difructose anhydrides in alcoholic and aprotic solvents, respectively. However, their formation is reversible, and high yields of HMF can be obtained at high fructose conversions.

ASSOCIATED CONTENT

Supporting Information

Details of fructose dehydration experiments in various solvent systems, quantitative tautomer distributions, and LC/MS fragmentation patterns used to identify intermediates. 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.

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