

UNIVERSITY OF CALIFORNIA  
RIVERSIDE

Understanding and Enhancing the Catalytic Production of 5-Hydroxymethylfurfural from  
Fructose in Aqueous Cosolvent Systems

A Dissertation submitted in partial satisfaction  
of the requirements for the degree of

Doctor of Philosophy

in

Chemical and Environmental Engineering

by

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December 2018

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The Dissertation of Glen Steven Svenningsen is approved:

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## ACKNOWLEDGEMENTS

I express my gratitude to the Department of Chemical and Environmental Engineering in Bourns College of Engineering at the University of California Riverside for giving me the opportunity to carry out graduate study towards a Doctor of Philosophy in Chemical and Environmental Engineering.

I am grateful for funding from the USDA through Agriculture and Food Research Initiative Competitive Grant-2015-67022-22843. The authors acknowledge Dan Borhardt for assistance with the Avance 600 performed at the Nuclear Magnetic Resonance Facility at UC Riverside.

I'm indebted to my advisers Prof. Phillip Christopher & Prof. Charles E. Wyman for making me part of their biofuel research team, support, patience, and caregiving over the past four and a half years. Their teachings and valuable guidance have helped me to perform research in the fields of catalysis and biofuels. I want to give a sincerely grateful acknowledgement to Dr. Rajeev Kumar who was the main reason for the funding of this project and collaboration; moreover, his suggestions, guidance, and support over the years has been an amazing resource.

I would like to acknowledge Prof. Charles E. Wyman's research team: Abhishek Patri, Ninad Kothari, Christian Alcaraz, Priyanka Singh, Priyanka Sengupta, Charles Cai, May Ling Lu, Rachna Dhir. Additionally, I would like to thank Prof. Phillip Christopher's research team: Leo Derita, Matt Kale, John Matsubu, and Talin Avanesian. Additionally, I would like to thank my friends Peter Bryley and Pedro Piqueras.

## ABSTRACT OF THE DISSERTATION

Understanding and Enhancing the Catalytic Production of 5-Hydroxymethylfurfural from Fructose in Aqueous Cosolvent Systems

by

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Doctor of Philosophy, Graduate Program in Chemical and Environmental Engineering  
University of California, Riverside, December 2018  
Dr. Phillip Christopher, Chairperson

US interest in biomass as an alternative energy source continues to increase in demand with growing political, economic and environment concerns with fossil fuels. One potential route for converting cellulosic biomass to fuels is through the dehydration of fructose to produce 5-hydroxymethylfurfural (HMF), followed by the catalytic conversion of HMF to renewable fuels, such as dimethylfuran (DMF). Economically viable production of HMF from fructose requires high yields. The formation of HMF has been thought to occur through the acid-catalyzed dehydration of the furanose form of fructose, while other fructose tautomers likely lead to unwanted side products. The tautomeric composition of fructose is highly dependent on the reaction temperature and solvent system; thus, HMF production is likely sensitive to these factors. In order to develop detailed insights into the factors that control HMF yields, we executed extensive kinetic analysis using a variety of solvent systems, reaction conditions, acid types and acid concentrations to determine the mechanism and selectivity controlling factors in fructose dehydration to HMF by homogeneous acid catalysts. Through these studies we were able to strongly support the hypothesis that selectivity in fructose conversion to HMF is controlled by the tautomeric distribution. Furthermore, we found that dimethyl

sulfoxide (DMSO) solutions produce the highest HMF selectivity, (up to 85%) and fastest conversion rates of any solvent system; however, DMSO is highly energy intensive to separate. To overcome separation costs, we aimed to develop novel heterogeneous catalysts which mimic the desirable solvation effects of DMSO in low boiling, aqueous co-solvent mixtures. We grafted DMSO-like functional groups near acidic sites on the surface of supports generate local conditions which mimic bulk solutions of DMSO, which increased HMF selectivity by ~30%. To synthesize these catalysts, the surface of silica was first functionalized by (3-mercaptopropyl)-trimethoxysilane. The grafted thiols were then converted into 1, 3-methyl propyl sulfoxides to mimic DMSO at the surface and characterized by RAMAN spectroscopy. A techno-economic analysis was performed on the conversion of fructose to dimethylfuran (DMF) by heterogeneous catalysts in aqueous tetrahydrofuran solutions, using Aspen Plus. We report a minimum selling price (MSP) of DMF of 1.74 \$/kg, with fructose feedstock, DMF yield, catalyst cost, and water treatment being the main contributors to the MSP.

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## **Chapter 1**

### **Introduction**

## **1.1 Motivation**

This work is a part of a United States of Agriculture (USDA) funded project which aims to transform inexpensive and abundant lignocellulosic corn stover through biological and catalytic processing to drop-in additive fuels. This dissertation focuses on the catalytic processing aspects and challenges of converting hexoses, derived from corn stover, to 5-hydroxymethylfurfural (HMF) and then to optimize production and separation of dimethylfuran (DMF), as a drop-in additive fuel.

The need to both decrease our dependence on foreign oil and reduce carbon emissions has attracted research towards domestically produced renewable energy sources. Lignocellulosic corn stover represents a unique, domestically produced energy resource for the sustainable production of drop-in additive fuels to reduce our dependence on petroleum. Corn stover is a highly abundant and inexpensive carbon-based energy source. At \$60 per dry ton, corn stover is equivalent in energy cost to petroleum at approximately \$20 per barrel.<sup>1</sup> In order to utilize this energy source, commercially viable processing technologies must be developed. To achieve this, a deeper understanding of the intermediate mechanistic steps involved in the conversion of corn stover to valuable products is needed.

## **1.2 Biomass-Derived Fructose to HMF**

Biomass processing to fuels begins with a pretreatment step, in which the cellulose and hemicellulose in the biomass are broken down to extract valued carbohydrates and chemicals. Recently, a pretreatment process, called Co-solvent Enhanced Lignocellulosic Fractionation (CELf), which utilizes tetrahydrofuran (THF) as a cosolvent in aqueous

systems, has seen high furfural yields in the liquid stream.<sup>2</sup> Additionally, this process produces highly enriched glucan solids, which are easily separated by filtration from the liquid stream. These glucan solids can then undergo biological saccharification to produce glucose monomers in aqueous phase solutions. In solution, glucose can then be isomerized to fructose, the primary intermediate to 5-hydroxymethylfurfural (HMF) production.<sup>3-6</sup> The final step involves the conversion of HMF to dimethylfuran (DMF), a high-valued gasoline blend-able fuel.

This dissertation aims to understand the factors that enhance sugar conversion to HMF. This will be accomplished by extensive kinetic analysis to determine the mechanism and selectivity controlling factors in fructose dehydration to HMF by homogeneous and heterogeneous acid catalysts. Moreover, this thesis aims to integrate the processing steps of biomass conversion to fuels. Specifically, extensive investigation will be performed on the dehydration of sugars to HMF by both homogeneous and heterogeneous acid catalysts, as well as, determining the optimization and integration of the conversion of HMF to DMF in a single-phase solution by functionalizing bimetallic heterogeneous catalysts. Lastly, an Aspen<sup>®</sup>-based techno-economic analysis will be performed on these systems to address the primary cost challenges towards commercialization.



### 1.3 Dissertation Organization

- 1) The first objective of this research is to understand the fundamental factors and mechanisms of processing fructose to HMF by homogeneous acid catalyzed dehydration. In order to achieve this goal, extensive analysis was performed by studying the kinetics and mechanism of sugar dehydration in terms of the effect of temperature, solvent system, type of catalysts, reaction time, and the impact of sugar loading on the production of HMF. Aqueous dimethylsulfoxide (DMSO) and other aprotic mixtures were utilized to demonstrate that the HMF production was primarily controlled by the isomeric distribution of fructose.
- 2) Porous silica supports were grafted with 3-mercaptopropyl trimethylsiloxane (MPTMS) and treated by oxidation and substitution reactions to generate unique surface functionality, mimicking high-yielding homogeneous solutions. These sulfoxide moieties were grafted to the surface of supports in order to generate unique microenvironments similar to that seen in dimethylsulfoxide (DMSO) solutions. They were then utilized in a lower boiling mixture of water and tetrahydrofuran (THF) to lower separation energy and still have high yields of HMF, similar to fructose dehydration in DMSO. These catalysts have been tested in a variety of dehydration studies to determine the effect of surface loading, type of functional group, pore size, and catalyst loading on HMF production.
- 3) In the final element, a techno-economic analysis was performed on the conversion of fructose to dimethylfuran (DMF) to determine its minimum selling price (MSP). Aspen Plus was utilized to estimate the mass and energy balances of the

systems. The process includes two reactors: 1) an heterogeneous acid dehydration reactor, converting fructose to HMF, and 2) a hydrogenation reactor to convert HMF to DMF. The DMF was then extracted via a series of distillations and decanters with the THF solvent being recycled. A sensitivity analysis was performed on this process to determine which factors most impact the MSP of DMF.

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## **Chapter 2**

### **A Review of the Catalytic Conversion of Fructose to 5-Hydroxymethylfurfural**

## **2.1 Abstract**

5-hydroxymethylfurfural (HMF) represents a key intermediate chemical linking the production of desired chemicals and fuels to biomass. One of the key steps to this is through the acid dehydration of biomass-derived fructose to HMF. This review simply focuses on the conversion of fructose to HMF production and mechanistic aspects of HMF formation in order to bridge the gap in understanding the selectivity controlling factors and optimize HMF yields. The direct transformation of fructose into HMF in recyclable organic solvents is most desired in terms of process economics and sustainability. This is generally due to the promotion of the furanose form of fructose and the formation of a protective solvation shell around HMF, preventing degradation. This review also ignores studies that report HMF production from aerated DMSO because DMSO will degrade to acidic species in the presence of oxygen distorting results. Additionally, present review is devoted exclusively to studies that determined the selectivity to HMF from fructose using either a homogeneous or heterogeneous acid. Technoeconomic studies for the fructose into HMF are examined in order to determine the commercial viability of HMF production and what is necessary to make the process more economical.

## **2.2 Introduction**

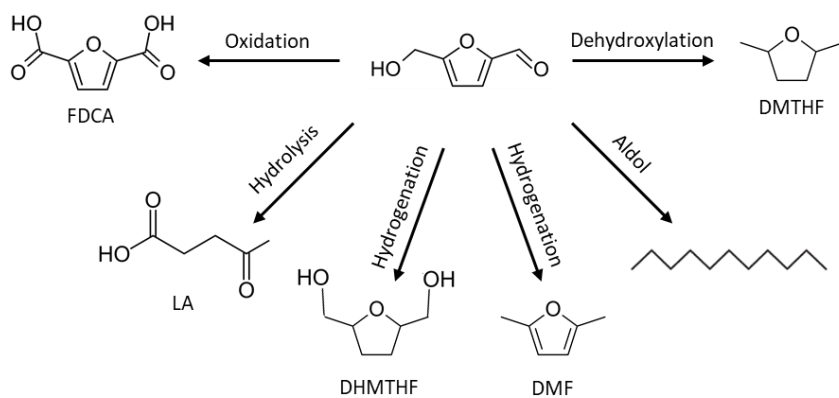
In recent years, the United States has moved towards becoming energy independent through domestically produced carbon sources. From 2005 to present, the net petroleum imports dropped from 12.6 to 3.8 MMb/day, the equivalent of 60% to 19% of total U.S. petroleum consumption.<sup>1</sup> To continue this decrease in net oil imports and

become more energy independent, increased use of domestic biofuels will be highly beneficial.<sup>2</sup> Accordingly, in order to become completely energy independent, research interest has focused on the effective utilization of domestically produced carbon sources, such as lignocellulosic biomass.

Lignocellulosic biomass is an abundant, domestic, and economically renewable carbon source that could potentially replace up to 30% of gasoline used in transportation.<sup>3</sup> Lignocellulosic biomass includes agricultural residues, such as corn stover or woody feedstocks, that could provide nearly one billion dry metric tons of lignocellulosic biomass in the United States for less than \$60/ton by the year 2022.<sup>4</sup> Lignocellulosic biomass refers to a plant's composition and is made of cellulose, hemicellulose, and lignin. Cellulose, in particular, is composed of energy rich  $\beta$ -(1-4) linked D-glucose units that can be extracted via chemical treatment,<sup>5</sup> enzymatic,<sup>6</sup> or biological processes.<sup>7</sup> For example, dilute acid treatment with metal chlorides of corn stover in aqueous tetrahydrofuran (THF) solutions demonstrated high extraction of glucan rich solids.<sup>5</sup> These solids can then be transformed through enzymatic hydrolysis to yield highly rich glucose streams.<sup>6</sup> Through catalytic or biological routes glucose released from cellulose can be converted into high valued fuels<sup>8</sup> and chemicals<sup>9</sup> via an array of mechanistic pathways.

Most pathways to desired chemicals and fuels require the intermediate chemical known as 5-hydroxymethylfurfural (HMF) that links biomass-derived C-6 sugars, such as glucose and fructose, with industrial chemicals and fuels usually derived from petroleum (**Fig 2.1**).<sup>10,11</sup> HMF and its derivatives could potentially be used to make plastics,<sup>12</sup> fine

chemicals,<sup>13</sup> liquid alkanes,<sup>5</sup> and fuels from renewable biomass resources instead of the current petroleum-derived building blocks. A common polyester building-block, 2,5-furandicarboxylic acid (FDCA), can be derived from HMF.<sup>14,15</sup> Acid hydrolysis of HMF can produce bulk chemicals, such as levulinic acid (LA) or formic acid (FA).<sup>13</sup> Additionally, multiple reports have demonstrated that HMF can be catalytically converted to 2,5-dimethylfuran (DMF), a high-octane biofuel miscible with gasoline.<sup>8,16,17</sup> However, in order to make the production of HMF and its products economically viable, better understanding of the mechanism and selectivity controlling factors is necessary.



**Figure 2.1.** HMF catalytic pathways to fuels and valued chemicals.

HMF production is presently limited from industrial applications due to low HMF yields, substrate loading, and/or high separation costs.<sup>18,19</sup> A process to produce pure HMF streams from biomass-derived carbohydrates in high yield and low-cost must be developed. A number of studies have indicated that it is difficult to economically improve the selective conversion of C6 sugars to HMF in aqueous solutions.<sup>20</sup> For example, Román-Leshkov and Dumesic determined that the addition of dimethylsulfoxide

(DMSO) to a biphasic solution increased fructose to HMF selectivity and yields to 90% and 80%, respectively.<sup>21</sup> However, they also demonstrated through techno-economic analysis (TEA) that the cost of DMSO separation was too high to be practical.<sup>21</sup> Generally, high HMF yielding aqueous reactions tend to require a combination of high catalyst loadings, co-solvents, or high temperature. High catalyst loadings require catalyst recycling, neutralization, and/or disposal.<sup>22</sup> Organic co-solvents tend to be expensive and also require high recyclability to be economical.<sup>23</sup> High temperature processes increase energy consumption/utilities and can lead to unwanted degradation pathways.<sup>11</sup> To minimize the costs, studies have focused on improving the catalyst and solvent solutions, as high recyclability can be designed into engineered processes, but lower utility costs are crucial to be economical. Therefore, acid catalyzed aqueous co-solvent processes are attractive systems for conversion of sugars to HMF, due to their potential low-cost and environmental impact. This has pushed numerous studies to explore a range of catalysts and/or organic solvents, which can significantly impact the selective conversion of sugars to furanic compounds.<sup>11,19,24</sup> These past research results have indicated that specific catalysts, temperature, and organic solvents significantly influence reaction rate and product selectivity. However, there has still been debate on the mechanism of HMF production from sugars and what factors control selectivity to HMF. Thus, this review focuses on which of the proposed mechanisms is likely correct and what factors control HMF production from biomass-derived sugars, specifically fructose. Such insights can be utilized to design new systems with novel catalysts and processing methods to increase the yield of HMF and reduce its production cost.

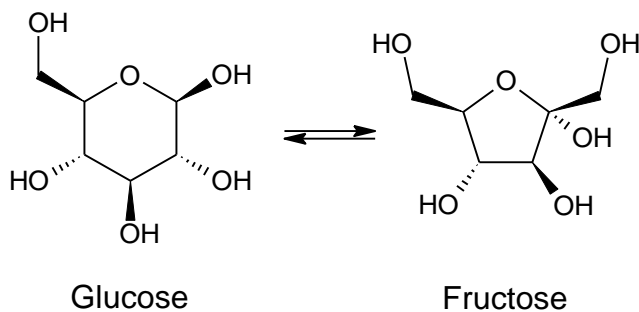


## 2.3 Mechanism

### 2.3.1 Glucose Isomerization to Fructose

Glucose is a C6-isomer of fructose (**Scheme 3.1**) that has been widely studied, as it is much cheaper and potentially readily available from lignocellulosic feedstock. Glucose streams are obtained from the saccharification of cellulose; however, HMF yields directly from glucose are far too low to be practical. Typically, the HMF yields from fructose are superior to those from glucose under the same reaction conditions. For example, a comparison of fructose and glucose dehydration studies at high temperatures in aqueous solution, in the absence of catalyst, reported a range of HMF yields between 4% to 51% for fructose as the substrate, which was much higher than when starting from glucose at just 0% to 16%.<sup>25</sup> It has been suggested that HMF yields are lower in glucose due to the far more stable pyranose form of glucose, reducing its likelihood to undergo dehydration.<sup>26</sup> Thus, glucose must first isomerize to the more reactive fructose molecule in order to have high HMF production. For high temperatures studies in aqueous solutions, a dissolved mineral acid<sup>27</sup> or organic acid<sup>28</sup> was added to promote isomerization of glucose to fructose; however, the amounts of observed fructose are always very small. This is because isomerization of glucose to fructose is a base-catalyzed reaction; in contrast, HMF production is an acid catalyzed dehydration reaction. This makes the rate of degradation to unwanted side products (often referred to as humins) faster than the dehydration rate to HMF for glucose.<sup>29,30</sup> Thus, this review will focus on understanding the underlying mechanism of fructose dehydration, what

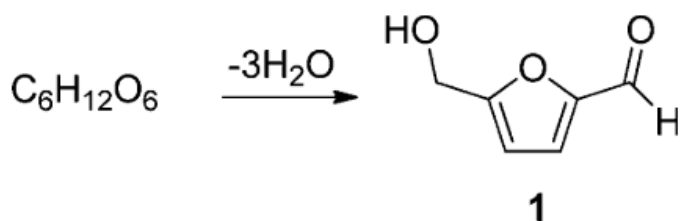
conditions maximize HMF production from fructose, and determine the feasibility of HMF production.



**Scheme 2.1.** Glucose to fructose isomerization.

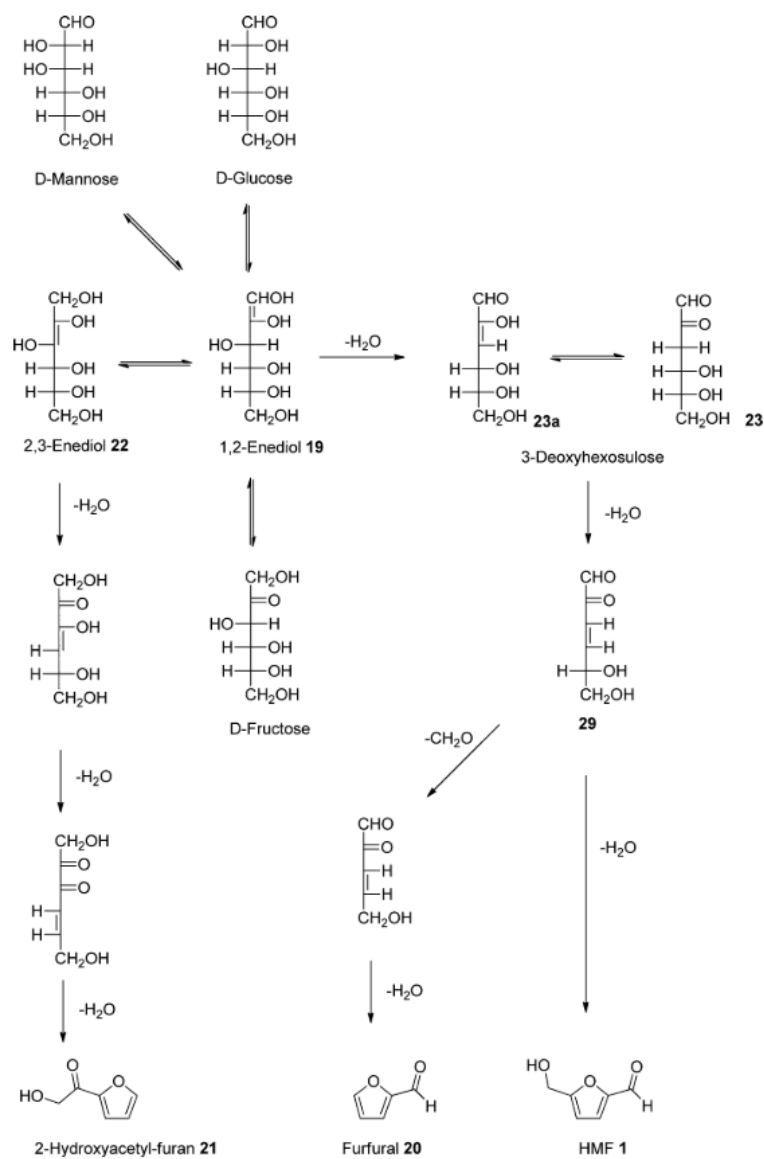
### 2.3.2 Fructose Dehydration to 5-HMF

The most generally accepted pathway for HMF production is the direct formation of HMF by acid catalyzed dehydration of a C6-sugar. This involves the removal three water molecules from the hexose, which are consecutively removed through several steps (**Scheme 2.1**). Presently, the mechanistic pathways proposed have either been for an acyclic pathway<sup>20,31</sup> or a cyclic pathway.<sup>32,33</sup> The body of experimental evidence to support either of the mechanistic routes is still small with most being performed in aqueous systems, leading to the majority of proposed mechanisms being in aqueous systems. In recent years, however, a shift toward the use of other solvent systems, such as aprotic solvents, was observed due to the low HMF yields generally observed in aqueous solutions. Therefore, it is important to examine all the mechanistic pathways as, depending on the solvent system, new mechanistic pathways may be operative.



**Scheme 2.2.** Simplified dehydration pathway of C6-sugar to HMF.

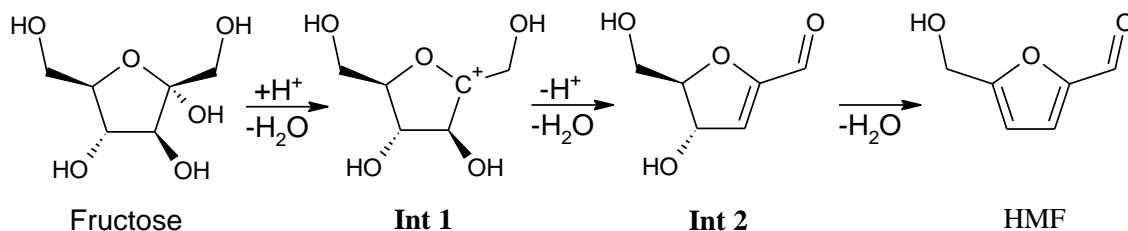
Some of the earliest studies first proposed that the rate-limiting step involved the formation of a linear 1,2-enediol **19**,<sup>20,27,34</sup> an isomerization intermediate between glucose and fructose. This was followed a  $\beta$ -dehydration to 3-deoxyglucose-2-ene, a second  $\beta$ -dehydration to 3,4-deoxyglucose **29**, and then a ring closure with a final water elimination to yield HMF. These acyclic pathways were primarily suggested in aqueous solutions due to the formation of furfural (**20**) and hydroxyacetyl furan (HAF, **21**). However, recent studies in organic solvents, such as DMSO, are beginning to favor the cyclic pathway to HMF.<sup>35-37</sup>



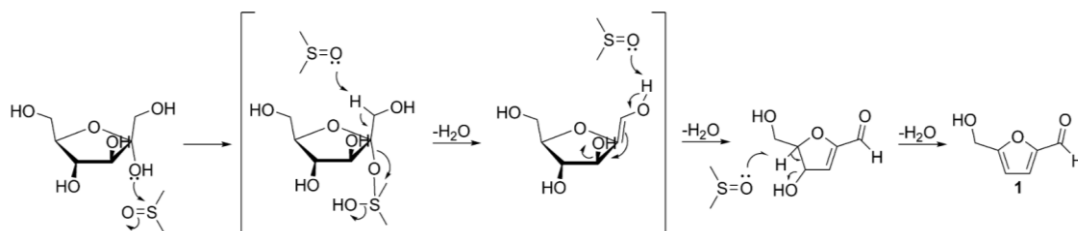
**Scheme 2.3.** Formation of HMF, Furfural, and Hydroxyacetyl-furan from Fructose.<sup>11</sup>

The generalized first step of the cyclic pathway begins with the cyclic ketofuranose form followed by the dehydration of the hemiacetal at C2, forming a tertiary carbenium cation (**Int 1** in **Scheme 2.2**). This is then followed by two consecutive  $\beta$ -dehydrations in the ring to form **Int 2** and then HMF.<sup>11,35,37,38</sup> This pathway is supported by multiple papers with the one of the first being a <sup>13</sup>C NMR study by Amarasekara et al. In this study, a

key intermediate in the reaction was identified as (4R,5R)-4-hydroxy-5-hydroxymethyl-4,5-dihydrofuran-2-carbaldehyde (**Int 2**) by using  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of the sample during the reaction in DMSO. Additionally, they proposed that DMSO acts as a catalysts for the conversion of fructose to HMF; however, they performed this studies in the presence of oxygen, which at elevated temperatures can cause the decomposition of DMSO to sulfuric acid, which will protonate the fructose molecule.<sup>35,39</sup> Akien et al. also performed  $^{13}\text{C}$  NMR studies in DMSO (again in open atmosphere), which assigned peaks in the NMR spectrum to both intermediates mentioned in **Scheme 2.4**.<sup>38</sup> Furthermore, experiments in the presence of  $\text{D}_2\text{O}$  showed that all steps after the first dehydration are irreversible. This was explained by the lack of deuterium incorporation in HMF and supports the cyclic pathway as the acyclic pathway would require deuterium in the HMF molecule.<sup>38</sup>

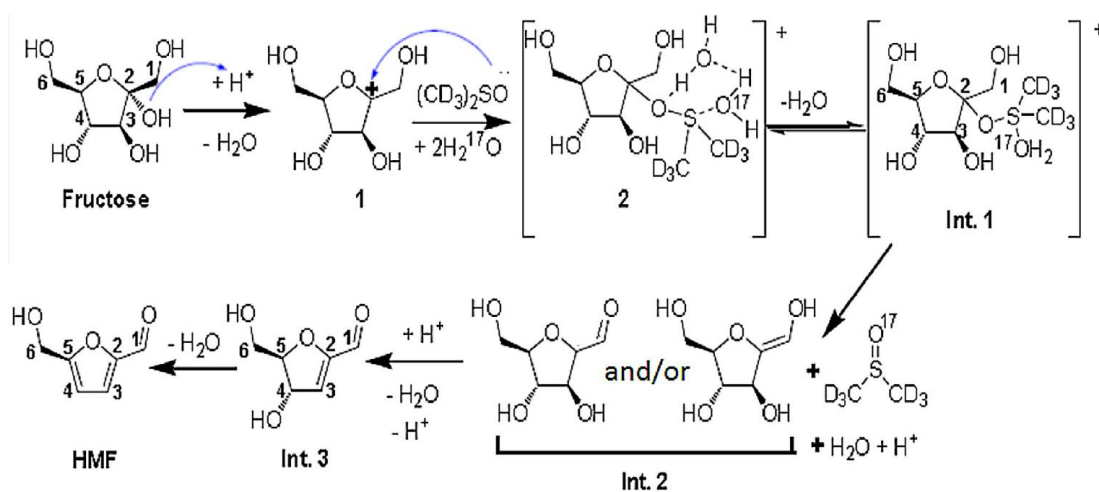


**Scheme 2.4.** Cyclic Pathway in the Dehydration of Fructose to HMF.



**Scheme 2.5.** Proposed Cyclic Mechanism for Fructose Dehydration in DMSO by Amarasekara.<sup>32</sup>

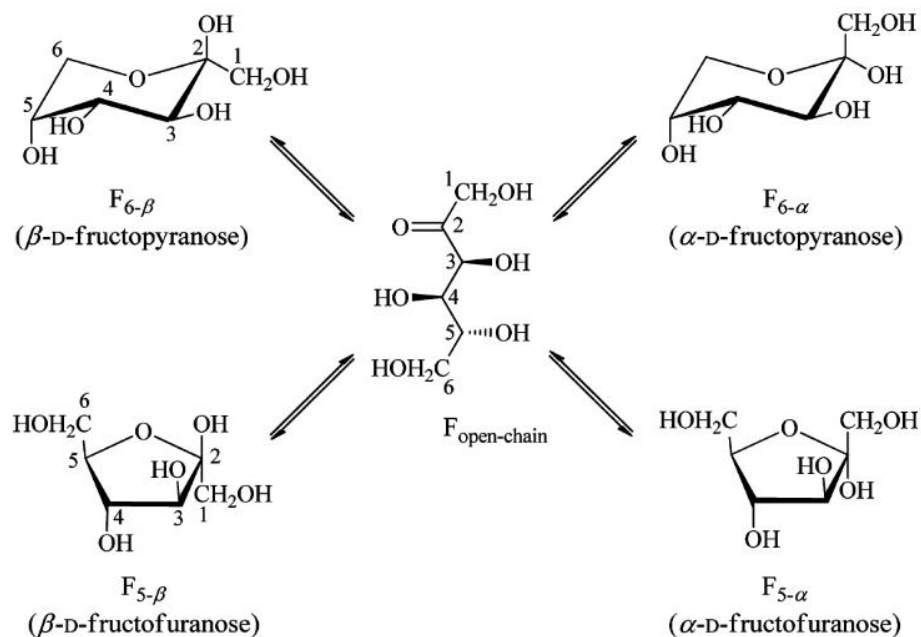
$^{13}\text{C}$  NMR studies by Zhang and Weitz using [ $^{13}\text{C}$ -1]fructose and [ $^{13}\text{C}$ -6]fructose confirmed that fructose C-1 forms the carbonyl carbon of HMF and fructose C-6 forms the hydroxymethyl carbon of HMF.<sup>37</sup> This agrees with both the acyclic and cyclic mechanisms proposed. However, their more recent study, performed in DMSO, identified three key cyclic intermediates: 2-(hydroxydimethylsulfinyloxy)-d-fructofuranose (**Scheme 2.66, Int. 1**), a secondary species pair (**Scheme 2.6, Int. 2**) between a keto-enol tautomerism, 4-dihydroxy-5-hydroxymethyl-tetrahydro-furan-2-carbaldehyde (the keto form)-2-(hydroxymethyl)-5-(hydroxymethylene)- tetrahydrofuran-3,4-diol (the enol form) and 4-(hydroxy)- 5-(hydroxymethyl)-4,5-dihydrofuran-2-carbaldehyde (**Int. 3**). All of these intermediates are cyclic and **Int. 3 (Scheme 2.6)** is a common intermediate reported in other studies.<sup>32,36,38</sup> Additionally, Zhang et al. reported a complex with the DMSO solvent that was characterized by means of  $^{13}\text{C}$  and  $^{17}\text{O}$  NMR spectroscopic techniques. They postulated that this complex could significantly lower energy barriers for both faster and more selective HMF production that is reported in DMSO.



**Scheme 2.6.** Proposed mechanism for the catalytic conversion of fructose to HMF in DMSO proposed by Zhang et al.

### 2.3.3 Selectivity Controlling Factors

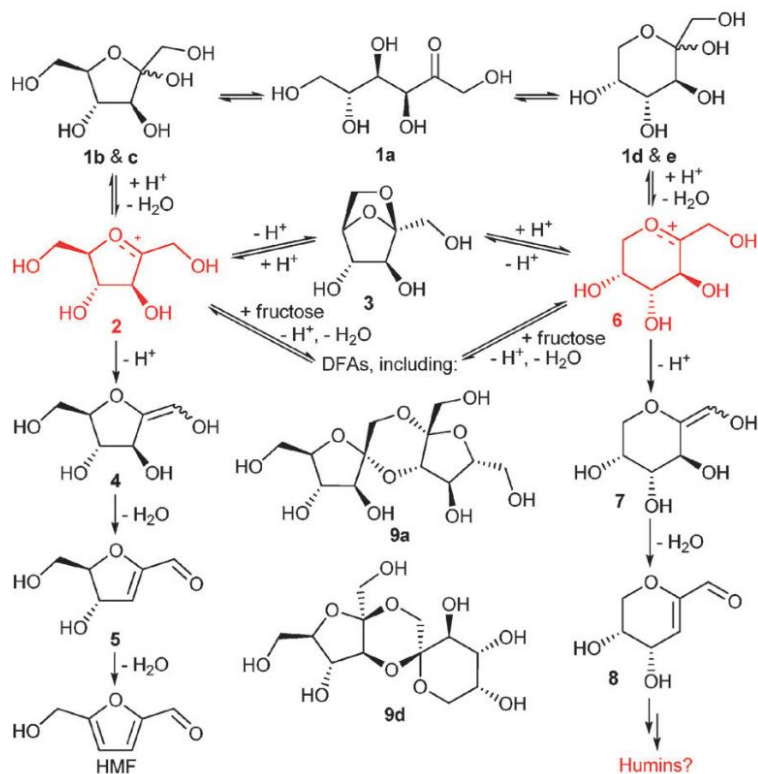
C6-sugars, such as glucose and fructose, exist in the follow isomeric forms:  $\alpha$ -ketofuranose,  $\beta$ -ketofuranose,  $\alpha$ -ketopyranose,  $\beta$ -ketopyranose, and the open-chain acyclic form. **Scheme 2.7** shows the isomeric pathways for fructose with the two  $\alpha/\beta$ -fructopyranose and  $\alpha/\beta$ -fructofuranose forms linked together through the acyclic intermediate.<sup>40</sup> In aqueous solutions, the isomerization of these isomers is rapid,<sup>38</sup> and maintain a constant distribution in water, which is temperature dependent.<sup>41</sup> Furthermore, recent NMR studies run under reaction conditions concluded that the tautomerisation of fructose is very rapid.<sup>42,43</sup> When tautomerisation proceeds at a significantly higher rate than dehydration this is not expected to be an important factor in influencing the selectivity of HMF formation.



**Scheme 2.7.** Structures and isomerization pathways of the D-fructose isomers.

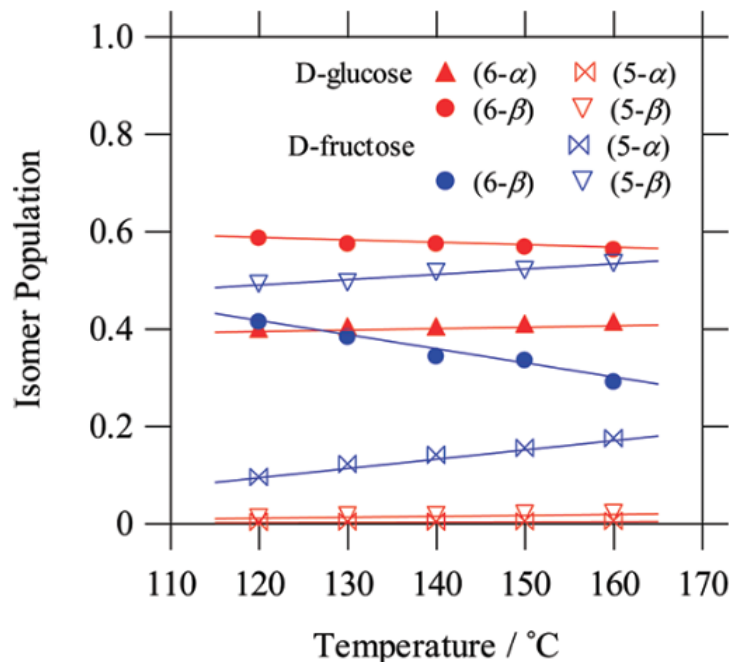
The mechanism proposed by Akien et al.<sup>38</sup> is of particular interest for determining what factors control selective to HMF, as it proposed two separate pathways: 1) the acid catalyzed dehydration of the fructofuranose isomer and 2) the acid catalyzed dehydration of the fructopyranose form. Through *in-situ* <sup>13</sup>C NMR analysis, they reported observing the reversible formation of 2,6-anhydro-β-D-fructofuranose (**Scheme 2.8, 3**) between the protonated cations of the fructose isomers. Difuctose dianhydrides (DFAs) were also observed (**9a–f**) by <sup>13</sup>C NMR. DFAs are slow to hydrolyze back to fructose in DMSO and were seen to remain in the solution long after about 99% of the fructose had been converted. It has been suggested by Tucker et al. that DFA formation protects the reactive anomeric hydroxyl groups from polymerization.<sup>44</sup> Akien then suggested that the linking between intermediate **3** and these cations could create intrinsic mechanistic limitation of selective HMF synthesis by providing an alternative connection between the preferred path to HMF and that of the formation of unwanted side-products due to pyranose degradation. However, this still links the original isomeric distribution between the furanose and pyranose forms, which can be controlled by factors such as temperature, solvent system, or catalyst.





**Scheme 2.8.** Dehydration pathways of fructose and glucose proposed by Akien.<sup>38</sup>

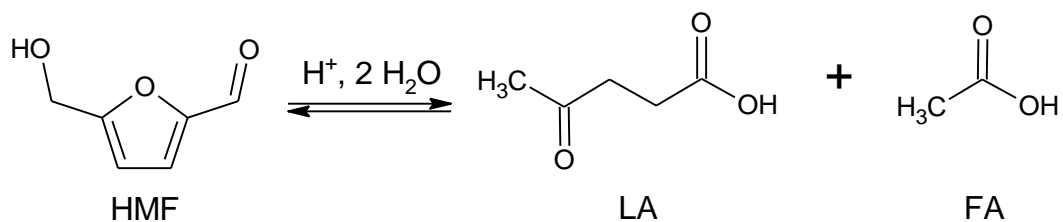
Kimura studied how the isomeric distribution of fructose and glucose in aqueous solution changes over temperature and found that the percent composition of the furanose form increases with temperature while the pyranose form decreases (**Figure 2.2**).<sup>41</sup> It was observed that the pyranose form of glucose is dominant with minuscule amounts of the furanose over all temperatures; in contrast, the pyranose form of fructose is always less than the furanose isomer and decreases with increasing temperature. It has been proposed that the high selectivity of HMF formation from fructo-furanose is due to their structural similarity; an extension of the observation that the fructofuranose ring system is more readily converted to HMF than the glucopyranose system.



**Figure 2.2.** Temperature dependence on the normalized fructose (blue) and glucose (red) isomeric distribution in water.<sup>41</sup>

An aqueous environment generally results in the non-selective conversion of fructose to HMF followed by the rehydration of HMF to LA and FA (**Scheme 2.9**), further reducing the total HMF yields.<sup>45,46</sup> Thus, numerous studies have explored different solvents that both inhibits the formation of byproducts and is easily separated from HMF. Many options have been analyzed, but some of them have been especially attractive since they increase reaction rates and have higher selectivity towards HMF. The choice of solvent greatly impacts the tautomeric distribution. For example, Kimura et al. observed that fructose dissolved in DMSO, at room temperature, has about 58% of the isomeric distribution in the fructofuranose form. This is considerable higher than their observation in water, which only has about 25% fructofuranose.<sup>40</sup> Thus, it has been proposed that by utilizing solvents that promote the furanose form, higher HMF yields

should be observed. This includes both organic solvents and ionic liquids as reaction media. Lastly, organic liquids have the potential to protect HMF from being hydrolyzed to LA and FA or even degrade into unwanted byproducts.



**Scheme 2.9.** Acid hydrolysis of HMF to LA and FA.

## 2.4 Solvent Systems

Solvents can be categorized into three types: polar protic solvents (water, methanol, ethanol, and acetic acid), aprotic solvents (DMSO, DMF, ketones, THF, and GVL), and ILs. Solvents can change the chemical reactivity, reaction rates, reaction pathways, product distributions, and product yields. Changes in interactions between the solvent and solute occur because of changes in hydrogen bonding and differing dipole moments, which can significantly alter the solubility and the thermodynamic state of reactants, transition states, activation energy, and products in a single reaction.<sup>47</sup> Therefore, reaction rates and product selectivity can be controlled to a certain degree by simply changing the solvent medium. Additionally, by mixing differing solvents together one can balance the advantages and disadvantages of each system to maximize economical production of HMF.

## **2.5 Aqueous Systems**

### **2.5.1 Monophasic**

The earliest studies of fructose dehydration first examined the non-catalytic dehydration to HMF.<sup>11</sup> However, non-catalytic dehydration of fructose in subcritical water has demonstrated slower rates and lower selectivity towards HMF than with a catalyst.<sup>27</sup> In consequence, research has shifted towards studying multitude of homogeneous and heterogeneous acids in aqueous solutions. However, no matter the catalyst chosen HMF yields from aqueous mixtures have generally not exceeded 70%.<sup>11</sup> This is largely due to sugar and HMF degrading to unwanted polymers and HMF hydrolyzing to LA and FA. Thus, most recent studies have moved away from pure aqueous systems with many imploring non-miscible solvents.

### **2.5.2 Biphasic**

As stated, one reason lower HMF yields are observed in aqueous solutions is caused by the degradation and hydrolysis of HMF. In addition, HMF is assumed to react with sugars, intermediate chemicals, and HMF to form humins and polycondensation byproducts. To address these problems, non-miscible organic solvents are utilized for in-situ extraction into the organic phase, removing HMF out of the aqueous phase. By continuously removing HMF, these undesired side reactions can be suppressed to a large extent and these solvents are generally easier to separate from HMF than water. Román-Leshkov and Dumesic<sup>48</sup> investigated the water immiscible organic solvent effect, primarily with methyl isobutyl ketone (MIBK) for the dehydration of fructose in a biphasic system. Utilizing MIBK as an extracting solvent, selectivity to HMF was shown

to increase from 51% to 73% selectivity, with HCl as the catalyst. While it is clear that biphasic solvents do help to increase selectivity to HMF, this is primarily only due to protecting the HMF from further degradation and not due to increased selectivity to HMF from fructose. Thus, we must examine other solvent systems to truly understand how solvents influence HMF production.

## **2.6 Organic Solvents**

### **2.6.1 DMSO**

DMSO is the most polar of the aprotic solvents; thus, it can dissolve polar carbohydrates and closely solvate these molecules, changing their chemical reactivity, isomeric distribution, and product selectivity.<sup>40,49</sup> DMSO has been the most widely studied organic solvents due to the high reported yields over a vast range of catalysts. However, DMSO decomposes at moderate temperatures ( $\sim 80$  °C) in the presence of oxygen to produce acidic species, including  $\text{H}_2\text{SO}_4$ .<sup>39</sup> This review does not overview the studies that utilized DMSO in open air, as the conversions and HMF selectivity have been affected by  $\text{H}_2\text{SO}_4$  production. This turns out to be the majority of the studies, only recently have experiments been taking this into account.<sup>35</sup> However, DMSO still is the most selective solvent for HMF production due to its unique solvent properties.

DMSO has been demonstrated to have nucleophilic action, interacting with carbonium ions to promote the dehydration of 1,4-diketones in furanic compounds.<sup>50,51</sup>  $^1\text{H}$  and  $^{13}\text{C}$  NMR studies have recently demonstrated that DMSO also greatly impacts the tautomeric distribution.<sup>32</sup> Dissolved in DMSO, the pyranose form of fructose changes to furanose the form, which can be more readily transformed into HMF. Several research

reports showed that DMSO could affect the equilibrium of sugar species by promoting the formation of the furanose form of fructose.<sup>40</sup> On increasing temperature, the furanose form of fructose increased with the decrease of the alternate pyranose form.<sup>36</sup> Nikolakis et al. analyzed the FTIR spectra of fructose in different solvents and observed a blue shift in the OH stretching vibration of fructose that was thought to be caused by the increase in the strength of the hydrogen bond between fructose and the solvent.<sup>52</sup> While these results point to a cyclic route for the dehydration of fructose to HMF, it is important to note that this tautomerization process has only been exclusively observed in DMSO.

Computational data from Ren et al.<sup>53</sup> however, suggests that fructofuranose form is the most stable isomeric form when dissolved in DMSO. It has also been shown that DMSO initiates HMF formation due to the arrangement of DMSO around the hydrogen atoms of the fructose molecule, reducing the formation of reversion and polymerization products from fructose.<sup>53</sup> Moreover, DMSO binds to HMF more strongly than water does, and reduces its susceptibility to nucleophilic attack, thereby minimizing undesirable side reactions. All these attributes result in HMF yields from fructose with DMSO as the solvent are often higher than in other solvents as HMF will be less likely to degrade to side products.

### **2.6.2 Protic Mixtures**

Organic protic solvents such as ethanol, butanol, or methanol are attractive solvents, as they are cheap, low-boiling point, and environmentally friendly solvents. However, these solvents cannot dissolve sugars at high concentrations and have only reported low yields of HMF. Aqueous mixtures of these alcohols are required to dissolve

fructose and obtain moderate yields. For example, reactions run in water/ethanol (3:7) mixtures with an acid carbon catalyst only reported 39% yields of HMF. However, this is much higher than in pure ethanol, which only reported 8.7% yields. The highest reported yield came from utilizing sulfonic cyclodextrin as the catalyst in isopropanol to dehydrate 1 wt% fructose to 63% yields of HMF.<sup>54</sup>

### **2.6.3 Aprotic Mixtures**

As stated before, all studies that utilized DMSO and did not deaerate the solvent have not be included in this review. Additionally, studies which did not quantify both conversion and yield are not taken into account as selectivity to HMF cannot be determined. This leaves a limited amount of studies utilizing aprotic solvents. Aprotic solvents are far more protective than protic solvents that hydrolyze or degrade HMF and fructose. Additionally, strongly polar aprotic solvents, such as DMF or DMA, can dissolve high concentrations of fructose and generate a solvation shell around HMF protecting it from unwanted side reactions.<sup>55</sup> Therefore, dipolar aprotic solvents have confirmed high yields of HMF from fructose. For example, it was demonstrated with the Lewis acid  $\text{FeCl}_3$  and  $\text{Et}_4\text{NCl}$  in NMP fructose was converted to HMF at 82% yield.

Low boiling point aprotic solvents are sought after due to the ease of separate; however, these solvents cannot dissolve fructose and require a more polar co-solvent. This tends to limit the dissolved fructose concentration in the stream. When 1 wt% fructose was dissolved in a 9 to 1 mixture of acetone to water and reacted with 10 mM  $\text{H}_2\text{SO}_4$  at 180°C for 2 minutes a maximum HMF yield of 75% was reported.<sup>56</sup>

**Table 2.1.** Fructose dehydration by homogeneous catalysts in organic solvents/mixtures. Catalyst loading percent are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Fructose Conc. (wt%)	Solvent	Catalyst	Catalyst Loading	Temp (°C)	Time (min)	Y (%)	C (%)	S (%)	Ref
2	1,4-dioxane	Sc(OTf) <sub>3</sub>	10 wt%	120	120	16	86	19	<sup>57</sup>
1	acetone/ water (9:1 v/v)	H <sub>2</sub> SO <sub>4</sub>	10 mM	180	2	75	98	77	<sup>56</sup>
2	DMA	Sc(OTf) <sub>3</sub>	10 wt%	120	120	50	98	51	<sup>57</sup>
5	DMF	NH <sub>4</sub> Cl	10 mol %	100	60	55	100	55	<sup>58</sup>
5	ethyl acetate	NH <sub>4</sub> Cl	10 mol %	77	30	58	100	58	<sup>59</sup>
9	NMP	FeCl <sub>3</sub> / Et <sub>4</sub> NCl	10 & 18 mol %	90	120	82	100	82	<sup>60</sup>

#### 2.6.4 Ionic Liquids

Ionic liquids typically consist of a combination of organic and inorganic ions and are liquid at low temperatures. Generally, the cations in ILs are organic groups, usually containing nitrogen or phosphorous, while the anion are an inorganic ion (HSO<sub>4</sub>, or Cl). The most common ionic liquids are N,N'-dialkylimidazolium, N-alkylpyridinium, alkylammonium and alkylphosphonium based. Ionic liquids are attractive due to their ability to dissolved high sugar concentrations, their range of functionality, and ability to tune their properties. However, they are currently too expensive to be economical and require large amounts of an extracting solvent to isolate HMF.<sup>24</sup> Nevertheless, these high HMF yields have still drawn large research attention. For example, fructose dehydration in the Brønsted acidic methylimidazolium chloride [AMIM]Cl reported a 92% HMF yield from a 23 wt% fructose solution. Moreover, it was reported that a 67 wt% loading



of fructose in 1-Butyl-3-methylimidazolium chloride ([BMIM][Cl]) with HCl as the dehydration catalyst had a 91% HMF yield, which are highly economical levels.<sup>61</sup> It is likely that these ionic liquids tune the isomeric distribution of fructose towards furanose, leading to higher HMF. Additionally, ionic liquids cannot hydrolyze HMF to LA or FA and may protect HMF from degradation.

**Table 2.2.** Fructose dehydration to HMF catalyzed by Bronsted acids in ionic liquids. Catalyst loading percent are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Solvent	Fructose		Catalyst Loading	Temp (°C)	Time (mins)	Y (%)	C (%)	S (%)	Ref
	Conc. (wt%)	Catalyst							
[BMIM][Cl]	4.8	H <sub>2</sub> SO <sub>4</sub>	0.75 mmol	120	30	97	100	97	62
[BMIM][Cl]	4.8	H <sub>2</sub> SO <sub>4</sub>	18 mol%	80	10	69	81	85	63
[BMIM][Cl]	9.1	H <sub>2</sub> SO <sub>4</sub>	10 mol%	100	50	83	100	83	64
[BMIM][Cl]	9.1	HCl	0.2 mmol	80	8	97	100	97	61
[BMIM][Br]	9.1	HCl	0.2 mmol	80	11.5	95	100	95	61
[AMIM][Cl]	9.1	HCl	0.2 mmol	80	25	96	100	96	61
[BMIM][Cl]	67	HCl	9 mol%	80	120	51	67	76	61
[BMIM][Cl]	33	HCl	9 mol%	80	35	82	90	91	61

## 2.7 Homogeneous Catalysts

### 2.7.1 Brønsted Acids

Past studies of fructose dehydration in aqueous solutions catalyzed by Bronsted acids reported mild differences between HMF production for each acid.<sup>29,65</sup> However, strong acids were limited to shorter reaction times or else LA production would dominant, lowering HMF yields. **Table 2.3** lists the results of of Bronsted acid catalyzed fructose dehydration experiments. From the table, it can be observed that the selectivity to HMF utilizing either HCl or H<sub>2</sub>SO<sub>4</sub> averages at about 48% and 40% in aqueous systems (Table 2.1). This lower selectivity to H<sub>2</sub>SO<sub>4</sub> can be attributed to faster HMF

hydrolysis than HCl.<sup>65</sup> Overall, Bronsted acids are necessary to initiate fructose dehydration; however, they only impact HMF selectivity through degradation of HMF.

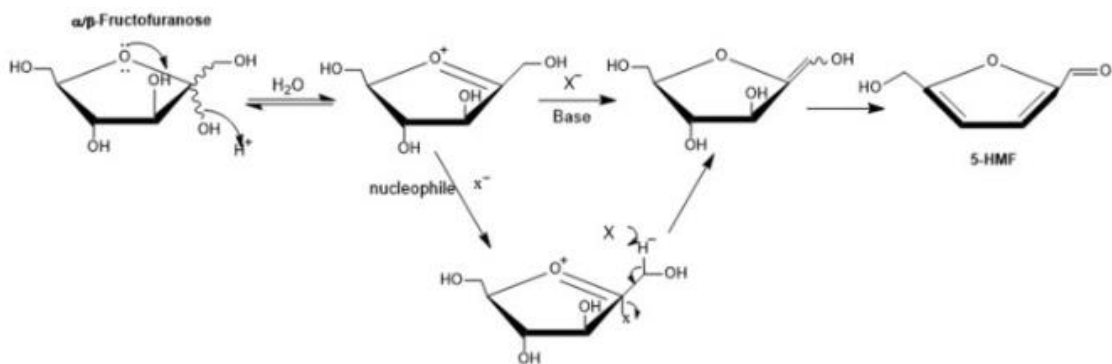
**Table 2.3.** Homogeneous Bronsted Acid Catalyzed Dehydration of Fructose to HMF in Aqueous Systems. Catalyst loading percentages are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Fructose Conc. (wt%)	Catalyst	Catalyst Loading	Temp. (°C)	Time (min)	Yield (%)	Conv. (%)	Selectivity (%)	Ref
3.6	PTSA	200 mol%	88	190	50	88	57	66
9	HCl	400 mol %	95	16	26	46	57	29
9	HCl	400 mol %	95	24	30	62	48	29
27	HCl	1000 mM	130	5	28	99	28	67
27	HCl	10 mM	200	1	53	95	56	67
30	HCl	250 mM	180	3	25	50	51	68
9	H <sub>2</sub> SO <sub>4</sub>	1 mM	200	5	23	93	25	69
2	H <sub>2</sub> SO <sub>4</sub>	50 wt%	200	5	47	97	48	70
0.9	H <sub>2</sub> SO <sub>4</sub>	4 mol %	250	0.53	50	95	53	71
1	H <sub>2</sub> SO <sub>4</sub>	10 mM	180	10	28	80	35	72
4.5	H <sub>3</sub> PO <sub>4</sub>	25 mM	240	2	65	98	67	73

## 2.7.2 Salts

Generally, salt have been utilized in biphasic solutions to increase the partition coefficient and separate more HMF into the organic phase. However, Binder and Raines<sup>74</sup> suggested that weakly paired anions from halide salts could increase the selectivity to HMF. They proposed that a fructofuranosyl oxocarbenium ion is formed and deprotonated, and that the halide anion formed a 2-deoxy-2-halo intermediate, which in turn formed an enol, leading to HMF (**Scheme 2.10**). Binder and Raines<sup>74</sup> performed these studies in N,N dimethylacetamide (DMA) with LiCl as a solution to hydrolyze and dehydrate cellulose to fructose to HMF. However, this proposed pathway was not

demonstrated experimentally and they concluded this route by comparing the salt effect at two differing temperatures.



**Scheme 2.10.** Proposed mechanism for fructose dehydration in the presence of halides.<sup>74</sup>

### 2.7.3 Lewis Acids

Brønsted acids have been extensively studied as catalysts for fructose dehydration. However, they are often corrosive and toxic, making them difficult to use in industrial processes. As an alternative, Lewis acids, particularly in the forms of salts, offer advantages such as an easier catalyst recovery, and less corrosiveness. The disadvantages of Lewis acids are that far lower yields have been reported compared to their Brønsted counterparts for the dehydration of fructose. The highest reported HMF yields from fructose heated in aqueous solution ( $140^\circ\text{C}$ ) with a Lewis acid ( $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ ) as the catalyst was only 20%.<sup>75</sup> Instead of promoting fructose dehydration these catalysts are generally used with glucose to promote isomerization to fructose.<sup>11,19</sup> Lewis acids do not effectively protonate fructose to form the carbocation intermediate, thus leading to low HMF yields.

## 2.8 Heterogeneous Catalysts

Solid catalytic materials have several advantages over homogeneous catalysts: they are easily recyclable, have adjustable properties, and are not as corrosive to the overall process.<sup>76,77</sup> However, these catalysts can be costly, lose reactivity due to fouling, and suffer from leaching of functionalized groups or metals into the solution.<sup>78</sup> The top heterogeneous catalyst utilized in research studies are functionalized silica supports, resins/polymers, carbon-based materials, zeolites, and metal oxides.

### 2.8.1 Functionalized Silica

Silica grafted with unique functionality can be generated through reacting tetraethyl orthosilicate with an organic functional silane/siloxane or can be formed by directly grafting an organic functional siloxane to the surface of a silica support. Functionalized silica has gained large research attention due to the control over porosity, surface acidity, and functionality. The choice of functional group has been shown to make a large difference in HMF production. For example, mesoporous silica (SBA-15) functionalized with thiopropyl showed no improvement in HMF production, but grafted polysulfonic groups on the surface demonstrated improved activity and selectivity.<sup>79,80</sup> Sulfonic acid functionalized SBA-15 was used to catalyze the dehydration of 30 wt% aqueous fructose, 11 wt% catalyst and 2 equiv of MIBK/2- butanol (7:3 w/w) at 180°C for 30 mins. This reaction yielded 49% HMF at a 66% fructose conversion. Additionally, when ordered, functionalized catalysts were compared to similar nonordered silicas, the SBA-15-based catalysts showed a much higher selectivity (75% vs 20% of non-ordered). SBA-15 organosilicas were also more thermally stable and less prone to leaching by

hydrothermal degradation.<sup>81</sup> Additionally, functionalized silica was prepared by reacting an acidic ionic resin with tetraethyl orthosilicate (TEOS).<sup>82</sup> The resin provided a stable template for TEOS to attach and source of sulfonic active sites. The catalyst was very effective in dehydrating fructose to 85% HMF yield (at 90 °C and 2 h).<sup>82</sup> Moreover, no leaching of the active groups was observed as no SO<sub>3</sub>H was seen in the solution. Past experimental results have demonstrated that functionalized silica can maintain high activity and selectivity to HMF from fructose, while still being easily separated from solution and stable in solution based on its synthetic method.

**Table 2.4.** Fructose dehydration to HMF catalyzed by functionalized silica supports. Catalyst loading percentages are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Solvent	Fructose Conc. (wt%)	Catalyst	Catalyst Loading	Temp (°C)	Time (mins)	Y (%)	C (%)	S (%)	Ref
Water/(MIBK:2-Butanol 7:3) 3:7	30	Taa-SBA-15	3 g	180	120	49	66	74	79
Water/(MIBK:2-Butanol 7:3) 3:7	30	TESAS-SBA-15	50 mg	130	140	60	84	71	79
Water/(MIBK:2-Butanol 7:3) 3:7	30	Tp-SBA-15	3 g	180	120	32	61	52	79
Water	4.8	SBA-SO <sub>3</sub> H	0.4 g	120	1440	20	84	24	83
NMP	33	Amberlyst-35	40 wt%	115	300	81	94	86	84

## 2.8.2 Resins and Polymers

Resins and polymers have been extensively used in past research to promote and catalyze HMF production. Some of the most used resins are Amberlyst and Nafion. Amberlyst and Nafion and can be produced from several types of biomass-derived waste materials.<sup>78,85,86</sup> Amberlyst is a sulfonic acid polystyrene resin and Nafion is a sulfonated

tetrafluoroethylene perfluoro-2-(fluorosulfonylethoxy)propyl vinyl ether copolymer. These catalysts are highly stable at temperatures below (120°C) and can be regenerated with a mobile phase and recycled. Additionally, these resins are often used in a flow-through system, which can continuously dehydrate fructose to HMF.<sup>87</sup> However, these resins tend to have lower surface area than other heterogeneous catalysts and can suffer from poor recyclability. A U.S. patent utilized Amberlyst-15 (one of the cheapest and most widely available resins) in NMP solution to dehydrate fructose to HMF at yields above 81%.<sup>84</sup> In aqueous solution, polyaniline, with acidic carbon nanotubes (CP30), was used to dehydrate fructose at 58% yields of HMF,<sup>88</sup> while the yields are good carbon nanotubes are still too expensive to utilize on large scale.

**Table 2.5.** Fructose dehydration to HMF catalyzed by acidic resins and polymers. Catalyst loading percentages are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Solvent	Fructose Conc. (wt%)	Catalyst	Catalyst Loading	Temp (°C)	Time (mins)	Y (%)	C (%)	S (%)	Ref
Water	4.8	Amberlyst-15	0.4 g	120	1440	15	57	26	<sup>89</sup>
N,N-DMF	3.2	Amberlyst-15	0.1 g	100	180	73	99	74	<sup>89</sup>
Water	2.5	Polyaniline w/ Carbon Nanotubes (CP30)	50 mg	160	30	58	80	73	<sup>88</sup>
Water	4.8	Nafion NR50	0.4 g	120	1440	6	78	8	<sup>89</sup>
N,N-DMF	3.2	Nafion NR50	0.1 g	100	180	45	99	45	<sup>89</sup>
NMP	33	Amberlyst-35	40 wt%	115	300	81	94	86	<sup>84</sup>
DMA	35	Amberlyst-35	40 wt%	105	300	62	75	83	<sup>90</sup>

### 2.8.3 Carbon Based Materials

Carbonaceous catalysts are desired due to their low cost, high stability, and can be synthesized from sustainable sources. Additionally, cheap biomass sources, such as agricultural and food waste, can be thermally and chemically treated to form highly stable, cost-effective, and sustainable catalysts.<sup>78</sup> Based on the processing method, the shape, particle size, and surface area of carbonaceous catalysts can be tuned for specific functions. Through oxidation and acid treatment, acidic sites can be generated and still retain high thermal stability. One disadvantage is that these current processes rely on using  $\text{H}_2\text{SO}_4$  or fuming  $\text{H}_2\text{SO}_4$  for functionalization, which requires washing the material with large quantities of water and other solvents to remove free acid and organic compounds. Still, carbon materials have shown high HMF yields in a variety of aprotic solvents. For example, at a low temperature of  $100^\circ\text{C}$  and a time of 45 mins cellulose sulfonic acid was the catalyst in DMA, DMF, and NMP in which each solvent had over 85% HMF yields.<sup>91</sup>

**Table 2.6.** Fructose dehydration utilizing a solid carbon catalyst. Catalyst loading percentages are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

Solvent	Fructose Conc. (wt%)	Catalyst	Catalyst Loading	Temp (°C)	Time (mins)	Y (%)	C (%)	S (%)	Ref
DMA	5.7	Cellulose-Sulfuric acid	27.8 wt%	100	45	91	98	93	91
NMP	5.7	Cellulose-Sulfuric acid	27.8 wt%	100	45	87	97	90	91
DMF	5.7	Cellulose-Sulfuric acid	27.8 wt%	100	45	86	98	88	91
Ethanol	5.7	Cellulose-Sulfuric acid	27.8 wt%	100	45	8.7	28	31	91
Water	5	Phosphorylated Carbon	20 wt%	120	480	43	68	63	92
DMF	7.7	Glu-TsOH	80 wt%	130	90	60	98	61	85
DMA	7.7	Glu-TsOH	80 wt%	130	90	60	97	62	85
Water/ Ethanol 3:7	5.6	C/MCF	30 wt%	140	240	39	93	42	93
Water/ Ethanol 3:7	5.6	C/SBA(45)	30 wt%	140	360	39	89	44	94

#### 2.8.4 Zeolites

Zeolites are microporous aluminosilicates that can hold exchangeable cations in their three-dimensional framework.<sup>95</sup> They are desired due to their high surface area, tailored active sites, and adsorption properties.<sup>96</sup> These catalysts have also demonstrated high yields to HMF. For example, Moreau et al.<sup>97</sup> utilized H-mordenites (H-MOR) to catalyze fructose dehydration to HMF with a 91% HMF selectivity and 76% fructose conversion in a biphasic mixture of water and MIBK. It was proposed that the shape selectivity properties of the catalyst, the Si/Al ratio, and the acidic sites controlled the selectivity to HMF. Additionally, Bhaumik et al.<sup>98</sup> performed fructose dehydration utilizing H-MOR and silicoaluminophosphate (SAPO) catalysts and obtained an HMF



yield of 63% with H-MOR versus 78% with the SAPO catalyst. It was proposed that the strong acid sites of the H-MOR lead to more decomposition products and hydrolysis of HMF, therefore reducing HMF yields compared to the SAPO catalyst. Wang et al.<sup>99</sup> performed experiments using HZSM-5 and observed that higher acid site density did change the dehydration reaction rate. Also, the reaction activation energy for the conversion of fructose to HMF reduced with the proximity of the Brønsted acid sites, which improved the results of the reaction. The stability of the zeolite at high temperatures and acid levels was also analyzed, showing that it did not suffer any structural changes, allowing for good recyclability.

### **2.8.5 Metal Oxides**

Metal oxides and phosphates offer low cost catalysts that can be generated with strong acid sites and have low toxicity. The most common metal oxides used are niobium oxide (NbO)<sup>100</sup> and phosphate (NbP).<sup>101</sup> Treatment of NbO with phosphoric acid increases its surface area as well as the amount of strong acid sites.<sup>102</sup> This pretreated catalyst was used to dehydrate 2.7 wt% fructose in a water, butanol mixture (2:3 (v/v)), gave HMF yields of 89% and at 160 °C.<sup>102</sup> Similar results were obtained by Antonetti et al.<sup>103</sup> when using this and phosphate zirconium under microwave heating (ZrP). Al<sub>2</sub>O<sub>3</sub> is another popular choice for a solid catalyst, particularly in its  $\gamma$  and  $\eta$  forms since they have a larger surface area and pore size than the  $\alpha$  form.<sup>104</sup> As with zeolites, it is their crystalline structure with multiple active sites and ease of recovery that makes them very interesting as catalysts.

**Table 2.7.** Fructose dehydration to HMF catalyzed by solid metal oxides. Catalyst loading percentages are referenced to substrate amount loaded. **Y** stands for yield, **C** for conversion, and **S** for selectivity.

<b>Solvent</b>	<b>Fructose Conc. (wt%)</b>	<b>Catalyst</b>	<b>Catalyst Loading</b>	<b>Temp (°C)</b>	<b>Time (mins)</b>	<b>Y (%)</b>	<b>C (%)</b>	<b>S (%)</b>	<b>Ref</b>
N,N-DMF	3.2	SO <sub>4</sub> <sup>2-</sup> /ZrO <sub>2</sub>	20 wt%	200	5	66	91	72	105
Water	2	ZrO <sub>2</sub>	20 wt%	200	5	21	59	35	106
Water	5	NbO	4 g	100	44	9	40	22	101
N,N-DMF	3.2	NbO	0.1 g	100	180	0	12	0	107
Water/Butanol 1:1.5	5.7	Phosphated tantalum hydroxide	0.1 g	160	100	90	94	96	108

## 2.9 Economic Analysis

In order to develop laboratory scale experiments to industrial scale, it is necessary to determine whether these laboratory results are practical or impractical. By using the values of substrate concentration, reaction time, and yield, it is possible to calculate the effective HMF output and price. The majority of U.S. oil consumption can be broken down into 2 main sectors: transportation and industrial. The transportation sector accounts for 71% of the oil consumption while the industrial sector accounts for 24%. Thus, the transportation sector requires about 2.02 million metric-tons/day of oil while the industrial sector requires roughly 688,000 metric-tons/day. To make a significant replacement within in these sectors, it is important to develop systems that are efficient, fast and can handle highly concentrated solutions.

A techno-economic analysis by Torres et al. focused on the production of HMF from fructose in aqueous phase and reported an HMF minimum selling price (MSP) of 2.16 USD/kg.<sup>109</sup> This MSP was determined by estimating a cost of fructose at 1.52 USD/kg and a process that utilizes a mixture of MIBK and 2-butanol as the extracting

solvent as the base case. A study by Kazi et al.<sup>110</sup> examined the processes for production of HMF from fructose. A biphasic (aqueous–organic phases) continuously stirred tank reactor (CSTR) was utilized with 300 metric tons/day of fructose being processed. They found that the MSP for HMF to be 1.25 USD/kg. Additionally, they reported a 20% increase in HMF yield could reduce the MSP by 15.7%. The study uses a highly concentrated 30 wt% fructose feed and estimates 83% HMF yield. It is important to mention that in this study, the costs of utilities and waste management is calculated as purchased from a third party, and the cost of storage facilities for raw materials, products and waste are not calculated, which can considerably increase total installed equipment costs, legal fees, utilities, and construction expenses. Both of these studies used HCl as model catalyst, which might also lead to increased maintenance and waste management costs.

These results highlight the importance of developing a process that can utilize cheap, sustainable feedstock and catalysts that can help reduce the production price of HMF and its derivate products. Further research into catalytic systems that can handle highly concentrated substrate solutions would greatly benefit the market viability of HMF as a platform chemical. Additional studies similar to the ones mentioned in this section are needed to assess the feasibility of catalytic systems.

## 2.10 Conclusion

This review overviews that the mechanism for fructose dehydration to HMF is likely controlled by the tautomeric distribution of fructose, with the fructofuranose form being the intermediate. While there has not been a direct study of this, it is a likely mechanism as HMF production is largely influenced by the temperature and solvent of the system. However, this review does not include the HMF yields of fructose dehydration for DMSO systems that have not been de-aerated. This is due to the formation of Bronsted acids which catalyze the system instead of the proposed catalyst. Early experimentation focused mainly on obtaining HMF using homogeneous Brønsted catalysts such as HCl and H<sub>2</sub>SO<sub>4</sub>. It is necessary to use a Bronsted acid to effectively catalyze the reaction; however, these catalysts do damage to the overall process. The use of heterogeneous catalysts, like resins, silica supported acids, or carbonaceous catalysts has become more prominent as they are less corrosive to the reactors and can be separated easier. Newer solid catalysts are being developed to have unique porosity and functionality which can improve HMF production.

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### Chapter 3

Unifying Mechanistic Analysis of Factors Controlling Selectivity in Fructose  
Dehydration to 5-Hydroxymethylfurfural by Homogeneous Acid Catalysts in Aprotic  
Solvents

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Svenningsen, Glen S.; Kumar, Rajeev; Wyman, Charles E.; Christopher, Phillip.  
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### 3.1. Abstract

The need for liquid fuels from inexpensive and abundant biomass sources continues to increase in light of the growing environmental and strategic consequences of relying on depletable petroleum. Fructose, a monomeric sugar derived from biomass, can be dehydrated to 5-hydroxymethylfurfural (HMF), an intermediate to furans that are high-energy-content compounds miscible with petroleum. To be economically competitive, production of HMF from fructose must achieve high selectivities and yields, but the design of catalysts that achieve high-yield HMF production is made difficult by the lack of understanding of the mechanistic aspects of fructose conversion to HMF. Various studies examining fructose conversion to HMF by homogeneous acids have proposed that different factors control selectivity, including the acid type, fructose tautomer distribution, and solvent type. A high-throughput system was utilized to develop detailed insights into mechanisms and factors controlling HMF selectivity from fructose dehydration by homogeneous acid catalysts. The high-throughput system utilized a 96-well Hastelloy plate reactor to facilitate the development of extensive data over a range of aqueous solvent systems, temperature, time, acid types, and acid concentrations. In situ NMR was also employed to analyze the relative distribution of fructose tautomers as a function of solvent type and temperature. HMF selectivity was directly correlated with the distribution of furanose and open-chain tautomers of fructose as a function of reaction temperature, time, and solvent composition. The observed correlation supported the hypothesis that selectivity in fructose conversion to HMF is primarily controlled by the equilibrium between the tautomeric forms of fructose in solution. Further, it was



identified that difructose anhydrides act as slow-converting, protective intermediates that increase HMF production during longer reaction times to a selectivity higher than that which would be predicted by the fructose tautomeric distribution alone.

### **3.2. Introduction**

CO<sub>2</sub> accumulation in the atmosphere resulting from the consumption of non-renewable petroleum resources can potentially be reduced by the transition to production of chemicals and fuels from renewable biomass feedstocks.<sup>1-4</sup> Biomass derived-furans have received attention as promising renewable intermediate chemicals, because they can be converted into an array of valuable fuels and chemicals.<sup>5-7</sup> Although furans can be produced directly from biomass at appreciable yields,<sup>8</sup> their production typically involves an initial liquid phase pretreatment coupled with biological conversion to release C5 and C6 sugars, such as xylose and glucose, followed by their selective conversion into value-added intermediates and chemicals.<sup>7,9-12</sup> 5-hydroxymethylfurfural (HMF) is a highly desirable chemical as it is an intermediate to attractive fuel components, such as furans<sup>13-15</sup> or alkanes.<sup>16</sup> Additionally, HMF can be oxidized to produce 2,5-furandicarboxylic acid (FDCA) and 2,5-bishydroxymethylfuran (BHMF),<sup>17</sup> which are potential derivatives for biopolymer production. Thus, polyesters and fuels can be derived from renewable biomass sources through HMF as an intermediate, although the commercial viability of these routes requires high yields in each process step.

The production of HMF from fructose has been of interest because higher HMF yields can be obtained from fructose compared to other sugar precursors.<sup>18</sup> The conversion of fructose to HMF involves three sequential dehydration steps and is

typically catalyzed by a Bronsted acid.<sup>19,20</sup> In addition to the pathway for HMF formation from fructose, various unwanted side reactions can be catalyzed by acids, which result in decreased HMF yields. For example, fructose and HMF can be converted to polycondensation products and humins through acid or base catalyzed degradation.<sup>21,22</sup> Furthermore, HMF can be rehydrated into formic acid (FA) and levulinic acid (LA). Previous studies have suggested that reaction temperature, catalyst choice, and solvent composition may all influence yields in fructose conversion to HMF. However, no comprehensive analyses have been applied to determine how reaction selectivity relates to process parameters through mechanistic insights.

A wide variety of Lewis and Bronsted acids, as both heterogeneous and homogenous catalysts, have been applied to dehydration of fructose.<sup>23–25</sup> Generally, heterogeneous acid catalysts are preferred due to their ease of separation. However, soluble polymers and humins foul heterogeneous catalysts, requiring regular catalyst regeneration. As a result, homogenous acids offer benefits as they are sufficiently inexpensive to avoid the need for costly catalyst regeneration. In particular, experiments that utilized mineral acids, such as sulfuric acid (H<sub>2</sub>SO<sub>4</sub>) or hydrochloric acid (HCl), have shown the highest HMF yields compared to other homogeneous acids.<sup>6</sup> Previous studies have proposed that HMF selectivity in fructose dehydration may be influenced by Bronsted acidity,<sup>26</sup> or that the acid anion may be involved in stabilizing carbocation intermediates that lead to HMF formation.<sup>9</sup> Effects associated with anion stabilization of carbocation intermediates should be more noticeable in aprotic solvents, as anions are less solvated in these systems compared to water and therefore more reactive.<sup>27</sup> However,

direct comparisons of Bronsted acid anion influences on HMF formation in aprotic solvents have been not reported.

In addition to the potential influence of acid catalyst characteristics, efforts have been made to analyze how HMF production from fructose is influenced by solvents including water,<sup>19,26,28,29</sup> alcohols,<sup>30</sup> aprotic solvents,<sup>9,31-36</sup> ionic liquids (ILs),<sup>37-39</sup> and organic co-solvent mixtures.<sup>30,40-42</sup> Aqueous systems have received the most attention, however, HMF yields have generally been reported to be low (<65%) due to HMF rehydration to LA and FA and humins production. Polar aprotic solvents have been utilized as co-solvents in aqueous systems to increase HMF production.<sup>5-7</sup> For example, it was reported that the addition of 20 wt% dimethyl sulfoxide (DMSO) to an aqueous biphasic system increased fructose conversion from 91% to 94% and HMF selectivity increased from 60% to 67%.<sup>40</sup> Higher contents of DMSO have shown to increase selectivity to HMF to above 80%.<sup>42</sup> These outcomes are clear evidence that the solvent significantly influences both the rate and selectivity of fructose dehydration. However, the majority of reports that utilize DMSO as a solvent have been performed in the presence of oxygen, with the result that DMSO will undergo radical decomposition at temperatures > 80°C to form methyl sulfonic acid and other acidic species.<sup>43</sup> As a result, it is unclear whether DMSO or acid produced from DMSO is the primary cause of increased HMF production. The use of other aprotic solvents such as dimethyl acetamide (DMA),<sup>9</sup> N-methyl-2-pyrrolidone (NMP),<sup>44</sup> and dimethyl formamide (DMFA)<sup>45</sup> have also been reported to enable high HMF yields from fructose when catalyzed by homogeneous acids. Developing mechanistic insights into why these aprotic solvents

enable high selectivity for HMF production is critical for the design of optimized fructose conversion processes.

Various mechanistic studies have attempted to understand the primary pathway for HMF formation from fructose and identify elementary steps that dictate selectivity and reaction rates.<sup>6,46,47</sup> Results from *in-situ* <sup>13</sup>C NMR spectroscopy have led to the conclusion that cyclic intermediates are the primary species that lead to HMF formation.<sup>33,48,34</sup> The exclusive involvement of cyclic intermediates in HMF formation supported a proposed mechanism based on the fructofuranose tautomer (fructose can exist in pyranose, furanose, and open chain tautomeric forms) being the primary fructose tautomer that leads to HMF formation, due to their similar five-member ring structures. This hypothesis is supported by broader trends observed across solvent systems, for which the tautomeric distribution of fructose in solution has been proposed to control HMF selectivity.<sup>30,32,40</sup> In this proposed mechanism, it has been suggested that the fructofuranose form dehydrates to HMF, while the fructopyranose form dehydrates to humins.<sup>35,49</sup> However, to date, no conclusive relationship has been demonstrated between the tautomeric distribution of fructose in solution and HMF selectivity. As a result, there is a lack of mechanistic insights to guide the design of optimal catalysts and solvents for HMF production.

To develop detailed insights into factors that control HMF selectivity in fructose dehydration by homogeneous acids in aprotic solvents, a high-throughput reactor was employed to allow an extensive kinetic analysis from application of a variety of solvent systems, reaction conditions, acid types, and acid concentrations. In particular, we

focused on DMSO solutions due to the high HMF yields reported in previous studies. In addition to kinetic analyses, *in-situ*  $^{13}\text{C}$ -NMR experiments were utilized to quantify the distribution of fructose tautomers in solution as a function of reaction conditions. The results of this study are expected to serve as a guide for the rational design of HMF producing processes with maximized yields. Through these mechanistic studies, it was concluded that fructose dehydration in DMSO solvent systems must be executed under deaerated conditions to avoid production of acidic species by DMSO oxidation. Furthermore, these systematic kinetic analyses showed that the primary factors controlling selectivity are temperature, solvent composition, and time. The observed HMF selectivity was quantitatively correlated with distribution of fructose existing in the furanose form under reaction conditions. This supports the hypothesis that fructofuranose dehydrates to HMF and the fructopyranose degrades to humins, while the open chain form rapidly equilibrates to maintain a constant furanose/pyranose ratio that controls selectivity. Further, it was identified that difructose anhydrides (DFAs), oligomers of fructose, act as slow converting, protective intermediates that increase HMF production during longer reaction times to selectivity higher than what would be predicted by the tautomeric distribution.

### **3.3. Experimental Detail**

#### **3.3.1. Materials**

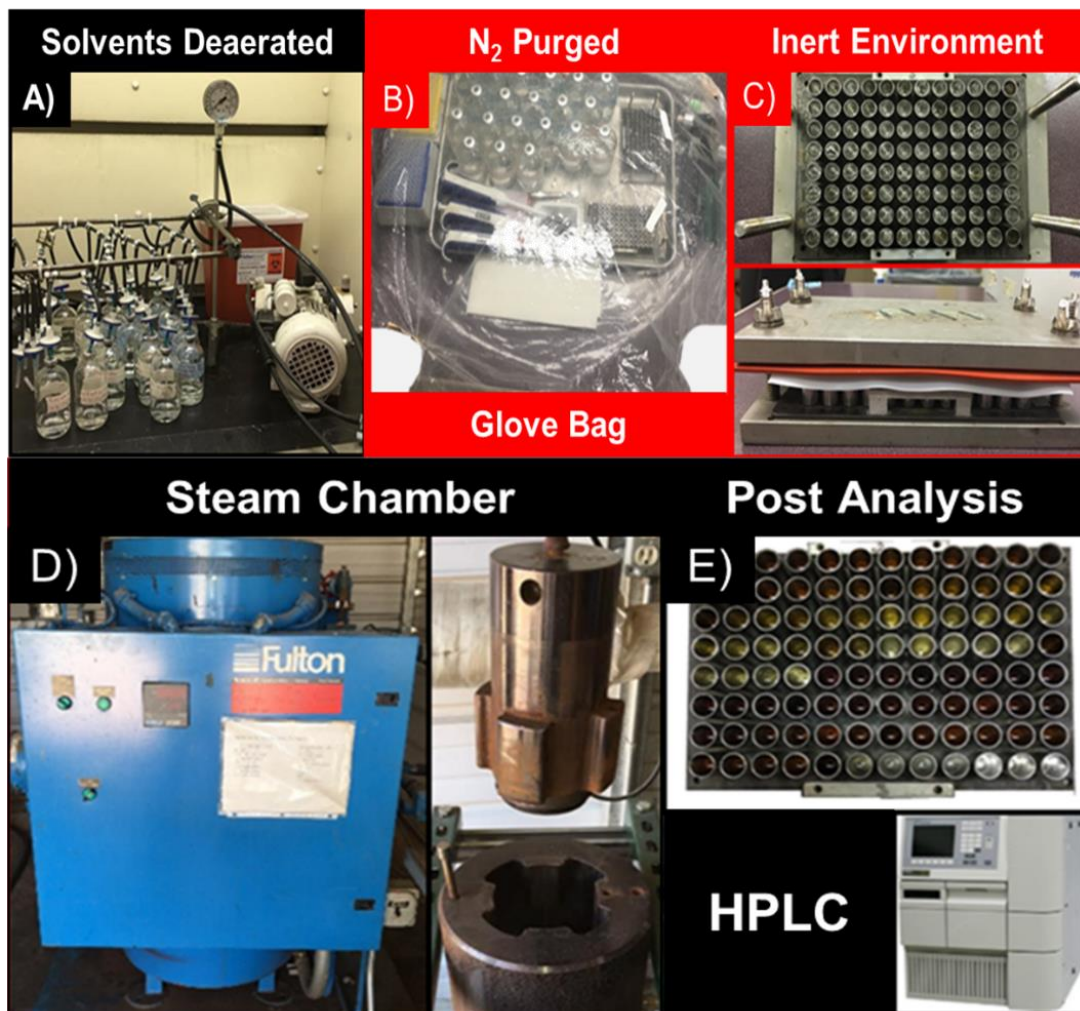
The following materials were purchased from Sigma Aldrich (Carlsbad, CA): D-fructose ( $\geq 99\%$ ), glucose ( $\geq 99\%$ ), DMSO (99.995%), NMP ( $\geq 99.5\%$ ), DMA ( $\geq 99\%$ ), DMF ( $\geq 99.8\%$ ), HMF ( $\geq 99\%$ ), levulinic acid (LA) ( $\geq 97\%$ ), formic acid (FA) ( $\geq 95\%$ ),

hydrochloric acid (HCl, 37%), hydrobromic acid (HBr, 48%), hydriodic acid (HI, 57% ), N-methyl -2-pyrrolidinone-d9 (NMP-d6, 98 %), and N,N-dimethylformamide-d7 (DMFA-d6,  $\geq 99.5\%$ ). Sulfuric acid (H<sub>2</sub>SO<sub>4</sub>,  $\geq 99.999\%$ ) and nitric acid (NO<sub>3</sub>, 70%) were purchased from Fisher Scientific. D-[2-<sup>13</sup>C]-Fructose (>99%), DMSO-d6 (99.9%), and deuterium oxide (D<sub>2</sub>O, 99.96%) were purchased from the Cambridge Isotope Lab (Tewksbury, MA) and N,N-Dimethylacetamide-d9 (DMA-d9,  $\geq 99\%$ ) from CDN Isotopes (Pointe-Claire, QC). All chemicals were used without further purification.

### **3.3.2. High-Throughput Procedure for Fructose Dehydration Studies**

Aqueous dipolar aprotic solutions (EMD<sup>®</sup> Millipore<sup>®</sup> Milli-Q<sup>®</sup>) were prepared in a graduated flask with 25 g/L fructose and 10 mM of acid, unless otherwise stated. Solutions were prepared in open air, loaded into 100 ml serum bottles (Supelco<sup>®</sup>), sealed with a Teflon rubber stopper and crimped in position with open-center aluminum crimp. As shown in Figure 3.1a, the serum bottles were then taken to a custom-made Schlenk line, where they were degassed and purged with N<sub>2</sub> for 25 cycles to remove excess air from the solutions. The serum bottles and the custom-made Hastelloy 96 well-plate (Figure 3.1b) were loaded into a two-hand, non-sterile glove bag (Aldrich<sup>®</sup> AtmosBag). The custom 96 well-plate has the same dimensions as a standard well-plate;<sup>50</sup> however, the individual wells are removable and made from Hastelloy bars cut to a length of 23.14 mm and the core milled to a well volume of 640  $\mu$ L. The glove bag was purged and degassed by N<sub>2</sub> for 25 cycles. Once oxygen was removed from the bag, the bottles were decrimped and desired solutions were loaded into the 96-well plate by pipet, under N<sub>2</sub>, see Figure 3.1c. The wells were then sealed by direct contact with Teflon<sup>®</sup> PTFE film

(0.012" thick, durometer hardness R58) and Silicone gasket (thickness 1.5875 mm, durometer hardness A40), which were compressed onto the wells by two 304 stainless steel well-plates using four 1/4 inch-20 threaded bolts (6.35 mm-20) placed in each corner of the plate together with spring washers (flat load 1,500 N) and wing nuts. The 96 well-plate was then sealed within the glove bag before being removed. The well-plate was then placed in a custom made high pressure vertical chamber that was heated by saturated steam generated in a 75 kW boiler (FB-075-L Fulton Companies, Pulaski, NY) at the appropriate pressure and temperature, **Figure 3.1 (d)**. When the desired reaction time was reached, the steam inlet valve was closed, steam was released from the chamber, and the chamber was filled with cool water to quench the reaction. The plates were then unsealed and the reaction solution was pipetted into vials for high pressure liquid chromatography (HPLC) analysis, **Figure 3.1 (e)**. All similar experiments follow the same deaerating, loading, reaction, and analysis procedure. The molar water content was determined by the volume of water added plus the water content within both the organic solvent and fructose added. Each experiment was run with four replicates, where four of the 96 wells were filled with identical sample solutions.



**Figure 3.1.** Experimental procedure for high-throughput fructose dehydration with control atmosphere. A) Multiple sealed pressure bottles containing desired solvents, acid, and fructose repeatedly degassed under vacuum and purged with nitrogen. B) 96- well plate reactor is enclosed in a glove bag purged with nitrogen, along with sealed vials containing deaerated reactants and solvents. C) While still in purged glove bag, reactor wells were loaded and sealed with Teflon film, silicone rubber, and steel plate (in listed order). D) The 96- well reactor was transferred to a steam chamber and heated with pressurized steam at controlled temperatures for controlled times. E) The 96-well reactor was unsealed and the solution was analyzed via HPLC.



### 3.3.3. Analytical Procedures

The majority of the resulting mixtures formed a single phase and were analyzed without dilution. For samples in which insoluble humins production was observed, the samples were centrifuged at 5000 rpm for 10 min (Allegra<sup>®</sup> X-15R Centrifuge, Beckman Coulter), and the solid free supernatant was analyzed for sugars, organic acids, and furan concentrations using a Waters<sup>®</sup> Alliance HPLC (model e2695, Waters Co., Milford, MA) equipped with a Waters<sup>®</sup> 2414 RI and PDA detector. The Aminex<sup>®</sup> HPX-87H column (Bio-Rad Life Science, Hercules, CA) utilized in the HPLC was conditioned at 65°C with a 5 mM sulfuric acid mobile phase at flow rate of 0.6 ml/min. The amounts of the fructose, HMF, and DFA were determined by comparison to measurements with external standards. The fructose conversion and product yields and selectivity were calculated according to the following equations:

$$Conv. (mol\%) = \left(1 - \frac{M_{RF}}{M_F}\right) * 100\% \quad (1)$$

$$Y_{HMF} (mol\%) = \left(\frac{M_{HMF}}{M_F}\right) * 100\% \quad (2)$$

$$Y_{DFA} (mol\%) = \left(\frac{2 * M_{DFA}}{M_F}\right) * 100\% \quad (3)$$

in which  $M_F$ ,  $M_{RF}$ ,  $M_{HMF}$ , and  $M_{DFA}$  represents the moles of initial fructose, remaining fructose, HMF, and DFA, respectively. Additionally,  $Y_{HMF}$  and  $Y_{DFA}$  are yields of HMF and DFA, respectively.

### 3.3.4. NMR Study of D-Fructose and DFA Tautomeric Distributions

NMR spectra of the 2-[<sup>13</sup>C]-fructose tautomeric distribution were recorded on a Bruker Avance 600 spectrometer equipped with a 5 mm BBO variable temperature

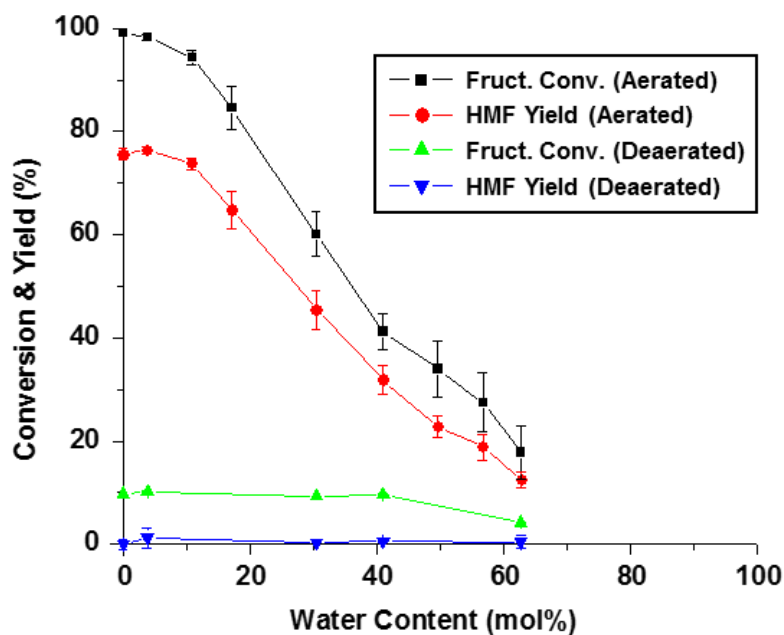
probe. The  $^{13}\text{C}$  NMR were obtained over 128 scans with a standard gradient pulse sequence and a relaxation delay of 10 s. The percentage of each tautomer was calculated and normalized with respect to one another, using Bruker TopSpin software. All samples were loaded into pressure bottles and deaerated, via the custom-made Schleck line described above. Within a deaerated glove bag, the samples were transferred into a Norell® valved 5 mm NMR tube (thick walled). The fructose tautomeric distribution in DMSO-d<sub>6</sub> (99.9%) was recorded at temperatures of 70, 80, 90, 105, 120, and 150°C using the variable temperature probe *in-situ*. Dehydration studies analyzing the tautomeric distribution of DFAs were carried out at 80°C in DMSO-d<sub>6</sub> with 10 mM H<sub>2</sub>SO<sub>4</sub>. The tautomeric distribution of 2- $^{13}\text{C}$ -fructose (25 g/L) was also analyzed in DMA-d<sub>9</sub>, NMP-d<sub>9</sub>, and DMFA-d<sub>9</sub> at 120°C.

### 3.4. Results

#### 3.4.1. Influence of Environment on HMF Yield

The role of DMSO oxidation and *in-situ* production of acidic species for the fructose dehydration reaction were analyzed in aqueous-DMSO mixtures containing fructose over a range of water molar percent without an acid catalyst at a temperature of 150°C for 30 minutes under aerated and de-aerated conditions. **Figure 3.2** reports the fructose conversion and HMF yields as a function of water molar percent in aerated and deaerated conditions. As shown, HMF was produced at significant yields for aerated conditions, while under deaerated conditions little to no HMF production was observed. This result contrasts with previous reports that stated DMSO acted as a catalyst that facilitated full fructose dehydration to reach high HMF yields.<sup>33,48</sup> This contradiction can

be accounted for by the thermal decomposition of DMSO above 80°C in the presence of oxygen<sup>43</sup> to produce acidic species, such as H<sub>2</sub>SO<sub>4</sub>, that can catalyze the reaction.<sup>35,43</sup> Additionally, it can be seen that under aerated conditions water content significantly hindered the conversion rates. However, water contents up to about 40 mol% had minimal impact on HMF selectivity, which remained roughly constant at 78%, in agreement with other reports of fructose dehydration in pure DMSO under aerated conditions.<sup>35</sup> The slight conversion of fructose under de-aerated conditions can be accounted for by the caramelization of fructose, indicated by an observed light brown color. Based on these results, subsequent experiments were performed strictly under de-aerated conditions to solely analyze the role of DMSO as a solvent.



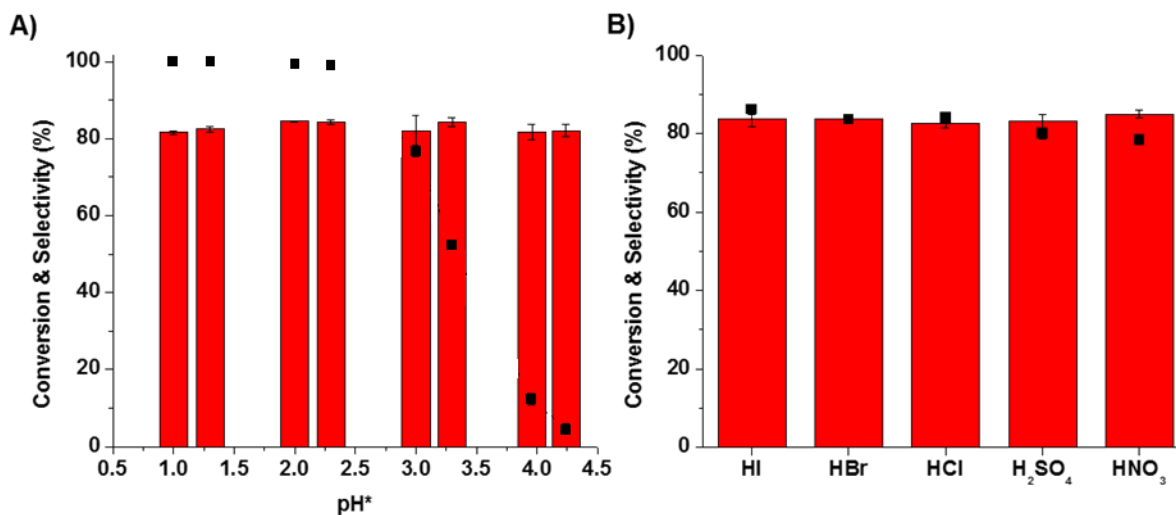
**Figure 3.2.** Conversion of fructose and yield of 5-HMF as a function of water content (mol%) in the DMSO mixture with a 25 g/L fructose loading and reaction volumes of 300  $\mu$ L in 600  $\mu$ L wells. Experiments were performed at 150°C for 30 mins after the solvent and head-space had been deaerated ( $\blacktriangle$ : fructose conversions;  $\blacktriangledown$ : 5-HMF yields) by nitrogen purging and with solvents and head-space without deaeration ( $\blacksquare$ : fructose conversions;  $\bullet$ : 5-HMF yields).

### 3.4.2. Influence of Acidity and Mineral Acid Type

Fructose conversion and HMF selectivity were measured as a function of calculated pH ( $\text{pH}^*$ ) that was determined based on  $\text{H}_2\text{SO}_4$  concentration added to the solution. The experiments were executed by filling the 96 well plate reactor with 25 g/L of fructose over a range of pH and holding the reactor at 150°C for 30 mins. **Figure 3.3 (a)** shows that the fructose conversion dropped with increasing pH, while the selectivity to HMF remained constant at between ~80-85%. Only trace amounts of LA and FA were

observed, as water is necessary for the conversion of HMF to LA and FA. Non-quantified products were mostly in the form of soluble humins, as evidenced by a deep dark color of the solution, and DFAs that are discussed further below. Importantly, it was observed that while fructose conversion varied significantly as a function of acid loading, the HMF selectivity remained essentially constant. The constant HMF selectivity as a function of fructose conversion provides evidence that HMF selectivity was controlled by a thermodynamic equilibrium, rather than by competing kinetic pathways.

In addition to the influence of acid loading, the effect of acid type was examined to determine if the weak base pair of the acid catalyst influenced the fructose dehydration reaction. In particular, the mineral acids HI, HBr, HCl, HNO<sub>3</sub>, and H<sub>2</sub>SO<sub>4</sub> were applied to catalyze fructose dehydration in DMSO mixtures at an acid loading of 10 mM, temperature of 120°C, and reaction time of 12.5 minutes. The results in **Figure 3.3 (b)** show that the selectivity to HMF was ~83% for all five acids. The rate of fructose conversion increased slightly from about 78% to 84% as the acid strength was increased. Because HI has a K<sub>a</sub> over 9 orders of magnitude higher than that of HNO<sub>3</sub> (3.9\*10<sup>9</sup> versus 2.4, respectively), the very small increase in conversion with significant variation in acid strength demonstrated that the initial protonation of fructose by a Bronsted acid is not the rate-limiting step in the reaction.

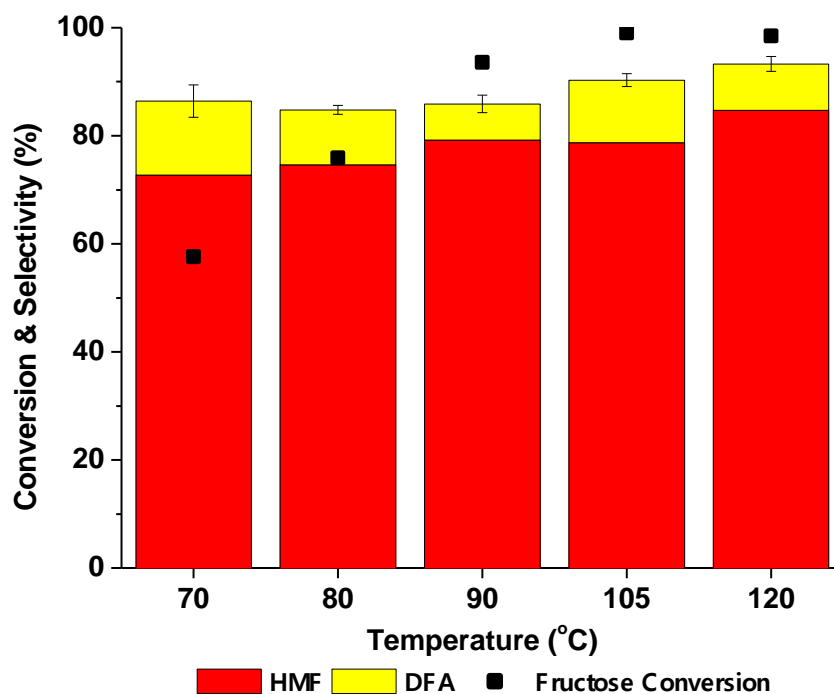


**Figure 3.3. A)** Fructose conversion (black dots) and HMF selectivity (bars) vs. the calculated pH (pH\*) based on initial H<sub>2</sub>SO<sub>4</sub> concentration for acid catalyzed dehydration of fructose in anhydrous DMSO at deaerated conditions. **B)** Effect of acid type on fructose conversion and HMF selectivity. For **A)**, H<sub>2</sub>SO<sub>4</sub> concentrations were varied from 0.01 to 100 mM and reactions were performed at 150°C for 30 mins. For **B)**, reactions were performed with 10 mM HI, HBr, HCl, H<sub>2</sub>SO<sub>4</sub>, and HNO<sub>3</sub> at 120°C for 12.5 minutes. All reactions were run with 25 g/L fructose in DMSO for reaction volumes of 300 μL in 600 μL wells, deaerated with nitrogen gas.

### 3.4.3. Influence of Temperature

Next, the influence of reaction temperature on fructose dehydration rate and selectivity was analyzed. Fructose was dehydrated for 30 mins in DMSO at temperatures of 70, 80, 90, 105, and 120°C at a fructose loading of 25 g/L and catalyst loading of 10 mM H<sub>2</sub>SO<sub>4</sub>. Two major products were identified and quantified by HPLC: DFAs and HMF, as shown in **Figure 3.4**. It was observed that selectivity to HMF increased from 74% to 84% as the temperature was increased from 70°C to 120°C. In contrast, DFA selectivity dropped with increasing temperature from 70°C to 120°C, but more directly decreased with increasing HMF selectivity, suggesting that DFAs serve as an

intermediate for HMF formation. Fructose conversion rates also increased with temperature. Unlike the effect of increasing acid loading, which did not change HMF selectivity, the selectivity to HMF increased with temperature. This result again suggests that HMF selectivity is thermodynamically controlled in aqueous DMSO mixtures.

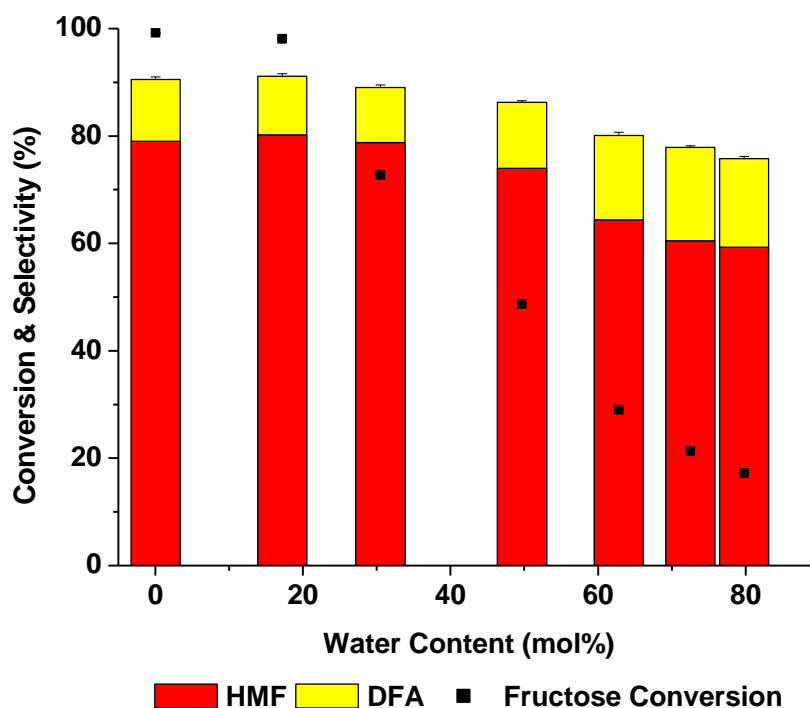


**Figure 3.4.** Fructose conversion (black dots), HMF selectivity (red bars), and DFA selectivity (yellow bars) for acid catalyzed dehydration of fructose in anhydrous DMSO under deaerated conditions. Reactions were performed at 70, 80, 90, 105, and 120°C. All reactions were performed with 25 g/L fructose in DMSO with reaction volumes of 300  $\mu\text{L}$  in 600  $\mu\text{L}$  wells, deaerated with nitrogen gas.

#### 3.4.4. Influence of Water Content

To determine how water content plays a role in HMF production, aqueous DMSO mixtures of 25 g/L fructose with 10 mM  $\text{H}_2\text{SO}_4$  were prepared in combination with water

amounts from ~0-80 mol% and heated at 105°C for 30 min. The results in **Figure 3.5** show that both DFA and HMF selectivity stayed roughly constant (~10% and ~80%, respectively) up to water contents of 40 mol%. Above 40 mol% water content HMF selectivity began to drop until it reached ~60% at a water content of 80%, at which point the DFA selectivity had increased to ~15%. Increasing water content was observed to also hinder fructose conversion. These results demonstrate that water content influences both HMF selectivity and yields.

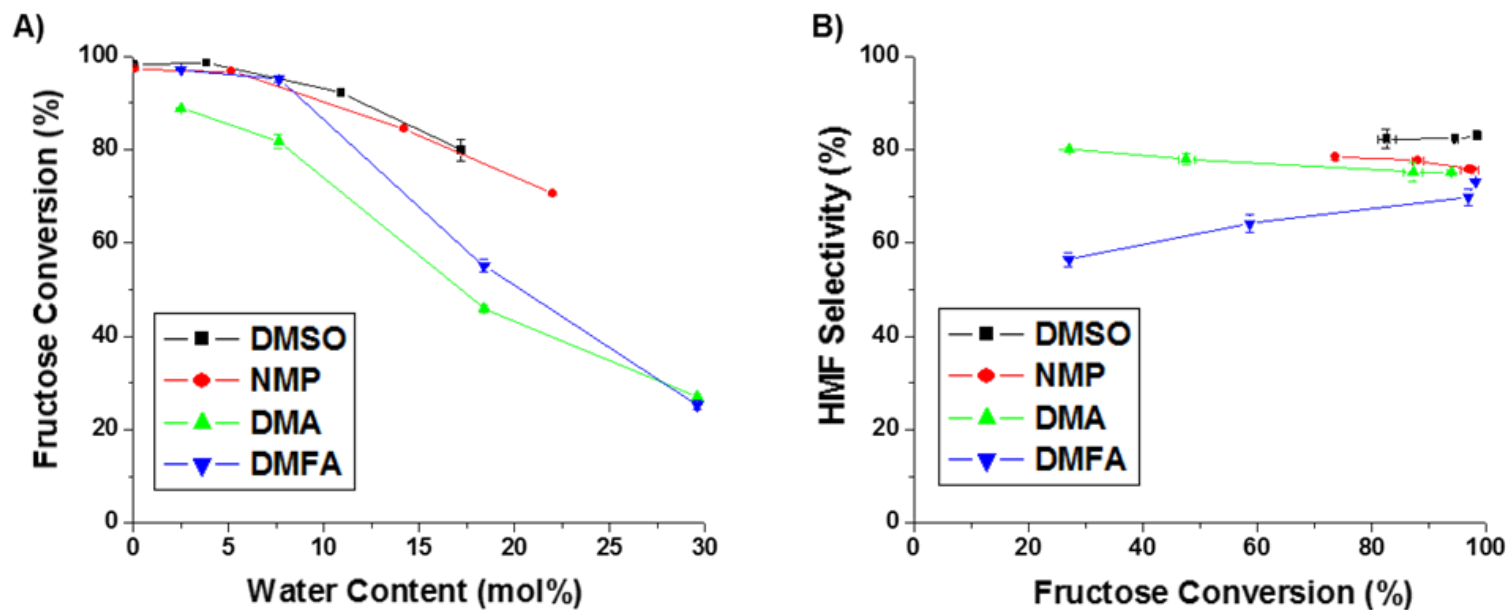


**Figure 3.5.** Fructose conversion (black dots), DFA selectivity, and HMF selectivity (red bars) for acid catalyzed dehydration of fructose with increasing water content (mol%) in DMSO mixtures under deaerated conditions. Reaction conditions: 25 g/L fructose in DMSO with 10 mM H<sub>2</sub>SO<sub>4</sub> at 105°C for 30 mins. 300 μL of solution was added to 600 μL wells that were then deaerated with nitrogen gas.



### 3.4.5. Effect of Solvent

To further understand the influence of the solvent environment, fructose dehydration reactions were performed in different aqueous dipolar aprotic mixtures with varying water content. 25 g/L of fructose was loaded into aqueous mixtures of DMSO, NMP, DMA, and DMF and heated to 120°C for 10 mins with 10 mM HCl as the acid catalyst. **Figure 3.6 (a)** shows fructose conversion as a function of water content (mol%) for each solvent, as water content was varied from ~ 0 to 30 mol%. In DMSO and NMP nearly identical fructose conversions were observed over a range of water contents, whereas fructose conversion in DMFA and DMA followed similar dependences on water content. In **Figure 3.6 (b)**, HMF selectivity is plotted as a function of fructose conversion for each of the aqueous solvent mixtures. Fructose conversion in DMSO was greatest at the lowest water content and exhibited the highest HMF selectivity (~84%), followed by DMA (~78%), NMP (~77%), and DMFA (~74%). For DMA, NMP, and DMSO, the HMF selectivity did not change with fructose conversion, consistent with the observation that below ~40% water content, solvent composition had little influence on HMF selectivity. The drop in HMF selectivity in DMFA with increasing water content will be discussed in more details later.



**Figure 3.6.** A) Conversion of fructose as a function of water content (mol%) and B) 5-HMF selectivity as a function of fructose conversion for DMSO (black), NMP (red), DMA (green), and DMFA (blue). Experiments were performed in 10 mM HCl catalyst for 10 min with de-aerated solvent and head-space.

To summarize the observations from these studies:

- (1) Operating in de-aerated DMSO solutions without additional acid resulted in no observable fructose conversion. This outcome demonstrated that DMSO is itself not a catalyst that can drive fructose conversion and further that the influence of DMSO on HMF production must be a solvent effect.
- (2) Acid loading and acid strength (type) had no measurable influence on HMF selectivity, whereas variations in reaction temperature and solvent composition (type of solvent and aqueous dilution above 40%) influenced HMF selectivity.
- (3) DFA formed and its selectivity tended to drop as HMF selectivity increased, suggesting DFA is an intermediate to HMF formation.

In the following discussion, a unifying mechanism will be developed to explain how the experimentally observed rate and selectivity of fructose dehydration to HMF are controlled.

### **3.4.6. Mechanism of Fructose Dehydration**

The dehydration of fructose to HMF has been previously reported for DMSO systems with and without an added acid catalyst.<sup>6</sup> Previous reports suggested that DMSO acts as both a catalyst and as a solvent.<sup>33</sup> However, it is known that DMSO undergoes radical decomposition in the presence of oxygen at elevated temperatures to form acidic species.<sup>34,43</sup> To determine the effect of DMSO decomposition on HMF production, fructose dehydration in aqueous DMSO mixtures was compared for aerated and de-aerated conditions without adding an acid catalyst. HMF production was only observed under aerated conditions in all aqueous mixtures while minimal fructose conversion

(<10%) was observed, likely due to sugar degradation. This result demonstrates that DMSO does not act as a catalyst by itself. HMF production can be attributed to *in-situ* production of acidic species (e.g., H<sub>2</sub>SO<sub>4</sub>, CH<sub>3</sub>SO<sub>3</sub>H) that then catalyze fructose dehydration to HMF. These results demonstrate conclusively that obtaining accurate kinetic and mechanistic understanding of fructose conversion in DMSO solvent mixtures requires de-aerated conditions.

Several mechanistic pathways have been proposed for acid catalyzed dehydration of fructose to HMF in aqueous and aprotic systems in attempts to identify the selectivity controlling factors. For example, Akien et al.<sup>35</sup> based on application of <sup>13</sup>C NMR to fructose dehydration in DMSO suggested that the homogenous acid catalyzed dehydration of fructose has two irreversible pathways: 1) fructofuranose to HMF and 2) fructopyranose to humins. It was proposed that these pathways could be linked by a secondary equilibrium formed after protonation between the fuctosyl cation intermediates. This equilibrium was justified by the observed formation of 2,6-anhydro-b-D-fructofuranose that was thought to be reversibly formed between the carbocation intermediates.<sup>35</sup> Additionally, it has been proposed by both Zhang et al.<sup>34</sup> and Binder et al.<sup>9</sup> that the carbocation intermediates or charged nucleophiles could form complexes with a dipolar aprotic solvent. This complexation can possibly lower energy barriers and stabilize intermediates from unwanted side reactions, promoting HMF production and selectivity.<sup>34</sup> While various assertions have been made regarding factors that could control HMF selectivity, such as the tautomeric distribution controls selectivity,<sup>35</sup> no previous direct quantified analysis demonstrated how reaction pathways control HMF

selectivity or the direct influence of reaction conditions (e.g., temperature, solvent composition).

In this study, increasing sulfuric acid concentration primarily impacted the rate of HMF production, but not HMF selectivity. Over a range of sulfuric acid loadings at 150°C for 30 mins, the selectivity to HMF held steady at roughly 80% over all fructose conversions (**Figure 3.3 (a)**). This result suggests that HMF selectivity is independent of the acid catalyzed rate-limiting step. Additionally, comparison of several strong mineral acids in aqueous DMSO mixtures (**Figure 3.3 b**) showed minor variations in HMF selectivity - from 81 to 85% over a range of fructose conversions. If the anions of these mineral acids played a role in stabilizing intermediates, then HMF selectivity would be expected to change significantly with acid catalyst type. Thus, the mineral acid catalyst had a minor effect on the selectivity to HMF in aqueous DMSO mixtures. The differences in the conversion of the dehydration reactions can be accounted for by the strength of the acid. However, even though the strength of the acids varied by several orders of magnitude, the type of acid had minimal effect on conversion. This result demonstrates that the initial protonation step for fructose conversion to a cation intermediate is not rate-limiting. Furthermore, the fact that HMF selectivity remained constant as fructose conversion increased with acid loading demonstrated that selectivity is controlled by a thermodynamic equilibrium prior to the rate-limiting step. Overall, our results clarify mineral acid catalysts control the rate of fructose dehydration to HMF but do not control selectivity to HMF.

The temperature dependent analysis of fructose dehydration in DMSO shown in **Figure 3.4** resulted in two important observations. First, both the rate of fructose conversion and selectivity to HMF increased with temperature, further supporting the hypothesis that HMF selectivity is thermodynamically controlled by an equilibrium before the rate-limiting step. Second, selectivity to DFAs decreased with increasing temperature, and the decrease in DFA selectivity was roughly compensated by an increase in HMF selectivity. This result indicates that DFA is a secondary pathway intermediate to form HMF.

To elucidate the relationship between fructose tautomeric distribution and HMF selectivity, we proposed that the fraction of fructose existing in the furanose form controls HMF selectivity, whereas the pyranose form of fructose degrades to humins. Furthermore, because the equilibration between the furanose, pyranose, and open-chain forms of fructose is very rapid, we also proposed that the fraction of open-chain fructose that ultimately converts to HMF or humins is dictated by the existing furanose/pyranose ratio. Based on this hypothesis equation 6 was developed, in which  $\theta_{HMF}$  represents the predicted HMF selectivity based on the tautomeric percentages of furanose ( $\theta_F$ ), open chain ( $\theta_{OC}$ ), and pyranose forms of fructose( $\theta_P$ ):

$$\theta_{HMF} = \theta_F + (\theta_{OC}) * \frac{\theta_F}{\theta_F + \theta_P} \quad (6)$$

To understand whether variations in HMF selectivity as a function of reaction temperature could be explained on the basis of variations in equilibrated fructose tautomeric distributions, *in-situ*  $^{13}\text{C}$  NMR spectroscopy of solutions containing D-[2- $^{13}\text{C}$ ]-fructose dissolved in DMSO at temperatures of 70, 80, 90, 120, and 150°C and the

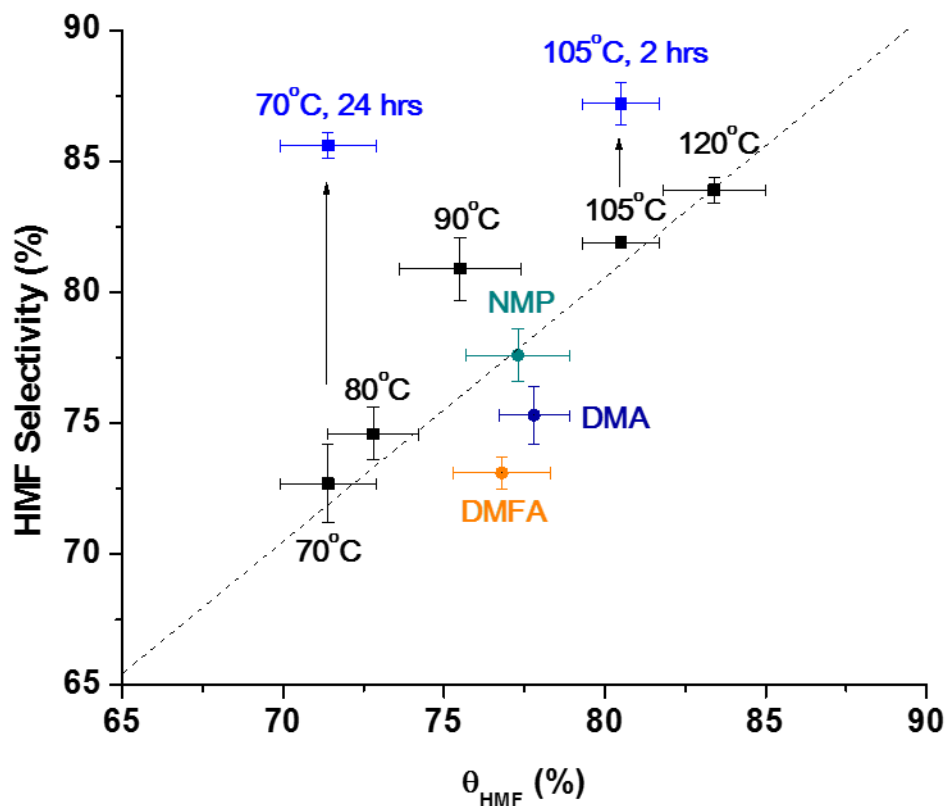
fraction of fructose existing in the furanose, pyranose, and open-chain tautomers were quantified. A parity plot of the predicted selectivity ( $\theta_{HMF}$ ) measured by NMR versus the actual selectivity from the dehydration experiments is shown in **Figure 3.7** for fructose dehydration in DMSO at several different temperatures and a reaction time of 30 minutes (black dots). There is an excellent agreement between the predicted and measured HMF selectivity, with the parity plot showing a slope of close to 1. Both the NMR predicted selectivity and experimentally measured selectivity increased with temperature due to shifting of the fructose tautomeric equilibrium toward the fructofuranose form. The strong correlation between NMR predicted and measured HMF selectivities provides direct evidence that selectivity is controlled by the branching ratio of the furanose and pyranose forms of fructose, which are in equilibrium, and dehydration of the fructopyranose form leads to humins while dehydration of the fructofuranose form directly converts to HMF.

To determine whether the dependence of HMF selectivity on solvent composition could also be quantitatively predicted by the tautomeric distribution, fructose dehydration catalyzed by HCl was compared in DMSO, NMP, DMA, and DMFA, and  $\theta_{HMF}$  was measured in each solvent at 120°C. As shown in **Figure 3.6**, HMF selectivity was the highest in DMSO followed by NMP, DMA, and DMFA. Correlation between the measured HMF selectivity and NMR predicted HMF selectivity at 120°C in each solvent is also included on the parity plot in **Figure 3.7**. **Figure 3.7** shows that the measured solvent dependent HMF selectivity is predicted quite well by  $\theta_{HMF}$  from NMR measurements. The agreement between the predicted HMF selectivity from the

tautomeric distribution and the measured selectivity as a function of reaction temperature and solvent composition is strong evidence that HMF selectivity is primarily controlled by the fraction of fructose existing in the furanose form under reaction conditions. Differences in the tautomeric distribution between solvents can be attributed to the solvents interaction with fructose. NMP, DMA, and DMFA have similar solvent properties, each including an amide group and their polarity indexes are similar, 6.7, 6.5, and 6.4, respectively. However, DMSO contains a sulfoxide group rather than amide and a higher polarity index of 7.2. This suggests that either the polarity of DMSO or specific interactions between the sulfoxide group and fructose promote enhanced stabilization of the furanose form by DMSO and thus higher HMF selectivity.<sup>48, 51</sup>

Additionally, water content was observed to play a significant role in HMF production as seen in **Figure 3.5**. It was observed that selectivity to HMF remained roughly constant (~80%) up to water contents around 40 mol% then decreases with further increasing water content. It is likely that DMSO is able to preferentially solvate fructose molecules, creating a solvation shell, which hinders interaction of the fructose with surrounding water molecules.<sup>52</sup> This could prevent the tautomeric distribution of fructose from shifting towards fructopyranose due to increasing water; however, at certain water content, the DMSO solvation shell weakens allowing for water to interact with fructose. This would shift the tautomeric equilibrium towards the pyranose forms of fructose, lowering HMF selectivity.





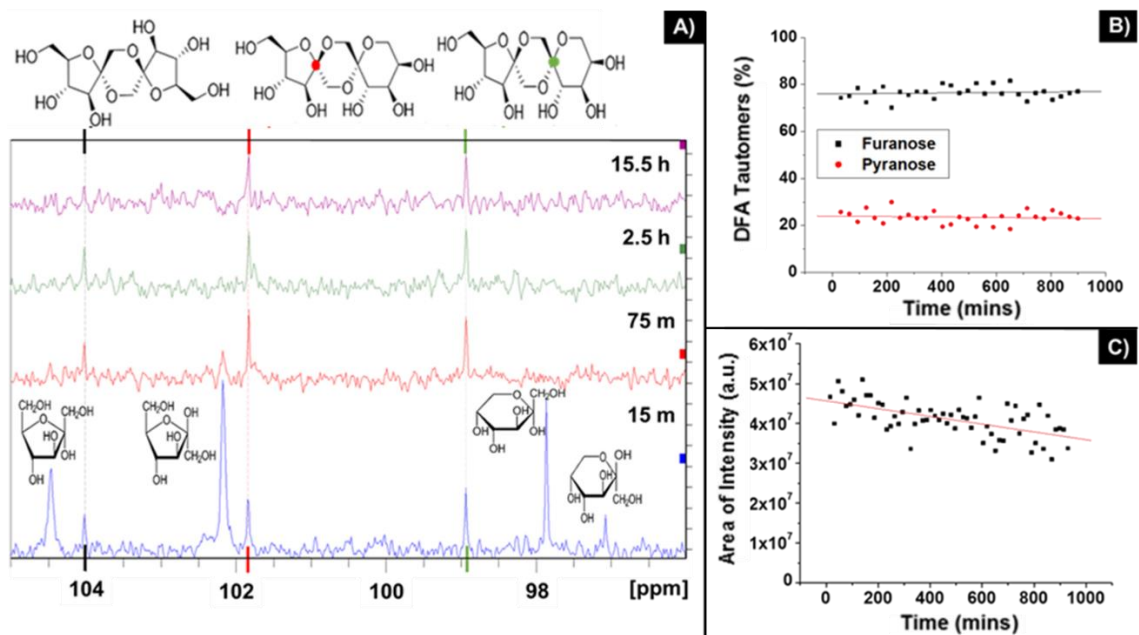
**Figure 3.7.** Experimentally observed HMF selectivity plotted as a function of  $\theta_{HMF}$ , the HMF selectivity predicted from the NMR measurements. Black squares represent experiments performed in DMSO with 10 mM H<sub>2</sub>SO<sub>4</sub> at a reaction time of 30 minutes at temperatures of 70, 80, 90, 105, and 120°C. Blue squares represent experiments in DMSO with 10 mM H<sub>2</sub>SO<sub>4</sub> over longer durations: 24 hours for 70°C and 2 hours for 105°C. Fructose dehydration in 10 mM HCl in NMP (green), DMA (navy blue), and DMFA (orange) were run at 120°C for 10 min. All reactions and NMR experiments were carried out with 25 g/L fructose under de-aerated conditions.

While  $\theta_{HMF}$  based on the NMR measured fructose tautomer distribution was an excellent predictor of the influence of solvent composition and reaction temperature at short reaction times, this correlation cannot account for DFAs produced during fructose dehydration or the conversion of DFAs to HMF over long reaction times. It was observed

that DFAs were consumed at longer reaction times, and as a result the selectivity to HMF increased proportionally. Results in **Figure 3.7** that show that HMF selectivity increased for longer reaction times, which was not predicted by the NMR measurements of the fructose tautomer distribution. This outcome suggests that either all DFAs are in the furanose form or that DFAs are a protective intermediate to HMF production by blocking the humins pathway.

It has been proposed that DFA production occurs after the first dehydration step of fructose.<sup>30</sup> In that mechanism, fructose is first dehydrated to a fructosyl cation intermediate, which can then react through a parallel and reversible pathway with another fructose molecule. The result is a strong six-membered ring between the two fructose tautomers. Two primary DFA tautomers can form from fructose: 1) fructofuranose-fructofuranose anhydride or 2) fructofuranose-fructopyranose anhydride. Due to the stable six member ring structure of DFAs, hydrolysis of DFAs back to fructose tends to be comparatively slower than fructose conversion to HMF.<sup>53</sup> This slower reverse reaction is evidenced by our observations of the presence of significant quantities of DFAs (~10% yields) at near quantitative conversions of fructose. Thus, DFAs can possibly isolate fructose tautomers from equilibrating in solution and slowly release fructose through reversible acid catalyzed hydrolysis. Therefore, it has been suggested that DFAs could act as a protective intermediate, preventing sugar degradation and increasing selectivity to HMF more than expected, based on the estimated tautomeric distribution.<sup>30</sup> It may also be possible that HMF is formed directly from DFAs as an intermediate; however, this process would likely be far slower than direct conversion from fructose.<sup>53</sup>

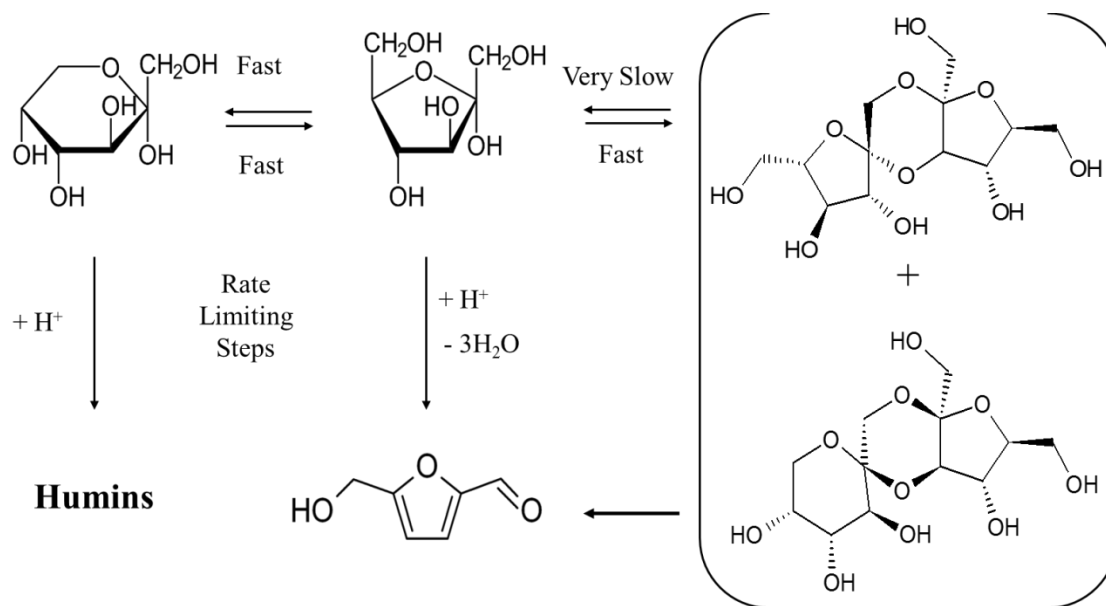
To examine how DFAs increase HMF selectivity, NMR studies were employed to measure the tautomeric distribution within DFAs for acid catalyzed dehydration of 2-[C-13]-fructose in D6-DMSO at 80°C. **Figure 3.8 (a)** shows *in-situ* C-13 NMR spectra for 15 min, 75 min, 2.5 hours, and 15.5 hours of reaction. At 15 min, fructose tautomers were still seen and had not been fully consumed, consistent with the data in **Figure 3.4**. However, after 75 mins, all the fructose had been converted into either HMF or DFAs. The DFA signals for the two 2-[C-13]-carbons can be seen for fructofuranose-fructofuranose dianhydride, and the two distinct 2-[C-13]-carbon signals for the fructofuranose-fructopyranose dianhydride are observed. These signals were seen throughout the reaction due to the stable structure of DFA, slowly undergoing hydrolysis to fructose, or directly converting to HMF instead of fructose. **Figure 3.8 (b)** shows the tautomeric distribution of the fructose monomers in DFAs over time is roughly constant at ~78% fructofuranose and 22% fructopyranose, a result consistent with the tautomeric distribution of fructose in solution under these reaction conditions. Additionally, the slow consumption of DFAs in **Figure 3.8 (c)** suggests that DFAs acted as a protective intermediate to HMF formation and while those containing the fructopyranose form seem to hinder its degradation to humins.



**Figure 3.8.** A) Selected <sup>13</sup>C-NMR spectrums for times of 15 min, 75 min, 2.5 h, and 15.5 h. B) furanose and pyranose DFA tautomeric percentages over time from 0 to 900 min. C) Total <sup>13</sup>C NMR area of DFA peaks over time from 0 to 900 min. For <sup>13</sup>C-NMR, the dehydration of 2-<sup>13</sup>C-fructose was performed in 10 mM H<sub>2</sub>SO<sub>4</sub> in deaerated DMSO-d<sub>6</sub> solution at 80°C.

Our results suggest the main factors controlling HMF selectivity are the fructose tautomeric distribution and the protective nature of DFAs. Scheme 3.1 below highlights our proposed simplified mechanism controlling selectivity to HMF. A fast equilibrium exists between the fructose tautomers in solution that can be shifted towards the furanose form of fructose by increasing temperature or changing the solvent environment to dipolar aprotic solvents. The dehydration of fructopyranose leads to humins formation while fructofuranose leads to HMF. Several past studies have proposed that HMF can form through the acyclic pathway. However, our results suggest that the open chain form remains relatively unreactive, as the ratio between the furanose and pyranose forms were the primary controllers of HMF selectivity, likely due to a faster rate of tautomerization

between the acyclic tautomer and the cyclic tautomers than any acyclic conversion pathways.<sup>29</sup> Additionally, a secondary pathway to HMF involves the formation of DFAs, which act as a protective intermediate. While it is not clear how DFAs convert to HMF, either by hydrolyzing back to fructose or by directly converting to HMF, it is clear that DFAs increase selectivity to HMF at longer reaction times.



**Scheme 3.1.** Proposed simplified mechanism of the acid catalyzed dehydration of fructose.

### 3.5. Conclusions

In this study, the influence of reaction conditions (de-aeration, acid type/loading, water concentration, temperature, time, and solvent composition) on acid catalyzed fructose dehydration to HMF was systematically analyzed. The experimental results, along with *in-situ* NMR analysis, suggest that the primary factor controlling selectivity in this reaction is the fructose tautomer distribution under reaction conditions, which were most effectively controlled by varying reaction temperature and solvent composition. Furthermore, it was demonstrated that elucidation of the role of environmental conditions

on fructose dehydration in DMSO requires application of de-aerated conditions to mitigate *in-situ* oxidation of DMSO to form acids. Additionally, it was shown that selectivity is controlled secondarily by the formation of DFAs that slowly convert to HMF under reaction conditions, acting as a protective intermediate. By understanding the primary factors that control selectivity, the development of higher yielding processes and conditions can be developed for conversion of fructose to HMF.

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## **Chapter 4**

### **Designing Micro-Environments in Porous Silica Supports via Surface Functionalization for Increased HMF Production**

#### 4.1 Abstract

Fructose dehydration to 5-hydroxymethylfurfural (HMF) in dimethylsulfoxide (DMSO) has reported the highest HMF yields compared to other solvent systems; however, due to the high energy costs to separate HMF from DMSO, it is not economically viable. In contrast, higher-volatile solvents, such as tetrahydrofuran (THF), are more economical to separate, but have lower HMF yields. To raise HMF yields, we aim to attach sulfoxide groups with acidic sulfonic acid groups on the surface of a porous silica supports to mimic the acidic environment in DMSO, while in aqueous THF mixtures. An organic silane, (3-Mercaptopropyl)trimethoxysilane (MPTMS), was utilized to graft acidic and sulfoxide sites on the surface of porous silica by co-condensation. Three silica particles of differing porosities were compared: 30, 60, and 150 Angstrom. The thioether group of MPTMS was either oxidized by  $\text{H}_2\text{O}_2$  to a sulfonic acid group or reacted with iodomethane and then oxidize to produce methyl sulfoxides on the surface. By varying the amount of iodomethane ( $\text{ICH}_3$ ), the ratio of sulfonic acid groups and sulfoxide groups was controlled. Then these changing functional groups were assessed by Raman spectroscopy. The materials were studied and compared in the selective dehydration of fructose to 5-hydroxymethylfurfural (HMF). These reactions were performed in a 1:1 THF to water solution at  $120^\circ\text{C}$ . The 150 A diameter pores showed the highest selectivity to HMF which was further increased by the increase amount of iodomethane, 40% with 1000 mg  $\text{ICH}_3$ / 250 mg MPTMS-silica to 66% selectivity with 1000 mg  $\text{ICH}_3$ / 250 mg MPTMS-silica. We propose this increase is due to microenvironments formed in the pores that mimic acid dehydration in DMSO.

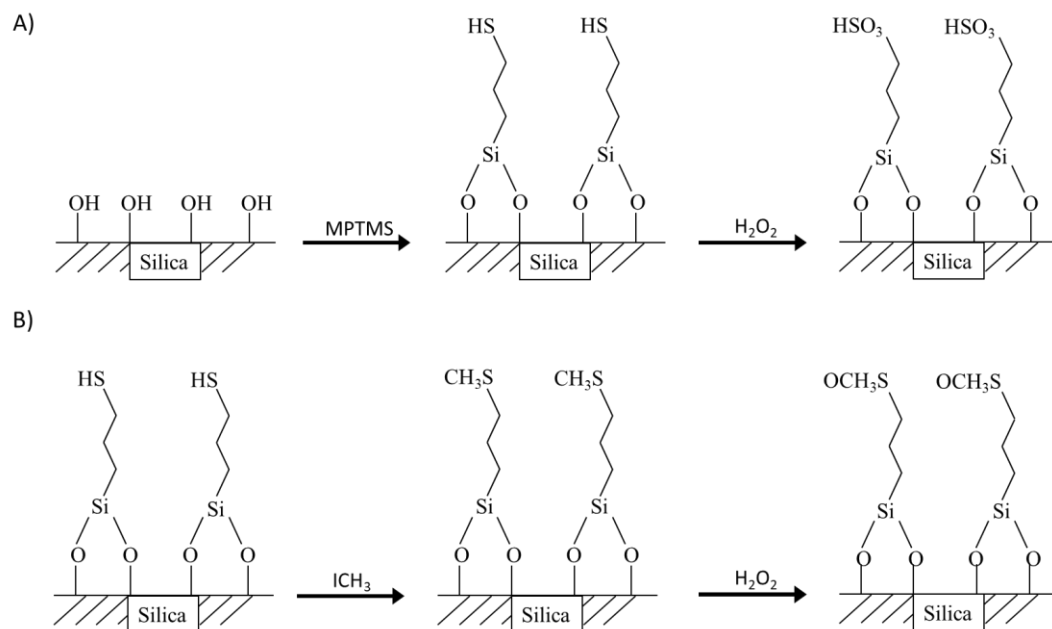
## 4.2 Introduction

Acid catalyzed fructose dehydration to 5-hydroxymethylfurfural (HMF) in dipolar aprotic solvents, such as dimethylsulfoxide (DMSO), have demonstrated some of the highest HMF yields and production rates. It has been proposed that the fructofuranose form is the direct intermediate to HMF, while other isomers of fructose lead to unwanted degradation products.<sup>1</sup> DMSO has been demonstrated to shift the isomeric distribution to the fructofuranose form; thus, increasing HMF production and selectivity.<sup>2</sup> Additionally, it has been reported that DMSO creates strong solvation shells around DMSO, protecting it from hydrolysis to levulinic acid (LA) and formic acid (FA), as well as, polymeric degradation reactions.<sup>3</sup> However, the isolation of HMF from DMSO is far too energy intensive to be commercially practical.<sup>4</sup>

In order to overcome the separation costs of extracting HMF, low boiling point solvents are necessary. However, acidic aqueous solutions produce major byproducts that are soluble oligomers and insoluble humins, as well as FA and LA formed by rehydration.<sup>5</sup> Moreover, low boiling point solvents, such as tetrahydrofuran (THF), cannot dissolve fructose to practical concentrations.<sup>6</sup> Aqueous mixtures of THF and water have demonstrated higher yields of HMF compared to pure water; however, they are still far lower than reported yields in DMSO.<sup>7</sup> Therefore, unique catalysts must be developed to selectively increase the concentration of the fructofuranose form and dehydrate to HMF.

Mesoporous silica can be functionalized to generate unique microenvironments within the porous structure.<sup>8</sup> This can be accomplished with organic silanes reacting onto the surface of silicas. The reactivity of the functionalized silica depends on the nature and extent of surface functionalization, pore structure, and pore dimensions.<sup>9–11</sup> Grafting occurs when the functional groups are incorporated by addition of an organosilane with surface silanols.<sup>12</sup> Silanes and siloxanes can attach to the surface of silica producing grafted sites that are typically bound by two siloxane bonds.<sup>13,14</sup> Past reports have demonstrated that SBA-15-type materials with differing particle morphologies<sup>15</sup> have pronounced changes in their catalytic properties.<sup>7,16</sup> For example, longer retention of a substrate inside the pore channels may alter product selectivity.

Here, we show that it is possible to increase HMF selectivity by functionalizing silica surfaces with functional groups similar to DMSO. This was accomplished by grafting 3-mercaptopropyl-trimethoxysilane (MPTMS) to mesoporous silica. The surface thiols can then be converted to methyl-thioethers by the addition of  $\text{ICH}_3$ , with the ratio of thiol to thioether controlled by the amount of  $\text{ICH}_3$  added. Afterwards, hydrogen peroxide solutions were used to convert the thiols to sulfonic acid and the thioether to methylsulfoxide (**Figure 4.1**). The ratio between sulfonic acid and sulfoxide groups on the surface was varied and utilized as the catalysts, in 1:1 THF, water solutions, for fructose dehydration. Additionally, we report the effect of pore size on HMF production by determining the change in fructose conversion and HMF selectivity with sulfonic acid functionalized catalysts.



**Figure 4.1.** A) Functionalization of silica surface with 3-mercaptopropyl-trimethylsiloxane, followed by oxidation to propyl-sulfonic acid by hydrogen peroxide. B) Conversion of mercaptopropyl-functionalized silica to 3-methylthioether-functionalized silica by iodomethane, followed by oxidation to 3-methyl-propyl-sulfoxide by hydrogen peroxide.

### 4.3 Experimental Methodology

#### 4.3.1 Reagents and Materials

3-mercaptopropyl-trimethoxysilane (MPTMS, 95%), fructose ( $\geq 99\%$ ), Iodomethane ( $\geq 99\%$ ), dimethylformamide (DMFA,  $\geq 99.8\%$ ), toluene ( $\geq 99\%$ ), THF ( $\geq 99\%$ ), and 3-mercaptopropyl-functionalized silica gel (200-400 mesh) were purchased from Sigma Aldrich. THF and MilliQ water were mixed into a high-pressure bottle and deaerated by vacuum and purging three times with nitrogen gas.

#### 4.3.2 Catalyst Synthesis

3-Mercaptopropyl-functionalized silica was generated by refluxing a ratio of 4 mL/mg of MPTMS/silica at  $115^\circ\text{C}$  in toluene (20 mL for 250 mg silica) over 8 hrs. All catalysts



were then filtered and washed with 5 mM HCl water and ethanol then dried in an oven 105°C. Thioethers were generated by refluxing ICH<sub>3</sub> with the 3-mercaptopropyl-functionalized silica in dimethylformamide (20 mL of DMFA for 250 mg catalyst) at 80°C for 8 hrs. Afterwards, the catalyst was filtered, washed, and dried as before. Lastly, the catalyst was reacted with 25 wt% H<sub>2</sub>O<sub>2</sub> at 100°C for 6 hrs. The catalyst was then filtered, washed and dried.

#### 4.3.3 Dehydration Reactions

Solutions of 1:1 THF, water solutions of 50 mg/ml fructose were prepared in open air, loaded into 100 ml serum bottles (Supelco<sup>®</sup>), sealed with a Teflon rubber stopper and crimped in position with open-center aluminum crimp. The serum bottles were then taken to a custom-made Schlenk line, where they were degassed and purged with N<sub>2</sub> for 5 cycles to remove excess air from the solutions. 2 ml of solution was loaded into a 5 ml Hastelloy tube reactor under a N<sub>2</sub> environment with a 1 cm long magnetic stir bar and catalyst and sealed. The tube reactors were placed in a silicon oil bath and heated at 120°C and stirred by the magnetic stir bar. The reactors were taken out and cooled by a water bath, dried, and solution was allowed to settle. The solution was decanted from the solid catalyst by pipette and filtered for analysis.

#### 4.3.4 Analytic Procedures

The majority of the resulting mixtures formed a single phase and were diluted by 1/4<sup>th</sup> with milliQ water and analyzed by high pressure liquid chromatography (HPLC). Samples were centrifuged at 5000 rpm for 10 min (Allegra<sup>®</sup> X-15R Centrifuge, Beckman Coulter), and the solid free supernatant was analyzed for sugars, organic acids, and furan

concentrations using a Waters® Alliance HPLC (model e2695, Waters Co., Milford, MA) equipped with a Waters® 2414 RI and PDA detector. The Aminex® HPX-87H column (Bio-Rad Life Science, Hercules, CA) utilized in the HPLC was conditioned at 65°C with a 5 mM sulfuric acid mobile phase at flow rate of 0.6 ml/min. The amounts of the fructose and HMF were determined by comparison to measurements with external standards. The fructose conversion and product yields and selectivity were calculated according to the following equations:

$$Conv. (mol\%) = \left(1 - \frac{M_{RF}}{M_F}\right) * 100\% \quad (1)$$

$$Y_{HMF} (mol\%) = \left(\frac{M_{HMF}}{M_F}\right) * 100\% \quad (2)$$

in which  $M_F$ ,  $M_{RF}$ ,  $M_{HMF}$ , and represents the moles of initial fructose, remaining fructose, HMF, and DFA, respectively. Additionally,  $Y_{HMF}$  is the yield of HMF.

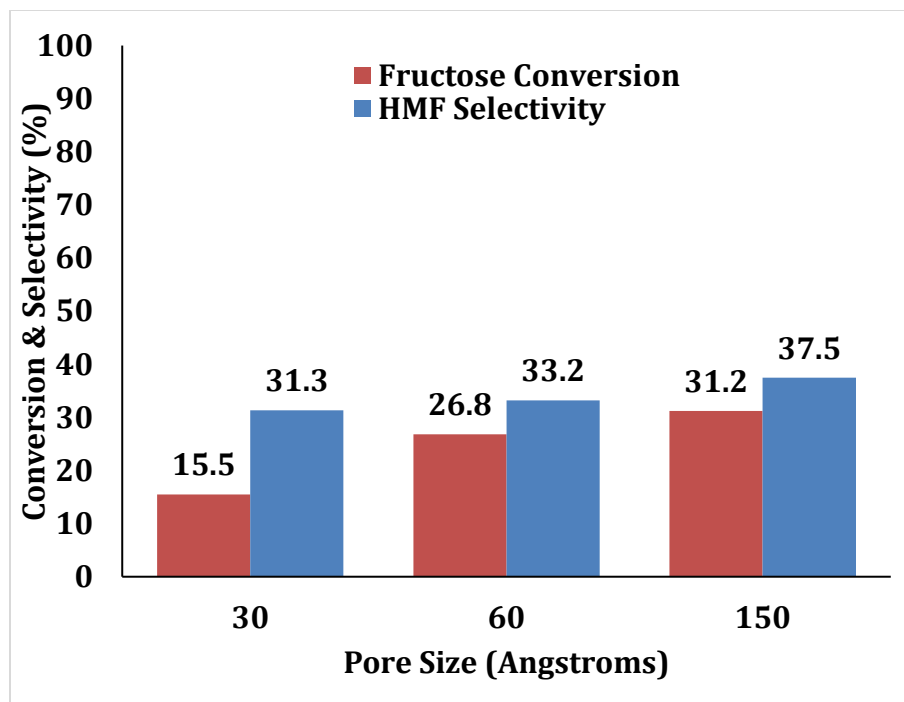
#### 4.3.5 Raman Spectroscopy

Raman spectroscopy measurements between were carried out at room temperature using the Raman spectrometer Dilor XY laser Raman with imaging microscope using a 532 nm diode laser. The spectra were obtained by focusing the laser beam through a 500 micron objective, with a numerical aperture close to 1. The laser power at the samples surface was kept below 5 mW. Samples were loaded into a capillary tube and spectrum was collected with an acquisition time of 2 s and a accumulation of 2.

## 4.4 Results & Discussion

We first theorized that in order to increase selectivity to HMF the majority of the acid catalyzed dehydration would need to occur within the pores. Thus, determining the

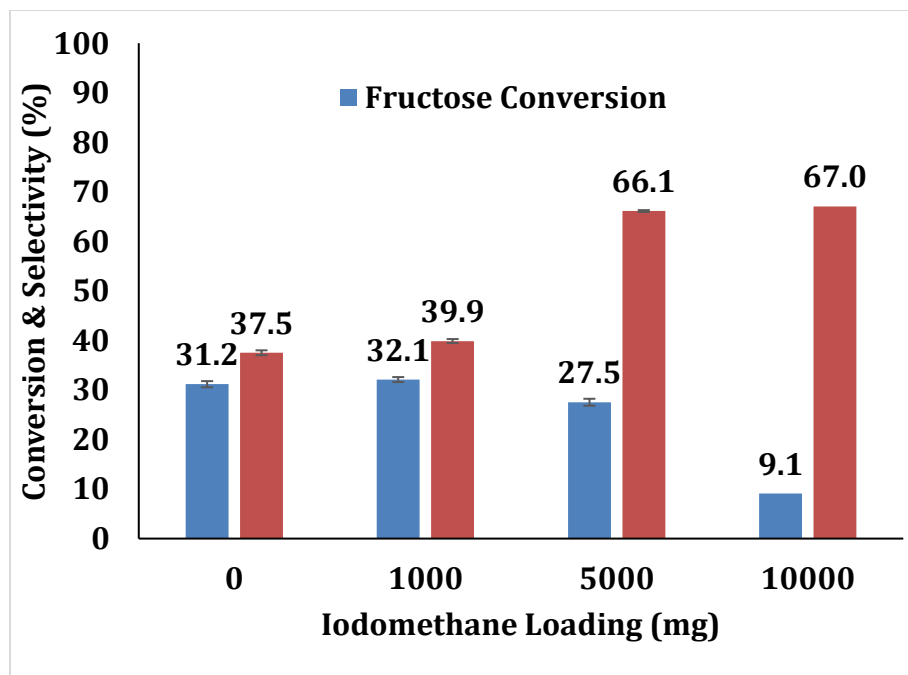
optimum pore size is essential as a unique microenvironment is to be generated throughout the pore channels that should promote the formation of the fructofuranose isomer. Thus, we first grafted MPTMS on the surfaces of 3 silica supports with varying pore diameter sizes: 30, 60, 150 angstroms. Then through H<sub>2</sub>O<sub>2</sub> treatment the thiol groups were converted to sulfonic acid groups. These catalysts were utilized to dehydrate fructose (50 mg/ml) at 120°C for 8 hrs. **Figure 4.2** demonstrates that the silica with 150 Å pore diameter had both higher HMF selectivity (37.5%) and higher fructose conversion (31.2%) than the 60 Å and 30 Å. Due to the higher conversions rates as pore size increases, it is likely that the smaller pore openings are blocked by the grafting of the MPTMS on the surface. Therefore, the silica support particles with 150 Å pore diameters was utilized for varying the ratio of sulfoxide groups to sulfonic acid groups grafted on the surface of the silica supports.



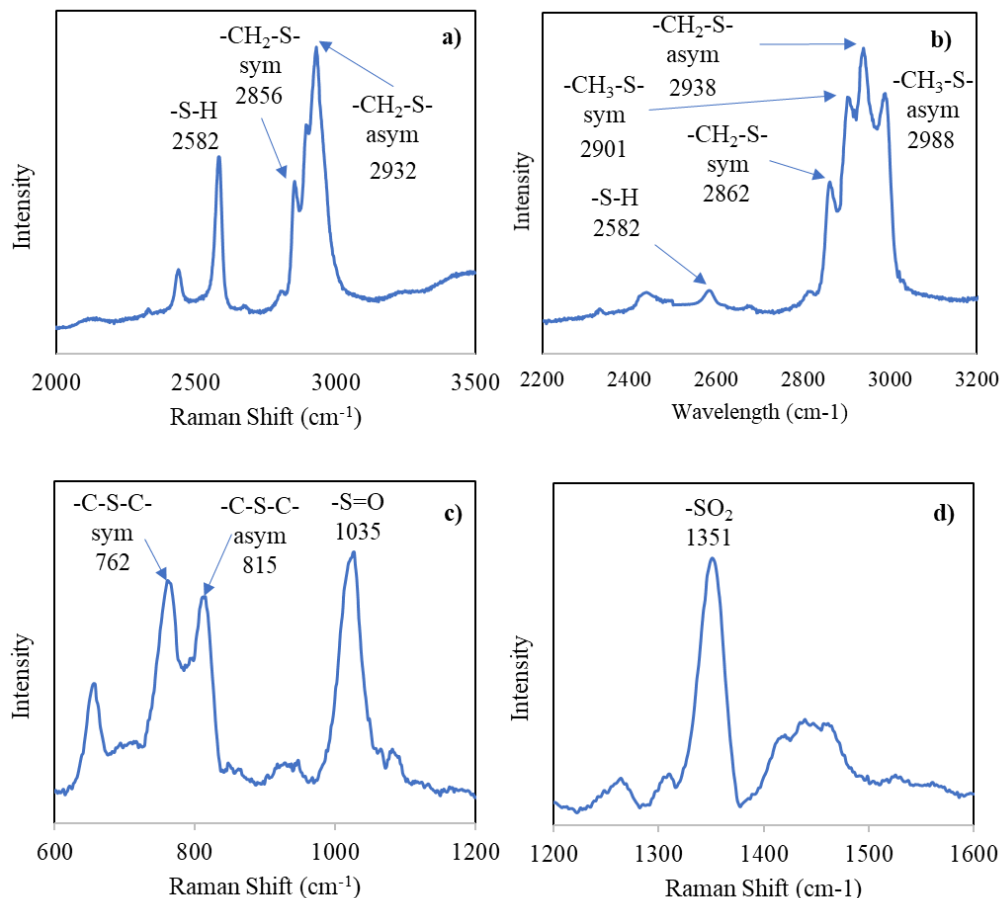
**Figure 4.2.** Fructose conversion and HMF selectivity over average silica pore diameter. Reactions were performed with sulfonic acid-functionalized silica. Reactions were performed with 50 mg/ml fructose dissolved in 1:1 (v:v) THF, water mixtures at 120°C for 8 hrs. The catalysts were loaded at 50 wt% to fructose.

The next goal was to determine how varying the loading of iodomethane effects HMF production. By oxidizing the thiols and methyl-thioether groups on the surface, we controlled the ratio between sulfonic acid and sulfoxides on the surface. We hypothesized that sulfonic acid groups surrounded by a sufficient number of methyl-sulfoxide groups on the surface could generate a micro-environment in the pores similar to that found in homogeneous acidic DMSO. By varying the loading of ICH<sub>3</sub>, we developed a qualitative approach to determine how iodomethane loading impacts fructose conversion and HMF selectivity. **Figure 4.3** demonstrates the change in fructose conversion and HMF selectivity for 0, 1000, 5000, and 10,000 mg iodomethane loading to 250 mg of

mercaptopropyl-functionalized silica. For loadings, of 0 and 1000 iodomethane there was little to no change in the conversion (~31-32%) or the selectivity (~38-40%); however, at a loading of 5000 mg the selectivity rises to 66.1% and the conversion drops to 27.5%. As the loading increased to 10,000 mg, fructose conversion dropped to 9.1%, while the selectivity to HMF remained the same. These results can be explained by the decreasing ratio between sulfonic acid groups/methyl-sulfoxide groups. We hypothesize that the increase in selectivity is due to the increased sulfoxide groups in the pores, shifting the isomeric distribution to the fructofuranose form. Furthermore, the decrease in conversion can be attributed to the decrease in the amount of acid sites per silica, as the sulfonic acid groups are replaced by the sulfoxide groups. This leads to a likely optimized ICH<sub>3</sub> loading between 1000 mg and 5000 mg for 250 mg of mercaptopropyl-functionalized silica.



**Figure 4.3.** Iodomethane loading vs fructose conversion and HMF selectivity. Reactions were performed with functionalized silica. Reactions were performed with 50 mg/ml fructose dissolved in 1:1 (v:v) THF, water mixtures at 120°C for 8 hrs. The catalysts were loaded at 50 wt% to fructose.

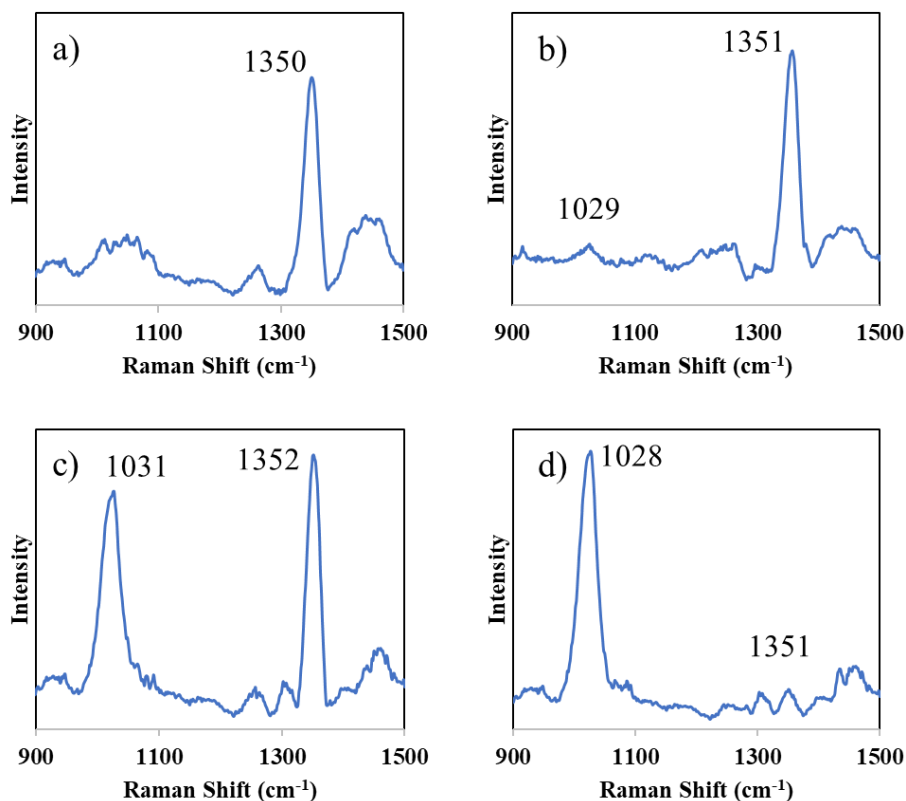


**Figure 4.4.** Raman spectrum of functional silica (pore diameter of 150 Å): a) 3-mercaptopropyl-functionalized silica, b) 3-methyl-propyl-sulfide-functionalized silica (250 mg 3-mercaptopropyl-functionalized silica treated with 5000 mg ICH<sub>3</sub>), c) methyl-propyl-sulfoxide-functionalized silica (3-methyl-propyl-sulfide-functionalized silica treated with 25wt% H<sub>2</sub>O<sub>2</sub>), d) propyl-sulfonic acid functionalized silica (3-mercaptopropyl-functionalized silica treated with 35wt% H<sub>2</sub>O<sub>2</sub>).

Raman spectroscopy was utilized to detect the surface functionalization on the surface of the silica supports, as the sulfur containing organic groups are easily detected due to their fairly intensive Raman scattering. In **Figure 4.4 (a)**, the characteristic Raman shifts of the mercaptopropyl-functionalized silica are observed. The strong band at 2582 cm<sup>-1</sup> in the upper spectrum is evidence that the thiol residue is attached to the silica support. This

band is assigned to the -SH stretching mode of the mercaptopropyl segment.<sup>17</sup> It appears between 2544 and 2583  $\text{cm}^{-1}$  depending upon its local environment. The -CH stretching vibration bands occur between 2850–3000  $\text{cm}^{-1}$  due to the presence of propyl chain these are observed at 2856 and 2932  $\text{cm}^{-1}$ . **Figure 4.4 (b)** shows the Raman spectrum of methylpropylsulfide-functionalized silica. The conversion of the thiol to a methyl sulfide group is observed by the vanishing of the peak at 2582  $\text{cm}^{-1}$  and the appearance of the symmetric and asymmetric methyl sulfide stretches at 2901 and 2988  $\text{cm}^{-1}$ , respectively.<sup>18</sup> **Figure 4.4 (c)** demonstrates the presence of sulfoxides on the surface of the silica, as the characteristic S=O peak is observed at 1035  $\text{cm}^{-1}$  with the symmetric and asymmetric -C-S-C- bonds at 762 and 815  $\text{cm}^{-1}$ , respectively.<sup>18</sup> The sulfonic acid peak is characterized by the 1351  $\text{cm}^{-1}$  peak in **Figure 4.4 (d)**.<sup>18</sup>





**Figure 4.5.** Raman spectrum of functional silicas (initial pore diameter of 150 Å): a) mercaptopropyl-functionalized silica (250 mg) treated with 0 mg ICH<sub>3</sub> and oxidized by H<sub>2</sub>O<sub>2</sub>, b) mercaptopropyl-functionalized silica treated with 1000 mg ICH<sub>3</sub> and oxidized by H<sub>2</sub>O<sub>2</sub>, c) mercaptopropyl-functionalized silica treated (250 mg) with 5000 mg ICH<sub>3</sub> and oxidized by H<sub>2</sub>O<sub>2</sub>, d) mercaptopropyl-functionalized silica treated (250 mg) with 10000 mg ICH<sub>3</sub> and oxidized by H<sub>2</sub>O<sub>2</sub>.

Raman spectroscopy helped to further illustrate the effect of ICH<sub>3</sub> loading on the surface functionality. **Figure 4.5 (a), (b), (c), and (d)** are the Raman spectra for mercaptopropyl-functionalized silica treated with 0, 1000, 5000, and 10000 mg, respectively, then oxidize with H<sub>2</sub>O<sub>2</sub>. The characteristic sulfonic acid peak at 1351 cm<sup>-1</sup> is observed in **Figure 4.5 (a), (b), and (c)**; however, **Figure 4.5 (d)** demonstrates the loss of the sulfonic acid group; while the sulfoxide group is maintained, as seen by the peak at

1028  $\text{cm}^{-1}$ . Moreover, the ratio of the sulfoxide to the sulfonic acid peak increases with  $\text{ICH}_3$  loading as observed by the growth of the peak at 1028  $\text{cm}^{-1}$

#### **4.5 Conclusion**

Here we demonstrate that the porosity and surface functionality of mesoporous silica supports can be utilized to increase the production and selectivity to HMF from fructose. By utilizing a simple synthetic process, sulfonic and sulfoxide groups were grafted on the surface by varying the loading of  $\text{ICH}_3$  followed by oxidation via  $\text{H}_2\text{O}_2$  treatment. These functional groups and the ratio between these two groups were observed by characteristic Raman shifts. The Raman spectrums revealed the emergence of a sulfoxide peak and a decrease in the sulfonic acid peak as the  $\text{ICH}_3$  loading increased. By utilizing silica with sufficiently large pores (150 Å diameter pores), transport and grafting of the  $\text{MPTMS}$  into the pore occurred, generating DMSO-like microenvironments within the porous structures. At a sufficient ratio of sulfoxides to sulfonic acid groups on the surface, the selectivity to HMF increased from roughly 32% to 66%; however, due to the reduced acid sites we saw a decrease in conversion. We propose that these sulfoxide groups within the pores of the silica support increase the fructofuranose, which is then dehydrated to HMF by the close proximity sulfonic acid groups. Further work is needed to optimize the synthetic procedure to lower the  $\text{ICH}_3$  loadings and find the optimized loadings to balance fructose conversion and HMF selectivity.

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## **Chapter 5**

### **Techno-Economic Analysis of the Acid Catalyzed Conversion of Fructose to DMF**

## 5.1. Abstract

Laboratory scale catalytic processes have been demonstrated to convert biomass-derived fructose to HMF and then hydrogenated to DMF at high yields. These tests have been performed in a single-phase aqueous solution of water and THF. The advantage to utilizing a single-phase solution is the ability to run a continuous stream without expensive separation steps between the dehydration and hydrogenation reactors to produce HMF and DMF, respectively. Additionally, DMF is not soluble in an aqueous stream and can be decanted and distilled without the need for an extracting solvent. Here we present a simplified plant process for converting 500 tonne/day of fructose, aimed to operate for 20 years. Installed equipment costs are estimated as \$4.9 million for the DMF process. The dehydration of fructose to HMF utilizes an acidic catalyst capable of 75% yields, the initial loading of the catalyst was estimated to cost \$20 million and a 99.5% recovery. These parameters averaged over 20 years amounted to \$3,420,000/year. Additionally, DMF process uses a copper–ruthenium–carbon (Cu–Ru/C) catalyst with initial capital cost at \$35 million and a 99.9% recovery that averaged \$1,890,000/year, over a 20-year period. Cost analysis is performed following the discounted cash flow method. The minimum selling price for DMF is estimated as \$1.74/kg (\$1.9/l). Sensitivity analyses are performed to assess the relative importance of key assumptions on minimum DMF selling prices. The most significant parameters are feedstock cost, product yields, catalyst cost and total purchased equipment costs.

## 5.2. Introduction

As CO<sub>2</sub> levels continue to rise at an ever-increasing rate, political and environmental concerns have grown regarding fossil fuel consumption and its future consequences. There has been growing interest towards the conversion of renewable carbon sources, such as biomass, to develop high yielding and economical processes for the sustainable production of fuels and chemicals, typically derived from petroleum.<sup>1-3</sup> In recent years, research has focused towards reductive upgrading of biomass-derived sugars to drop-in fuel additives, such as furans. Furans are more suitable for the transportation sector than ethanol due to their specific physical properties. One furan of particular interest is dimethylfuran (DMF). Compared to ethanol, DMF has a 40% higher energy density, a 20 K higher boiling point, and is immiscible with water.<sup>4</sup> Additionally, DMF can also be a renewable source of furan based compounds which have widespread use in the industrial solvent and pharmaceutical industry.<sup>5</sup>

The production of DMF from lignocellulosic biomass begins with the pretreatment of lignocellulosic biomass to separate cellulose, hemicellulose, and lignin from the other components.<sup>6</sup> One novel process, known as “CELFR” (Co-solvent Enhanced Lignocellulosic Fractionation), was discovered by researchers at the University of Riverside and utilizes dilute acid aqueous tetrahydrofuran (THF) mixtures to extract glucan rich solids at low severity conditions from soluble components such as lignin, xylose, proteins, etc.<sup>7</sup> These glucan rich solids can undergo enzymatic saccharification to release glucose monomers.<sup>8,9</sup> Glucose can then be isomerized to fructose by a selectivity glucose isomerase enzyme.<sup>10,11</sup> Fructose then undergoes acid catalyzed dehydration to 5-

hydroxymethylfurfural (HMF).<sup>12</sup> HMF is the intermediate to DMF through catalytically hydrogenation by supported metal catalysts.<sup>13-15</sup> The technological costs of producing furans from lignocellulosic biomass have been difficult to overcome.<sup>16-18</sup> One processing reason for these challenges is that the majority of processes have relied on biphasic solutions to extract and separate the components from biomass; however, biphasic solutions can be more expensive than aqueous monophasic solutions, due to the large amount of organic extracting solvents required and the need to add salts to increase the partition coefficient. In contrast, the CELF process extracts the solvent into a solid and liquid stream avoiding the need for an extracting biphasic solvent. Thus, this opens the possibility for a continuous mono-phasic catalytic conversion fructose to DMF without the need for a multitude separation steps. It has been proposed that such catalytic pathways from sugar to fuel can be more efficient and less expensive than biological methods.<sup>2</sup> Using fructose as the feedstock avoids energy-intensive steps common to thermochemical processes and catalytic methods for biomass.

In this paper we perform a techno-economic analysis (TEA) on the feasibility of a biorefinery based on processes for producing DMF from fructose in a 1:1 (w/w) water/THF solution. We overview the analytical methods utilized, describing the catalytic dehydration and hydrogenation process designs and estimating the minimum selling price of the DMF, assuming a 10% internal rate of return. Discussion of results includes a sensitivity analysis that examines the major component costs of the design and identifies the most significant technical and cost barriers to successful commercialization.



### 5.3. Materials and Methods

#### 5.3.1. Thermodynamic Modeling

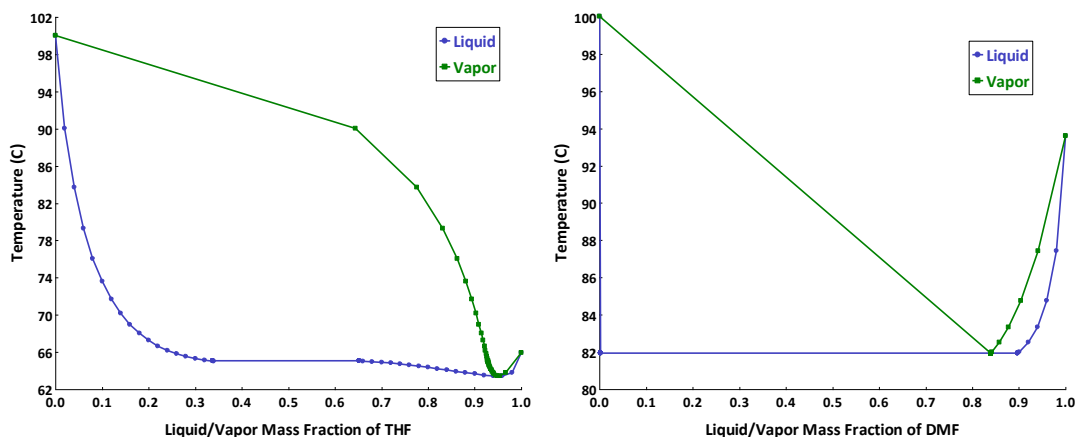
To begin this TEA model of the fructose to DMF process, short-range contributions of local compositions were estimated with Non-Random Two Liquid model (NRTL)<sup>19</sup> and UNiversal Functional Activity Coefficient (UNIFAC).<sup>20</sup> These models are ideal for low pressure (<10 bar) chemical processes with no estimation needed of electrolytic contribution of the electrolytes in solution. Binary interactions were estimated by the UNIFAC model from either the inputted structures of the functional group codes given by Aspen. Aspen Plus did not provide have the correct aromatic oxygen functional group for DMF; thus, DMF was estimate with the codes in table 5.1. A cyclic ether bonded to two sp<sup>3</sup> carbons was generally used to estimate the aromatic oxygen in DMF.

**Table 5.1.** Functional Groups Utilized by UNIFAC, UNIF-LBY, UNIF-DMD, and UNIF-R4 to estimate DMF interactions. Aromatic bonds are referred to by an \*.

UNIFAC			UNIF-LBY		
Number	Occurrence	Bond	Number	Occurrence	Bond
1160	2	C-CH3	1015	2	-CH3
1055	2	-CH=C<	1055	2	-CH=C<
1600	2	-CH2-O-*	1600	2	-CH2-O-*
UNIF-DMD			UNIF-R4		
Number	Occurrence	Bond	Number	Occurrence	Bond
1015	2	-CH3	1015	2	-CH3
1055	2	-CH=C<	1055	2	-CH=C<
1610	2	-CH2-O-	1600	2	-CH2-O-*

Utilizing the estimates generated by UNIFAC, the binary and ternary interactions of water, THF, and DMF could be estimated. The thermodynamic equilibrium of a binary mixture takes place when temperature, pressure and chemical potential of components are equated between the phases, for each component. Although there are other basic criteria

for system equilibrium, the minimization of Gibbs free energy is the condition which ensures equilibrium. Figure 5.1, demonstrates the temperature profiles vs liquid/vapor mass fractions of THF (Left) and DMF (Right) in H<sub>2</sub>O binary mixtures. It can be seen that at ~95wt% THF there is an azeotrope at ~62.5°C. While there is no azeotrope for aqueous DMF mixtures the system is biphasic up to ~85wt%, as seen in Figure 5.1.



**Figure 5.1.** Temperature Profiles vs Liquid/Vapor Mass Fractions of THF (Left) and DMF (Right) in H<sub>2</sub>O Binary Mixtures at 25°C and 1.0133 bar.

### 5.3.2. DMF Production Process Setup

Block diagrams of the conversion of fructose to HMF and then to DMF will be based on published literature in aqueous mixtures.<sup>21</sup> At present, the technologies are at the early stage of development and technical data are obtained primarily from published accounts of laboratory-scale experiments performed at CE-CERT and other public literature.<sup>6,15,22</sup> Individual unit operations are scaled and cost is estimated using scaling exponents for particular equipment categories or following the six-tenth exponential correlation when more specific information is not available.<sup>23,24</sup>

**Table 5.2.** Investment parameters per year used in estimating costs. Percentages based on purchased equipment cost.

<b>Cost category</b>	<b>Value (%)</b>
Tax Rate	20
Interest Rate	10
Project Capital Escalation	5
Raw Material Escalation	3.5
Labor Escalation	3
Utilities Escalation	3
Operating Charges	25
Working Capital Percentage	5
Plant Overhead	50

Table 5.1 shows the investment parameters used to estimate the plant based on typical purchased equipment cost and cost ratios.<sup>24</sup> This techno-economic analysis utilizes nth-plant economics in which a successful industry has been assumed to ignore artificial inflation of project costs associated with risk financing, delayed start-ups, equipment overdesign, and other costs associated with pioneer plants. This assumption allows plants simulations to ignore large capital cost overruns and performance deficits common to “pioneer” plants.<sup>25</sup> In the discounted cash flow analysis of the selling price for DMF is calculated when the net present value of the project (including a 10% internal rate of return) is equal to zero. The resulting product price is referred to as the Minimum Selling Price (MSP).<sup>23</sup> Utilities and wastewater treatment plants are not modeled explicitly, rather it is assumed instead that utilities are purchased and wastewater is treated by a third party at a fixed price per unit mass.<sup>24</sup> A range of additional assumptions are required for the analysis. The major assumptions are listed as follows:

- 1) Corn stover is the primary source of carbohydrates and has a 37.4 wt% glucan. A typical biorefinery plant processes 2000 metric ton/day of ligno-cellulosic feedstock.<sup>26</sup> Thus, this plant size is estimated to have a feed-rate of 500 metric ton/day of fructose (approximately 66.8 wt% theoretical yield). Sensitivity analysis is used to evaluate the effect of variation of fructose loading.
- 2) It is assumed that fructose is available at a fixed cost of \$300/metric ton. Sensitivity analysis is used to evaluate the effect of variation in cost of fructose.
- 3) Levulinic acid, formic acid, and humins are the primarily byproducts of the sulfuric acid catalyzed dehydration occurring in the aqueous co-solvent CSTR. The degradation solid byproducts (humins) will be assumed to be similar in structure to fructose.
- 4) Humins will be completely removed via filtration. This solid stream will be assumed to be waste and has zero value in this process.
- 5) The byproducts from the hydrogenation CSTR will be unidentified furan solids, so they are referred to as unknown byproducts and for design purposes we assume their physical properties to be similar to those of DMF. The unidentified byproducts will have no value on the market.
- 6) Product yields, selectivity and operating conditions are obtained from published literature, specific studies performed at CE-CERT.<sup>15,24</sup>
- 7) The aqueous co-solvent reactor (CSTR) operates at 150°C and 6 bar. Under these operating conditions fructose to HMF conversion is 100% and selectivity to HMF is 80%. 5% of HMF then hydrolyzes to LA and FA, making overall HMF selectivity 75%. The

catalyst used is based on an acidic heterogeneous resin. The cost of this catalyst is based on Amberlyst-15 at about \$7.5/kg. Selectivity analysis will be performed on the variation in HMF selectivity by varying humin production.

8) The hydrogenation reactor operates at 220°C at roughly 30 bar with a DMF selectivity of 100%.<sup>15</sup> Selectivity analysis will be performed on the variation in DMF selectivity by varying degradation product yields.

9) Cu–Ru/support-catalyst loading is estimated based on published bench scale data<sup>15,27</sup> and fed into a stoichiometric reactor at a 1/10 weight ratio of Cu-Ru (3:2 molar ratio) to catalytic support. The catalyst cost is estimated as the sum of 10 wt% of catalytic metals \$11/kg for carbon support. By totaling these costs, the stream cost equals about \$13/kg (\$3100/kg). The catalyst life is taken to be 2 years. It is assumed that the catalyst manufacturer will be able to recover 99.9% of the metals in the spent catalyst.

10) Cost of other raw materials are: \$1350/metric ton of THF, \$550/metric ton of H<sub>2</sub>, \$1.1/metric ton of water. THF remaining in the product and byproduct streams is assumed to be lost.

11) The plant is assumed to operate in a continuous, steady state mode for 350 days per year. The plant is depreciated in 7 years with zero salvage value.

12) Depreciation cost is estimated as 20% per year.

13) The plant life is 20 years. Income tax paid by the plant and depreciation is computed on an annual basis over the plant life.

14) All cost data are evaluated and reported on a present value basis.

15) The investment is assumed with a 100% equity financed, and has an internal rate of return (IRR) at 10%.

Sensitivity analyses have been performed to study the robustness of MSP for HMF and DMF. The parameters that have the largest influence on process operations and economics are subjected to sensitivity analysis. The effect of variation in multiple parameters was studied to identify the most prominent factors affecting MSP. Two-point values are selected to study the effect of upper and lower limits of the parameters to which the MSP is most sensitive and these are designated as Case-1 and Case-2.

### **5.3.3. Process Description and Flow Diagram**

**Figure 5.2** shows the block diagram with simulated mass balances of the DMF production process. DMF is produced from fructose through a 2-pot process, beginning with the dehydration of fructose by a heterogeneous acid catalyst in a stoichiometric reactor, which is then filtered and the stream is pressurized into another stoichiometric reactor for hydrogenation of HMF to DMF. For this process, water and THF are used to create a single-phase system throughout these steps. The dehydration reaction is carried out at 180°C in liquid phase. The conversion of fructose to HMF takes place in the aqueous stoichiometric reactor using an acidic catalyst, similar to Amberlyst-15 for the conversion of fructose to HMF. The THF acts as the co-solvent added to the solution to promote HMF production. In the aqueous phase, HMF degrades to LA and FA. The extent of degradation depends on the process parameters and reaction severity which have been set for 5% conversion of HMF to LA and FA. All fructose is assumed to convert to HMF (75% yields), LA (5% yields) and solid humins (20% yields).

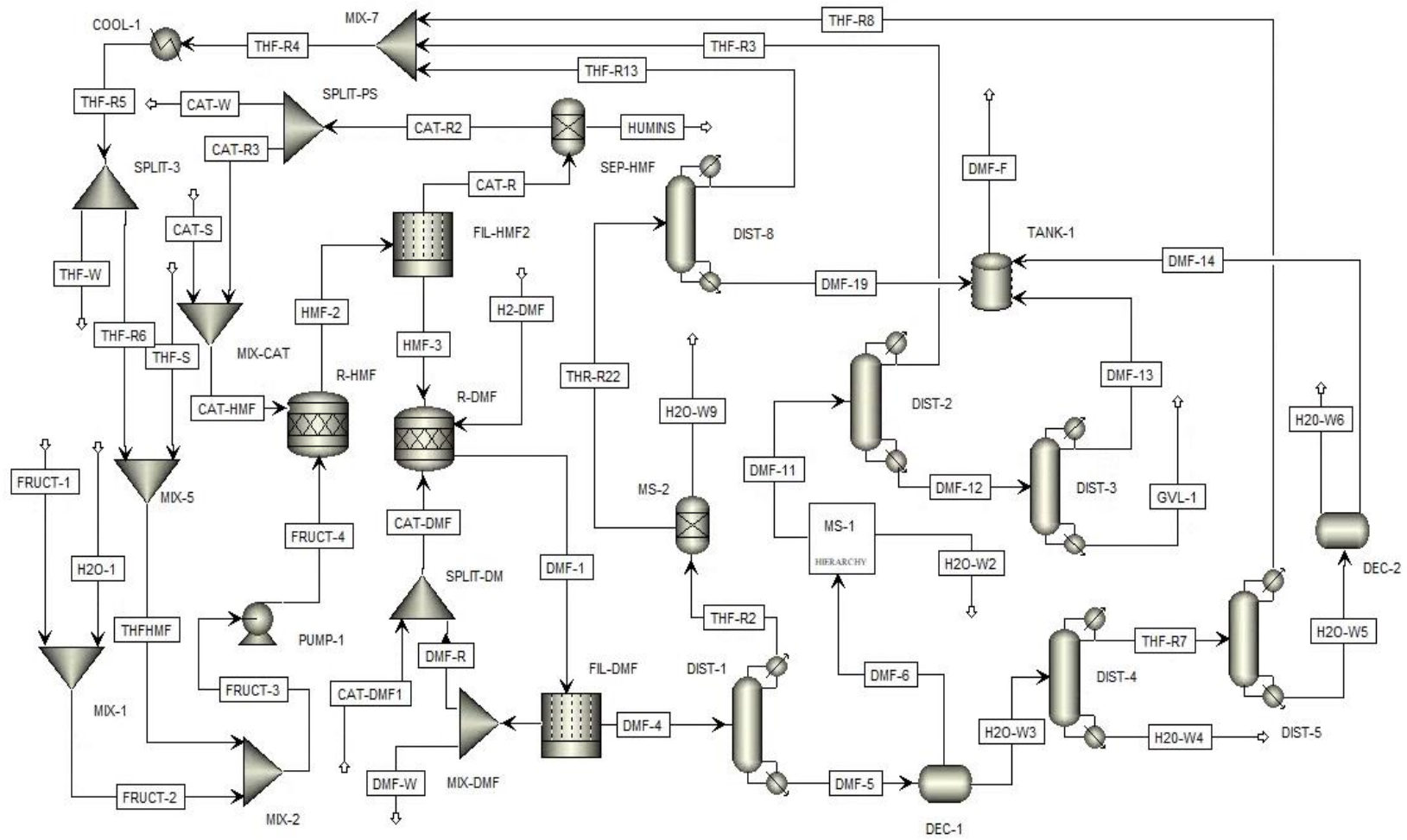


Figure 5.2. Aspen model flowsheet of the conversion of fructose to DMF.

HMF is transferred to the hydrogenation stoichiometric reactor and heated to 220 °C and 30 bar. Hydrogen is then added at ratio of 3:2 H<sub>2</sub> to HMF for the conversion of HMF to DMF in presence of Ru/C catalyst. The reactor is operated at 100% conversion of HMF and 100% yield of DMF. DMF is separated first by distillation with 93 wt% of the THF in the feed stream being separated to the distillate. The bottom stream from the distillation column is biphasic, containing 17.3 wt% DMF, and the top distillate contains 5.3% DMF and 86.6% THF. The bottom stream is sent to a decanter to separate the organic and aqueous phases. The organic phase is composed of 77.6% DMF, 11.2% THF, and 9.0% water and sent to a molecular sieve. The water stream flowing at 265,000 tonne/year is treated as waste and sent to a third-party waste water treatment facility, containing 0.87% DMF and 1.7% THF. The top distillate from the first distillation column and is sent to a molecular sieve assumed to remove all water into a waste stream. The subsequent THF/DMF stream is then distilled to extract 86.1% of the DMF to the product stream and the THF is then recycled. The organic stream from the first decanter is also sent to a molecular sieve removing the water and then distilled to once again extract both remaining DMF and GVL to the bottom stream which is then distilled a final time separating the DMF (99.8 wt% pure) to the main product stream and GVL (96 wt% pure) to a secondary stream valued at \$1/kg. In the decanting section, DMF is separated from water, formic acid, and levulinic acid as DMF forms a biphasic solution with water.



**Table 5.3.** Feed, product, and recycle flow rates for DMF production process.

<b>Feed Stream</b>		<b>Product and Wastewater Stream</b>		
<b>Raw Materials</b>	<b>Flow Rate (tonne/day)</b>	<b>Products/ Byproducts</b>	<b>Flow Rate (tonne/day)</b>	<b>Purity (wt%)</b>
Fructose	500	DMF	111.32	99
THF	8.8	GVL	12.32	99
Water	581	Humins	67.70	100
Acidic Polymer Catalyst	5	Wastewater	452.93	--
Hydrogenation Catalyst	0.01	<b>Recycle Stream</b>	<b>Flow Rate (tonne/day)</b>	
H <sub>2</sub>	13.8	THF	576	
		Water	3.4	

**Table 5.4.** Feed, price, and total cost per day for DMF Production Process.

<b>Feed Stream</b>			<b>Product and Wastewater Stream</b>		
<b>Raw Materials</b>	<b>Cost (\$/kg)</b>	<b>Total Cost (\$/day)</b>	<b>Products/ Byproduct</b>	<b>Price (\$/kg)</b>	<b>Profit/ Loss (\$/day)</b>
Fructose	0.3	150,000	<b>DMF</b>	<b>2.2</b>	488,374
THF	1.5	13,230	GVL	1	4,392
Water	1.1*10 <sup>-3</sup>	638	Humins	0.05	3750
Acidic Polymer Catalyst	7.5	56,634	Wastewater	-0.05	-35,534
Hydrogenation Catalyst	13	46,871			
H <sub>2</sub>	0.55	7585			

**Table 5.5.** Installed equipment cost for DMF production.

<b>Equipment</b>	<b>Installed Cost (\$)</b>	<b>(%)</b>
Dehydration Reactor	305,600	7.455
Hydrogenation Reactor	329,600	8.041
Distillers	2,656,200	64.8
Decanters	218,300	5.325
Molecular Sieves	286,300	6.984
Pumps	49,100	1.198
Heat Exchangers	158,000	3.854
Cooling Tank	96,100	2.344
<b>Total</b>	<b>4,099,200</b>	<b>100</b>

#### 5.4. Results and Discussion

**Table 5.2** overviews the simulated feed, product, and recycle stream mass flowrates for the reactants, solvents, catalysts, and byproducts of the overall production process. 500 tonne/day of fructose is mixed with a 1:1 (w/w) solution of THF, water and pumped into a stoichiometric reactor at a loading of 30 wt% fructose. This produces two product streams: 111 tonne/day of DMF (99% pure) and 12.3 tonne/day of GVL (96% pure) are co-produced. The process also generates formic acid as a byproduct, however the concentration of formic acid in the aqueous stream is too low to be economically recovered and this and other minor waste streams are modeled as being eliminated in the wastewater stream. Table 5.3 overviews the total installed equipment costs of the reactors, distillers, decanters, pumps, molecular sieves, and exchangers. Total installed capital cost for the base case scenario is estimated as \$14.98 million. The total purchased equipment cost for the HMF production process has been estimated as \$4.1 million. The most expensive equipment are the distillers which are 64.8% of the total equipment cost.

The MSP for DMF is obtained as \$1.74/kg. A summary of the DMF process engineering analysis results is shown in Table 5.4. The annual DMF production are 81.1 million kilograms produced from 182 million kilograms of fructose. The current process HMF yield from fructose is assumed at 75%, with 5% going to LA (and FA) production and the rest is assumed to be lost as solid humins which are filtered out. This loss is based on the maximum experimental results from multiple experiments utilizing heterogeneous acid catalysts. 100% of experimentally reported yields of HMF then 56 mega l (14.8 million gal) of HMF could be produced which would reduce the MSP of DMF to \$1.16/l (\$4.4/gal) or \$0.94/kg. Sensitivity analysis has been performed to study the relative significance of economic and process parameters on MSP. Based on our perception of uncertainty in the assumptions, the sensitivity of HMF MSP is measured for a plus or minus 20% change in the values for critical parameters (Fig. 3). It is evident that the yield of DMF from fructose is the most significant parameter affecting the MSP. Thus, a 20% increase in HMF yield can result in a 15.5% decrease in the MSP to \$1.47/kg. This process does not aim to extract HMF, but instead convert it to DMF; thus, the typical high costs of extracting HMF into an organic phase are ignored.

The price of fructose is the next most significant parameter affecting the MSP for DMF. A 20% change in the fructose price results in a 10.8% change in the MSP for DMF. An inexpensive source of fructose will be necessary to lower DMF price and promote its wide-scale use. Use of cheap lignocellulosic sources that do not compete with food prices, such as corn stover, may reduce the price of fructose; however, fructose production from lignocellulosic sources is still more expensive than other cellulosic

sources (such as corn). The large fraction of capital cost in the MSP of DMF creates an opportunity to take advantage of economies of scale that can be achieved through a larger scale of production. Reduction in capital costs for this process through better process design will make DMF more attractive by allowing derivatives to compete with petroleum-based alternatives.

**Table 5.6.** Summary of DMF process engineering analysis.

<b>DMF production process engineering analysis</b>	
Minimum DMF Selling Price	\$1.74/kg
DMF Production (kg/year at 25°C)	8.11*10 <sup>7</sup>
HMF Yield from Fructose	75%
LA Yield from Fructose	5%
DMF Yield from HMF	100%
GVL Yield from LA	100%
Internal Rate of Return	10%
Equity Percent of Total Investment	100%
Payout Period	20 years

**Table 5.7.** Summary of DMF Capital and Operating Costs.

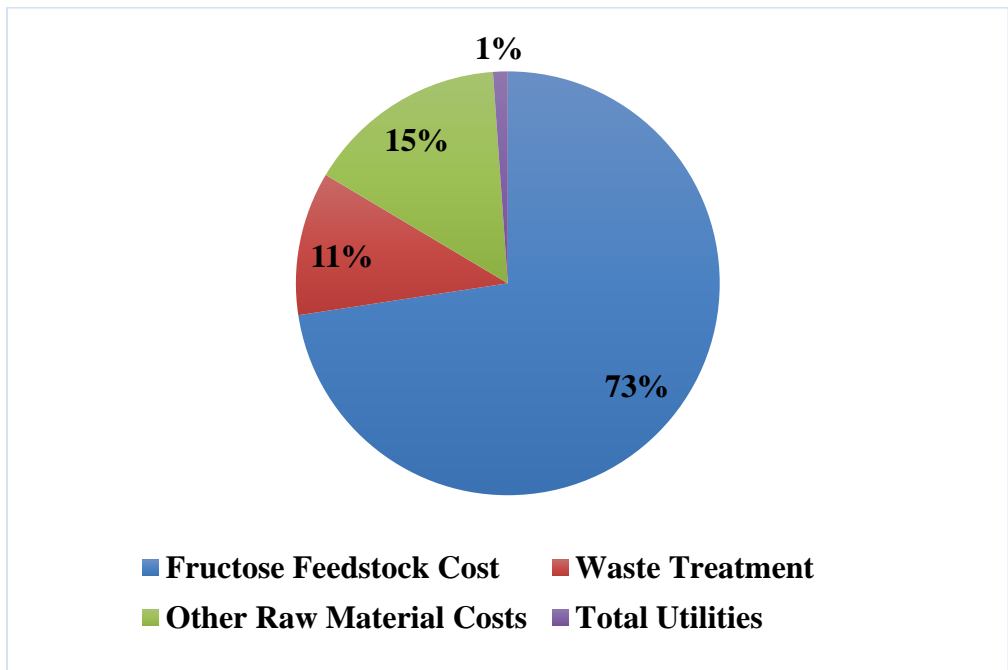
<b>Capital Costs</b>	
THF Recovery	98.5%
Total Installed Cost (TIC)	\$4,099,200
Total Capital Investment	\$14,983,900
Installed Equipment Cost/Annual kg	\$0.051
Total Capital Investment/ Annual kg	\$0.185
Loan Rate	N/A
Term (years)	N/A
Capital Charge Factor	0.15
Maximum HMF Yield	90%
Minimum HMF Yield	60%
Current HMF Yield	75%
HMF Production (kg/year)	$1.03 \times 10^8$
Current DMF Yield	100%
DMF Production (kg/year)	$7.91 \times 10^7$
Current GVL Yield	100%
GVL Production (kg/year)	$4.31 \times 10^6$
Isolated DMF (kg/year)	$7.86 \times 10^7$
Percent DMF Isolated	99.4%
Isolated GVL (kg/year)	$1.56 \times 10^6$
Percent GVL Isolated	36%
<b>Operating Costs (\$/Year)</b>	
Fructose Feedstock	54,787,500
Utilities	1,010,650
Other Raw Material Costs	11,570,400
Water Disposal	8,271,590
Electricity	150,892
Steam	156,018
Cooling Water	537,233
Total Utilities Cost	844,721
Capital Depreciation	20%
Average Return on Investment	20%
<b>Major Cost Contributors:</b>	<i>Fructose Feedstock, Catalysts, Distillation</i>

Techno-economic analysis shows that the MSP of DMF for the base case scenario is \$1.74/kg or \$1.95/liter. This price is quite high when compared to the average U.S. November 2018 gasoline price of \$0.68/liter (\$ 0.88/kg or \$2.54/gal).<sup>28</sup> However, the typical average price of DMF for chemical use at bulk purchase (>10 kg) is \$50/kg.<sup>28</sup> This cost is also high as compared to similar scale corn ethanol plants at \$0.60/l (\$2.30/gal) capacity or even cellulosic ethanol which is estimated to be \$1.60/l (\$6.10/gal) capacity.<sup>29</sup> The major contributors to the MSP for DMF are depicted in the pie chart of Fig. 3. Fructose feedstock contributes to 73% of the product price, while a significant expense is also incurred in the recovery of raw materials, such as THF and catalysts. Additionally, the production of DMF requires a 3 to 2 molar ratio of H<sub>2</sub> to HMF, amounting to 4444.5 kg/year of H<sub>2</sub> to convert HMF to DMF. This limits the process to an on-site H<sub>2</sub> production facility or on a hydrogen pipeline. Significant hydrogen use also reduces the renewable energy content of the DMF product since hydrogen is presently generated from natural gas or oil resources.

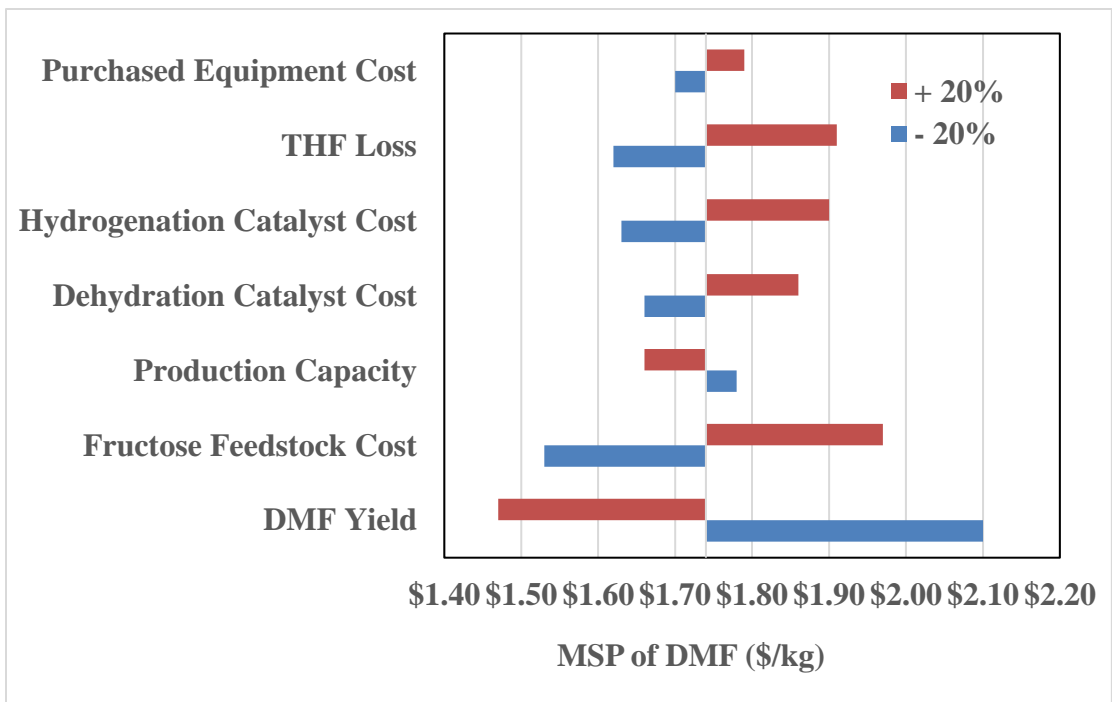
Sensitivity analysis has been performed on critical process and economic parameters to study their relative impact on the MSP of DMF. 1415 tonne/year of DMF is lost to the waste streams or about 0.14% of the DMF generated. This yield loss is due to the difficulty in fully separating DMF from the aqueous, THF streams. There are opportunities to minimize these losses through more lab and pilot trials. However, the main obstacles to the process are reactor yields and fructose feedstock cost.

If 100% DMF yields were obtained in the current process, the MSP for DMF reduces to \$1.47/kg (\$1.65/l). Following our earlier assumption of fructose at 500

tonne/day, the large-scale availability of inexpensive fructose is also a bottleneck for this process, which can be addressed through studies for fructose production from cellulosic sources. In this process 75% of inlet fructose is converted in the reactor and it is assumed that there is no remaining fructose. However, this is a best-case scenario and likely that some fructose will be left in stream and degrade into unwanted products, raising the MSP. A 20% change in other material costs results in a 9% change in the MSP. Currently the inlet ratio of catalyst to HMF in the reactor is maintained as 30% w/w and H<sub>2</sub> fed is at a rate that is 1.2 times more than the stoichiometric requirement. The conversion of HMF to DMF is enabled through use of a Cu–Ru/C catalyst. A 20% change in the price of catalyst results in a 10.2% change in the MSP for DMF. This catalyst is expensive due to the higher percentage of ruthenium. The catalyst contains 8.86% Ru, which is significantly higher than the usual 0.5–1% content of noble metals in catalysts. The use of ruthenium catalyst also has its limitations. Synthesis of cheaper catalysts with possible a mixture of non-noble metals, while maintaining or improving performance would certainly reduce the price for DMF. Additionally, research into low priced alternative catalysts is equally important to enable commercial production of DMF. The GLV by-product can also be a significant factor which affects the MSP of DMF. At the currently assumed price of \$1/kg, a 20% change in the GVL price results in 1% change in the MSP of DMF. However, the price that can be obtained for GVL depends on a variety of factors, including its purity, current market demand and potential applications.



**Figure 5.3.** Major Operating Costs to DMF price.



**Figure 5.4.** Sensitivity analysis on minimum selling price.



## 5.5. Conclusions

The process shown highlights the production of DMF from fructose in an aqueous THF solution. The immiscibility of DMF can be utilized to extract DMF from the solution without the need of an extraction solvent; while this can reduce the costs, there are still uncertainties that need to be overcome to achieve practical implementation. Fructose price, DMF yields, and waste water treatment cost are the most significant challenges to the successful commercial implementation of these processes. The dehydration of fructose to HMF requires a highly reusable acidic catalyst that can achieve yields up to 75%. The process for conversion of HMF to DMF uses an expensive Cu–Ru/C catalyst which will need to be replaced by a cheaper alternative in the future. Development of less expensive and effective catalysts with lower rare metal composition is essential for fuel applications. In addition, the use of hydrogen to make DMF makes it a non-green fuel source compared to ethanol and may need to be used as a solvent for other application. To benefit from synergies in a biorefinery it is imperative that new processes be developed which utilize byproducts like GVL. The availability of inexpensive fructose feedstock certainly holds the key to viable large-scale production of DMF. Hence it is necessary to develop economically feasible pathways to fructose from biomass.

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**Chapter 6**  
**Conclusions**

## 6.1. Summary

In conclusion, this dissertation first aims to examine the past literature to illustrate the how factors such as temperature, time, catalyst, and solvent systems have influenced past experiments. Higher temperatures and dipolar aprotic solvents tend to report the highest yields. This is inline with the hypothesis that the tautomeric distribution controls the selectivity to HMF. To explore this idea further, extensive dehydration tests were run with a high-throughput reactor in a variety of temperatures, Bronsted acid catalysts, and solvents. The selectivity to HMF, determined from these tests, in DMSO and other aprotic solvents, demonstrated a linear correlation between the fructofuranose isomer and HMF selectivity. We demonstrate that temperature and solvent system control the percentage of the fructofuranose form in equilibrium. This equilibrium can be further controlled in the pores of functionalized silica via the generation of unique micro-environments. By functionalizing silica supports, a ratio of methyl sulfoxide groups to sulfonic acid groups can be achieve which increases selectivity to HMF. Lastly, the techno-economic analysis revealed that the main factors controlling the MSP for DMF are fructose feedstock cost, DMF yield, and catalyst cost. We determined a MSP of \$1.74/kg for DMF, which is still far higher than gasoline. It may be highly difficult to obtain a lower price as fructose as well as H<sub>2</sub> are relatively expensive compared to a kg of oil.

## 6.2. Future Work

The goals for the future work of this dissertation is to fully integrate acidic hydrolysis of fructose together with hydrogenation to DMF to develop a continuous in-

situ dehydration and hydrogenation process for the production of DMF. The continued surface functionalization of porous silica will be further developed to explore the effect of larger pore sizes, more effective synthetic techniques to lower ICH<sub>3</sub> loading, and the optimum ratio of sulfoxides to sulfonic acid. Additionally, notable high-performance heterogeneous catalysts such as zeolites, vanadium phosphate, TiO<sub>2</sub> and SBA-15 will be examined over a variety of reaction conditions to optimize HMF production in aqueous THF and dioxane solutions. Moreover, the propyl carbon chain will be changed to long chains to determine the effect of chain length on the surface of supports. Low cost bimetallic catalysts will be deposited on surface of the metal oxide supports near the organic sulfonic and sulfoxide groups. We aim to have an in-situ process in which fructose will be converted to DMF in one pot. Overall, reaction parameters such as solvent type, HMF concentration, and acid/salt catalytic poisoning will be examined to optimize the overall process in terms of catalytic selectivity to HMF, activity, and recyclability. Lastly, Aspen Plus will be utilized to further develop the techno-economic analysis by adding a process flowsheet for the conversion of corn stover to fructose. We will determine the major cost contributors for the MSP of fructose and determine if this process is economically competitive compared to purchasing cellulosic fructose.