

# Mechanistic Study of a One-Step Catalytic Conversion of Fructose to 2,5-Dimethyltetrahydrofuran

Matthew R. Grochowski, Weiran Yang, and Ayusman Sen\*<sup>[a]</sup>

**Abstract:** Carbohydrates, such as fructose, can be fully dehydroxylated to 2,5-dimethyltetrahydrofuran (DMTHF), a valuable chemical and potential gasoline substitute, by the use of a dual catalytic system consisting of HI and RhX<sub>3</sub> (X = Cl, I). A mechanistic study has been carried out to understand the roles that both acid and metal play in the reaction. HI serves a two-fold purpose: HI acts as a dehy-

dration agent (loss of 3 H<sub>2</sub>O) in the initial step of the reaction, and as a reducing agent for the conjugated carbinol group in a subsequent step. I<sub>2</sub> is formed in the reduction step and metal-catalyzed hydrogenation reforms

**Keywords:** biomass • carbohydrates • hydrogenation • reduction • rhodium

HI. The rhodium catalyst, in addition to catalyzing the reaction of iodine with hydrogen, functions as a hydrogenation catalyst for C=O and C=C bonds. A general mechanistic scheme for the overall reaction is proposed based on identification of intermediates, independent reactions of the intermediates, and deuterium labeling studies.

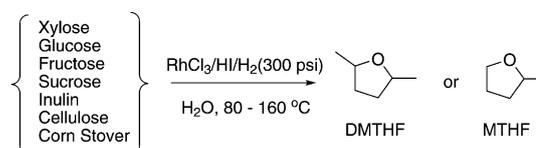
## Introduction

The catalytic transformation of abundant biomass into fuels offers the exciting possibility of the potential replacement of non-renewable fossil fuels.<sup>[1]</sup> Recent advances have been made in the conversion of biomass to fuels by combining the power of both metal- and acid catalysts.<sup>[2]</sup> Most current efforts have focused on a two-step process; the first step involves breaking down polysaccharides in biomass into their monomeric carbohydrate units by the use of acid-catalyzed hydrolysis, and then dehydration of the monosaccharides to 5-hydroxymethylfurfural (HMF). Subsequent chemical transformations involve the use of metal catalysts to produce valuable end-products, such as 2,5-dimethylfuran (DMF) and 2,5-dimethyltetrahydrofuran (DMTHF), which can be made from these transformations.<sup>[3]</sup>

There are several recent reports in the literature on the conversion of biomass to DMF. Dumesic and co-workers utilized a two-step process to convert fructose to DMF in good yield.<sup>[3a]</sup> The first step involved dehydration of fructose to 5-hydroxymethylfurfural (HMF) by HCl in a biphasic solvent system, whereas the second step employed a Cu–Ru/C catalyst for vapor phase hydrogenolysis to form DMF. Rauchfuss and Thananathanachon has also reported the synthesis of DMF starting from fructose; added formic acid resulted in dehydration to HMF, and then a Pd/C catalyst was added to the reaction mixture to form DMF. The

formic acid functioned as the hydrogen source in the second step and assists in the deoxygenation of HMF to DMF.<sup>[4]</sup>

Our work has involved the successful catalytic transformation of carbohydrates, both poly- and monosaccharides, to DMTHF in a single step (Scheme 1), whereas pentoses are



Scheme 1. One-step transformation of carbohydrates and cellulosic biomass to tetrahydrofuran derivatives.

converted to 2-methyltetrahydrofuran.<sup>[5]</sup> DMTHF is a valuable organic solvent that also has several desirable properties that make it an excellent candidate for gasoline replacement. For example, DMTHF has good volatility (b.p. 90 °C), low miscibility with water, and good combustibility (research octane number (RON)=82). The energy density of DMTHF (31 MJL<sup>-1</sup>) is comparable to gasoline (34.2 MJL<sup>-1</sup>) and far superior to ethanol (23 MJL<sup>-1</sup>). Our process is unique in that it combines the use of both hydriodic acid and a metal catalyst RhX<sub>3</sub> (X = Cl, I); the dual catalytic system allows conversion to occur in a single step. The system can even be used with raw corn stover as the starting material to obtain DMTHF in good yield.

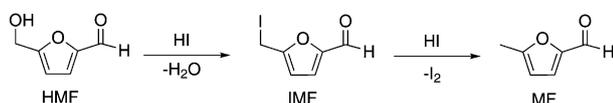
Here we describe the results of a mechanistic study undertaken to determine the roles of both the metal catalyst and the acid (HI) in the transformation.

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## Results and Discussion

**Role of HI:** The acid-catalyzed dehydration of carbohydrates to 5-hydroxymethyl-2-furaldehyde (HMF) has been extensively studied and is a well-established step in the reactivity of carbohydrates. A large number of inorganic-, organic-, and Lewis acids have been found to catalyze this dehydration.<sup>[6]</sup> Antal has conclusively shown, through deuterium labeling experiments, that the acid-catalyzed triple dehydration occurs through cyclic intermediates.<sup>[7]</sup> HI functions as a dehydration agent in this manner, however, in addition to its role in dehydration it is a versatile reducing agent for aryl carbinols.<sup>[8]</sup> We have recently reported that HI can also be used to convert fructose to 5-methylfurfural (MF) in good yield ( $\approx 50\%$ ) under mild aqueous conditions.<sup>[9]</sup>

Because of the strong acidity of HI ( $pK_a = -9.5$ ), combined with the excellent nucleophilicity of the iodide ion, an alcohol is easily protonated and then substituted by iodide. Fenton and Gostling reported the synthesis, isolation, and characterization of both chloromethylfurfural and bromomethylfurfural by the reaction of cellulose or carbohydrates with HCl and HBr, respectively.<sup>[10]</sup> They were able to reduce both of these derivatives in a separate step by reaction with stannous chloride. An external reducing agent is unnecessary in the presence of HI. The intermediate 5-iodomethylfurfural (IMF) is easily reduced in situ by HI under the reaction conditions, due to the weak C–I bond (the analogous aromatic compound benzylic iodide has a bond strength of  $43.2 \text{ kcal mol}^{-1}$ ),<sup>[11]</sup> and results in further reduction to MF with the concomitant formation of iodine ( $I_2$ ) as a byproduct (Scheme 2).<sup>[8]</sup>



Scheme 2. HI reduction of HMF to MF via the intermediacy of IMF.

When the reaction was repeated using HMF as the starting material, conversion to MF occurred in 47% yield, which is the same yield as that obtained with fructose. In both instances, some dark solid (humin) was observed to have precipitated out of solution. HMF, due to its reactive hydroxyl and carbonyl groups, is highly susceptible to the formation of humin polymers under aqueous acidic conditions.<sup>[12]</sup> In the reduction of HMF with HI, the intermediate IMF was observed by GC and  $^1\text{H}$  NMR spectroscopy, with the iodo-methylene resonance ob-

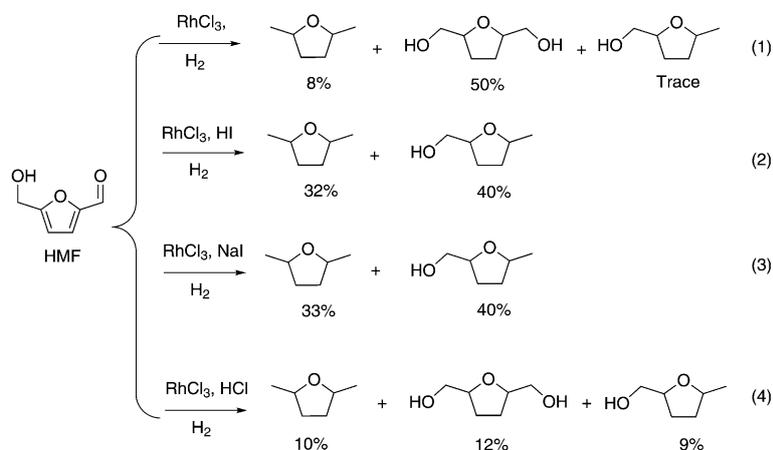
served at  $\delta = 3.50$  ppm, the aldehyde proton at  $\delta = 8.97$  ppm, and the ring protons at  $\delta = 5.49$  and  $6.19$  ppm. However, IMF could not be isolated in the pure form. The reaction of HMF with one equivalent of HI resulted in a mixture of MF, IMF, and unreacted HMF.

**Catalytic hydrogenation of  $I_2$  to HI:** As mentioned in the previous section, iodine is formed as a byproduct in the reduction of the alcohol moiety. The standard method in the literature to recycle iodine is to add hypophosphorus acid or red phosphorus as a reducing agent to reconvert the iodine back to HI.<sup>[13]</sup> This can be problematic because it results in the buildup of phosphorus byproducts in the reaction mixture. In our method, the iodine is catalytically converted back to HI by reaction of iodine with hydrogen during the course of the reaction.

The reaction of iodine with hydrogen is a thermodynamically favored process ( $K_{eq} = 408$  at  $100^\circ\text{C}$ ). However, the conversion is kinetically slow at lower temperatures such as those used in the reaction ( $80\text{--}140^\circ\text{C}$ ). We have found that catalytic amounts of rhodium ( $\text{RhCl}_3$ ,  $\text{RhI}_3$ ,  $\text{Rh/C}$ ), palladium ( $\text{Pd/C}$ ), and ruthenium ( $\text{Ru/C}$ ) can hydrogenate iodine to HI under the reaction conditions employed for fructose conversion.<sup>[9]</sup> Not surprisingly the conversion did not proceed without the presence of water under our moderate reaction conditions. Water provides significant added driving force because of the solvation of the ions derived from HI. The free energy of hydration of gaseous HI is  $-118 \text{ kJ mol}^{-1}$  at  $100^\circ\text{C}$  ( $K_{eq}(100^\circ\text{C}) = 3.3 \times 10^{16}$ ).<sup>[14]</sup>

### Rhodium-catalyzed hydrogenolysis of carbon–oxygen bonds:

The Rh catalyst also plays a role in carbon–oxygen bond hydrogenolysis, although to a lesser extent than with HI. When the intermediate HMF was allowed to react with  $\text{RhCl}_3$  (5 mol%) under a hydrogen atmosphere without HI (Scheme 3, reaction 1), DMTHF formed in only 8% yield; the major product, 2,5-dihydroxymethyltetrahydrofuran, resulted from the hydrogenation of the unsaturated bonds of



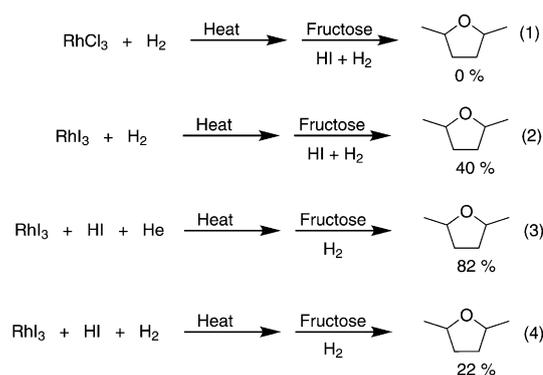
Scheme 3. Conversion of 5-hydroxymethylfurfural (HMF). Reaction conditions: HMF (1 mmol),  $\text{RhCl}_3$  (0.05 mmol), HI, NaI, or HCl (1.5 mmol),  $\text{H}_2\text{O}$  (1.8 mL), benzene (2 mL),  $\text{H}_2$ , (300 psi),  $140^\circ\text{C}$ , 16 h.

HMF. In contrast, when the same reaction was repeated with added HI or NaI the yield increased to 32 % (Scheme 3, reaction 2). The utility of using the iodide ion in the reaction was demonstrated when HCl was used in place of HI resulting in only a 10 % yield of DMTHF; most likely, the production of DMTHF in this latter reaction occurred exclusively from C–O hydrogenolysis by the Rh catalyst (Scheme 3, Eq. (4)). The experiments showed that the dehydration/reduction ability of HI combined with the hydrogenation/hydrogenolysis ability of the Rh catalyst results in an efficient dual catalytic system for the conversion of fructose to DMTHF.

**Identity of the active rhodium catalyst:** The identity of the active rhodium catalyst in the course of the reaction could not be precisely determined. Given the large excess of HI relative to  $\text{RhCl}_3$  (30 to 1 for a typical reaction) and the elevated temperatures employed, conversion of  $\text{RhCl}_3$  to  $\text{RhI}_3$  is a likely possibility. Moroz and co-workers found that heating  $\text{RhCl}_3 \cdot x\text{H}_2\text{O}$  with an excess of HI in boiling aqueous HCl resulted in the precipitation of  $\text{H}_n\text{RhI}_{3+n}$ . The amount of HI incorporation was dependent upon the amount of HI added (max  $n=0.81$ ).<sup>[15]</sup> The reactivity of  $\text{RhCl}_3$  and  $\text{RhI}_3$  were tested in separate experiments under the same conditions (1 mmol fructose, 5 mol % Rh, 1.5 mmol HI, 300 psi  $\text{H}_2$ ,  $\text{H}_2\text{O}$ /toluene, 125 °C, 1 day). Reaction yields were found to be identical (65 and 64 %), with the implication that both catalysts form the same catalytic reactive species.

However,  $\text{RhCl}_3$  and  $\text{RhI}_3$  have significantly different hydrogenation abilities.  $\text{RhCl}_3$  is a more active hydrogenation catalyst than  $\text{RhI}_3$ , as demonstrated by the extent by which the organic solvent (either toluene or benzene) is hydrogenated.  $\text{RhCl}_3$  was heated (140 °C) under hydrogen (300 psi) in a biphasic toluene/water solution (50:50). A large amount of the solvent was hydrogenated to methylcyclohexane ( $\approx 65\%$  by GC). In contrast, when  $\text{RhI}_3$  was used as the starting catalyst under the same conditions, only a small amount of toluene was hydrogenated to methylcyclohexane ( $\approx 0.1\%$  by GC). During the course of the actual catalytic reaction with fructose, only a trace amount of hydrogenated toluene was detected by GC, similar to the result obtained with  $\text{RhI}_3$ . The active catalyst is believed to form in the aqueous layer. We have previously shown that under optimal reaction conditions (HI (9 mmol), 80 °C, 300 psi  $\text{H}_2$ ) the catalyst is stable and can be recycled at least 10 times without loss of activity.<sup>[5]</sup> The activity was also observed to be unaffected even after filtration of the reaction solution, indicating that the active catalyst is homogeneous and water soluble.

At higher reaction temperatures, the catalyst deactivation was found to occur with the precipitation of black  $\text{Rh}^0$  particles. It is well established that hydrogenation of  $\text{RhCl}_3$  in aqueous solutions of HCl results in the formation of highly pure Rh metal.<sup>[16]</sup> This was observed when  $\text{RhCl}_3$  was first heated in toluene/water solution under a hydrogen atmosphere for 3 h (Scheme 4, Eq. (1)), and resulted in the precipitation of fine black rhodium(0) particles. Fructose and HI



Scheme 4. Reactivity of the Rh catalyst. Reaction Conditions:  $\text{RhI}_3$  or  $\text{RhCl}_3$  (0.05 mmol), HI (1.5 mmol), fructose (1 mmol),  $\text{H}_2$  or He (300 psi),  $\text{H}_2\text{O}$  (2 mL), toluene (2 mL) 125 °C; the first step was heated for 3 h; the second step was heated for at least 12 h.

were subsequently added and the reaction was heated under hydrogen, but no DMTHF formed in the reaction.

Repeating the same sequence with  $\text{RhI}_3$  resulted in the formation of DMTHF, but with a decreased yield of 40 % (Scheme 4, Eq. (2)). It appears that deactivation is slower starting with  $\text{RhI}_3$ . This is probably due to differences in solubility;  $\text{RhCl}_3$  is soluble in water whereas  $\text{RhI}_3$  is insoluble and undergoes reduction at a slower rate.

In contrast to catalyst deactivation in the presence of hydrogen, enhanced reactivity was found when  $\text{RhI}_3$  was preheated for 3 h at 125 °C with 30 equivalents of HI under an inert atmosphere (300 psi He). The aqueous solution phase went from colorless to orange and the addition of fructose and subsequent heating gave an enhanced yield of 82 % (Scheme 4, Eq. (3)), compared with an yield of 64 % without any catalyst pretreatment as discussed above. We propose that the reaction of  $\text{RhX}_3$  with HI forms the reduced active catalytic species through a redox reaction. James and Rosenberg found that aqueous acidic solutions of  $\text{Rh}^{\text{III}}$  and iodide underwent a redox reaction with the liberation of iodine.<sup>[17]</sup> The half cell reduction potentials for  $\text{Rh}^{\text{III}}$  to  $\text{Rh}(0)$  (0.76 V) and  $\text{I}_2$  to  $\text{I}^-$  (0.535 V) at pH=0 are favorable for this transformation.<sup>[18]</sup>

Finally, decreased reactivity was found when  $\text{RhI}_3$  was preheated for 3 h at 125 °C with 30 equivalents of HI under a hydrogen atmosphere (300 psi). Fructose was then added and the reaction was heated at 125 °C for 19.5 h. The yield of DMTHF was only 22 %, further indication that pre-treatment with hydrogen results in catalyst deactivation by precipitation of metallic rhodium (Scheme 4, Eq. (4)). This was confirmed in a separate experiment in which an aqueous solution of HI (9 mmol) and suspended  $\text{RhI}_3$  (0.30 mmol) was heated at 140 °C under  $\text{H}_2$  (300 psi) for 2 days. The suspended black particles were collected and analyzed by inductively coupled plasma mass spectrometry (ICP-MS) and the elemental composition was found to be 78.0 % Rh and 23.0 % I. The decrease in % I from the  $\text{RhI}_3$  starting material (18.7 % Rh and 79.4 % I) is indicative of reduction by  $\text{H}_2$ .

**Reaction intermediates:** The reaction intermediates were readily identified by GC. The reaction involving fructose was carried out in a bomb reactor charged with hydrogen and or helium gas (300 psi), and was heated at 80 °C and stopped after specific time intervals (Table 1). The organic layer was analyzed by GC and compared to known standards to determine the identity of the formed intermediates and final products, and then the relative percentages of the intermediates

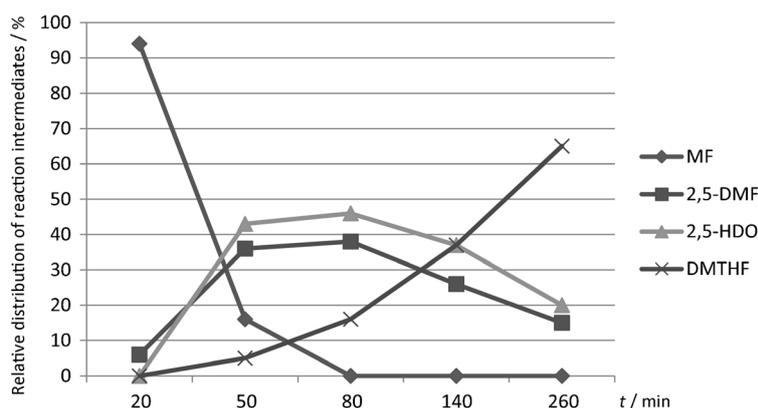


Figure 1. Graphical representation of Table 1 showing the distribution of reaction intermediates and products with time.

Table 1. Relative distribution [%]<sup>[a]</sup> (and [% change])<sup>[b]</sup> in reaction products with time.

Reaction conditions <sup>[c]</sup>				
9 h, 80 °C, 300 psi He	100	0	0	0
+20 min, 80 °C, 300 psi H <sub>2</sub>	94 [−6]	6 [+6]	0	0
+50 min, 80 °C, 300 psi H <sub>2</sub>	16 [−78]	36 [+30]	43 [+43]	5 [+5]
+80 min, 80 °C, 300 psi H <sub>2</sub>	0 [−16]	38 [+2]	46 [+3]	16 [+11]
+140 min, 80 °C, 300 psi H <sub>2</sub>	0	26 [−12]	37 [−9]	37 [+21]
+260 min, 80 °C, 300 psi H <sub>2</sub>	0	15 [−11]	20 [−17]	65 [+28]

[a] The percentages were obtained from the GC area of the intermediate divided by the total area of all intermediates. [b] The percentages in brackets are the % change from the preceding time interval. [c] Reaction conditions: fructose (1 mmol), HI (10 mmol), RhCl<sub>3</sub> (0.10 mmol), 300 psi He or H<sub>2</sub>, 80 °C, H<sub>2</sub>O (3 mL), toluene (4 mL). The toluene layer was analyzed by GC at the stated time intervals.

and final products were determined with respect to each other. A large excess of HI (10 equiv) was used initially without hydrogen in an effort to determine how far the reaction would progress without the use of hydrogen gas. Under an inert He atmosphere the reaction stops at the formation of MF, the only product detected in solution. When hydrogen was added, 2,5-dimethylfuran (DMF) began to form after 20 min of heating, and as the concentration of MF decreased, the concentration of DMF increased rapidly along with 2,5-hexanedione (HDO) (Figure 1). HI-catalyzed hydration of DMF results in ring-opening and keto–enol tautomerization to HDO, whereas the reverse reaction involves dehydration of HDO to give DMF with the two intermediates in equilibrium with each other as determined by deuterium labeling experiments (see below). It has previously been shown that the acid-catalyzed equilibration occurred with HCl,<sup>[19]</sup> and HDO was isolated in 93 % yield with the acidic cation exchanger Amberlyst 15.<sup>[20]</sup> Trace amounts of 5-methyltetrahydrofuranmethanol and 3-methylcyclopenta-

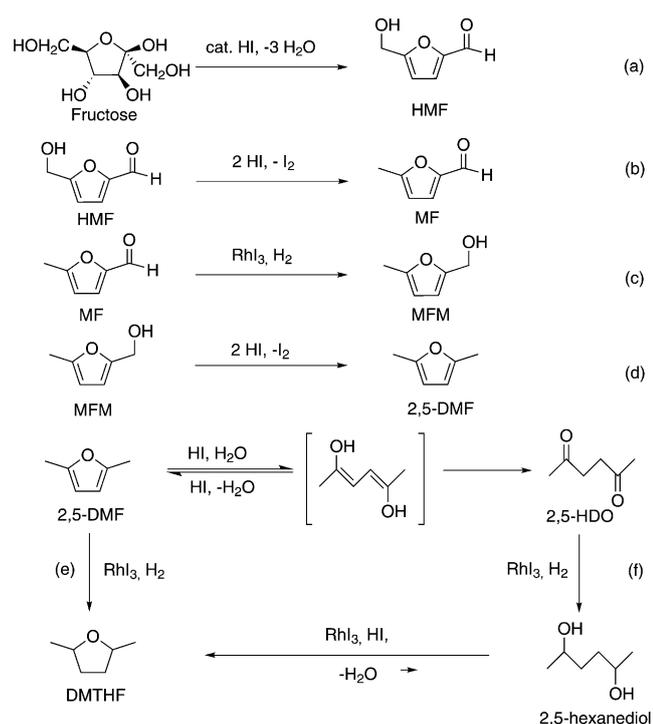
none were also identified in solution (determined by GC-MS). The former was likely produced from the hydrogenation of 5-methylfuranmethanol (MFM), whereas the latter may have formed from the enolization and intramolecular cyclization of HDO.

The amounts of both DMF and HDO decreased over time and an equal amount of DMTHF was formed. Thus, DMTHF formation is a direct result of the disappearance of these two intermediates from the reaction mixture. On the basis of these experimental results, we propose the reaction mechanism shown in Scheme 5. The mechanism involves HI acting as a dehydration/reduction agent, whereas the Rh catalyst acts as a hydrogenation/hydrogenolysis agent.

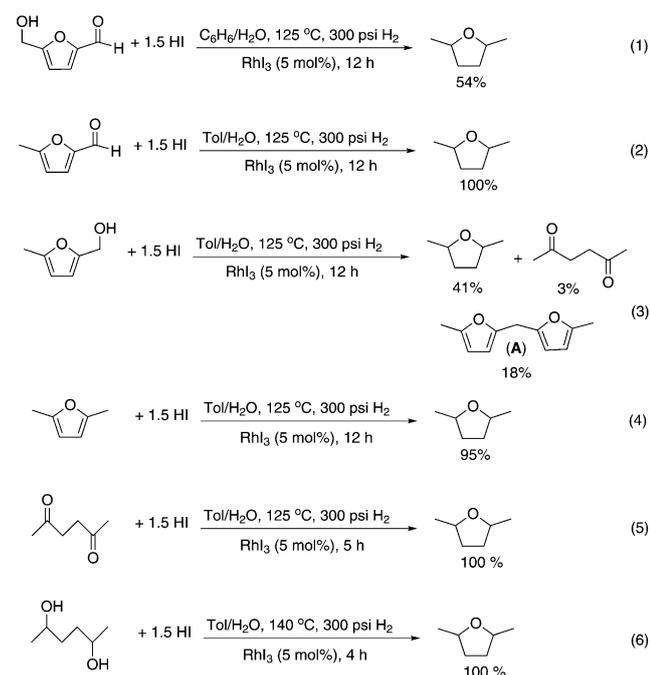
#### Independent synthesis of DMTHF starting from the intermediates:

The viability of each of the proposed intermediates was determined by examining their respective reactions under the same reaction conditions as the fructose starting material. All six of the proposed intermediates tested resulted in the formation of DMTHF as the end product, supporting their validity as proposed intermediates. Although DMTHF was formed in each case, the yields of DMTHF ranged widely depending on the starting intermediate. MF, DMF, HDO, and 2,5-hexanedione all gave quantitative or near quantitative yields of DMTHF, whereas HMF (54 %) and MFM (41 %) gave DMTHF in lower yields (Scheme 6).

The differences in yields starting with the various intermediates can be attributed to their different susceptibilities to the formation of polymeric humin. It is well established that HMF readily forms humin under highly acidic aqueous conditions.<sup>[12]</sup> Our recent work has shown that MF can be made in 51 % yield from the reaction of fructose and HI without the aid of a metal catalyst.<sup>[9]</sup> A <sup>1</sup>H NMR spectrum of the water layer showed that fructose conversion was 67 %, a significant portion (≈20 %) was converted to the undesired humin byproduct.



Scheme 5. Proposed reaction mechanism for the conversion of fructose to DMTHF.



Scheme 6. Reaction of proposed reaction intermediates used as the starting reagent. Reaction conditions: starting intermediate (1 mmol), HI (1.5 mmol),  $\text{RhI}_3$  (0.05 mmol), 300 psi  $\text{H}_2$ ; 140 °C,  $\text{H}_2\text{O}$  (2 mL), and toluene (2 mL).

MFM was also found to be highly reactive, and a substantial amount of the condensation product 2,2-methylenebis(5-

methyl-furan) (**A**) was found to form from the reaction (18%). Product **A** was not observed when fructose was used as the starting material. The formation of **A** has been previously documented by Lund, who found that it is formed in 50–60% yield under electrochemical reduction of MFM in a biphasic medium consisting of  $\text{HCl}/\text{NaI}/\text{CH}_2\text{Cl}_2$ .<sup>[21]</sup> Product **A** was proposed to be formed from the carbocationic condensation of MFM with concurrent loss of formaldehyde. This result, combined with the lack of observed MFM during the reaction of fructose, suggest that MFM is a highly reactive low concentration intermediate in the reaction. The low concentration minimizes the amount of side products formed when fructose is used as the starting material.

The intermediates also have vastly different solubilities. MF and DMF are insoluble in water making them less susceptible to side product formation in the reaction with aqueous HI, and accounts for their near quantitative conversions to DMTHF. In comparison, HMF and MFM are water soluble making them more susceptible to side product formation in highly acidic aqueous HI. HDO and 2,5-hexanediol are also highly soluble in water, but are less susceptible to side product formation with HI compared to MFM and HMF, and as a result their conversion to DMTHF was quantitative.

**Deuterium labeling experiments:** Deuterium labeling experiments were carried out in an effort to provide further insight into the reaction mechanism. The formed DMTHF was analyzed by both GC–MS, and NMR spectroscopy ( $^1\text{H}$ , and  $^{13}\text{C}$ ). According to the proposed mechanism given in Scheme 5, Rh-catalyzed hydrogenation first occurs in step (c), when the aldehyde group is hydrogenated to an alcohol (leading to  $[\text{D}_1]\text{MFM}$  when using  $\text{D}_2$ ). The MFM intermediate is then reduced by HI to DMF. Two routes to the final DMTHF product are now possible: Direct hydrogenation of DMF to DMTHF with  $\text{D}_2$  would result in the incorporation of four additional deuterons ( $\text{D}_5$  total); in contrast, the alternative route involves hydrogenation of the two carbonyl groups of HDO (two additional deuterons using  $\text{D}_2$ ) followed by cyclization-dehydration to DMTHF ( $\text{D}_3$  total). Note that any deuterium on the hydroxyl group will rapidly wash out by exchange with  $\text{H}_2\text{O}$ .

Ideally the molecular ion peak for DMTHF ( $m/z = 100$ ) should be used, however its small size (5.7%) makes it unreliable in terms of measuring deuterium incorporation. Instead the peak corresponding to the loss of a methyl group ( $m/z = 85$ ) which is more abundant (72.2%), was analyzed for all of the labeling experiments. In the first experiment deuterium gas ( $\text{D}_2$ ) (60 psi, 24 h) was used in place of hydrogen. An analysis of the isotope ratios for the  $m/z$  85 peak ( $\text{D}_0$ ) in the mass spectrum showed a  $\text{D}_1$  incorporation of 32% ( $m/z = 86$ ) and  $\text{D}_2$  incorporation of 3% ( $m/z = 87$ ), far less than the predicted isotope ratios.

In a different experiment,  $\text{D}_2\text{O}$  was used as the deuterium source whereas standard hydrogen gas ( $\text{H}_2$ ) was used. This experiment was based on the expectation that the high ex-

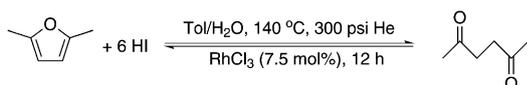
change rate between D<sub>2</sub>O and HI generates DI in situ. The end result was a large amount of deuterium incorporation in the DMTHF end product. Analysis by GC-MS of the *m/z* = 85 peak showed incorporation for D<sub>5</sub>–D<sub>8</sub>, with a D<sub>6</sub> incorporation of 31.3% (*m/z* = 91) and a D<sub>7</sub> incorporation of 34.9% (*m/z* = 92) (Table 2). The amount of D<sub>0</sub>–D<sub>4</sub> products was negligible. Broad resonances were observed in the <sup>13</sup>C NMR spectrum with a large amount of hyperfine splitting indicative of deuterium incorporation.

Table 2. Isotope ratios for the DMTHF C<sub>5</sub>H<sub>9</sub>O fragment. HI/D<sub>2</sub>O reaction conditions.<sup>[a]</sup>

D <sub>n</sub>	<i>m/z</i>	[%] <sup>[b]</sup>
D <sub>5</sub>	90	16.5
D <sub>6</sub>	91	31.3
D <sub>7</sub>	92	34.9
D <sub>8</sub>	93	17.3

[a] Reaction conditions: fructose (1 mmol), HI (1.5 mmol), RhCl<sub>3</sub> (0.05 mmol), H<sub>2</sub> (300 psi), D<sub>2</sub>O (2 mL), C<sub>6</sub>D<sub>6</sub> (2 mL), at 140 °C for 6 h. The C<sub>6</sub>D<sub>6</sub> layer was analyzed by GC, GC-MS, and NMR spectroscopy (<sup>1</sup>H and <sup>13</sup>C). [b] Percentages were determined from the integration of peak areas in GC/MS.

The above labeling studies indicate that deuterium incorporation into DMTHF occurred almost exclusively from HI. However these results are misleading. As shown in Table 1, when helium was used at the onset of the reaction, product formation stopped at MF, demonstrating that H<sub>2</sub> is necessary for the reaction to proceed to completion. The need for H<sub>2</sub> was also demonstrated in a separate reaction when the intermediate DMF was used as the starting material. DMF was allowed to react with 6 equivalents of HI under a helium atmosphere with RhCl<sub>3</sub> added as a control to determine if DMTHF would form in the absence of hydrogen (Scheme 7). After heating for 5 and 17 h, no DMTHF formed, instead an equilibrium ratio was established between DMF and HDO (*K* = 2.3).



Scheme 7. Reaction of DMF with HI under an inert (He) atmosphere.

The equilibrium mixture converted completely to DMTHF when the reaction vessel was recharged with hydrogen (300 psi) and reheated for 4 h at 140 °C, demonstrating that hydrogen was necessary to obtain DMTHF in line with the results from Table 1. The experiment was repeated using the typical amount of HI (1.5 equiv) with D<sub>2</sub>O as the solvent under an inert atmosphere. The DMF and HDO formed were analyzed by GC-MS and NMR spectroscopy (<sup>1</sup>H and <sup>13</sup>C). A large amount of deuterium incorporation was observed in both products. HDO had D<sub>5</sub>–D<sub>9</sub> incorporation (GC-MS) when the molecular ion peak of 114 (D<sub>0</sub>) was examined (Table 3), whereas the amount of D<sub>1</sub>–D<sub>4</sub> products

Table 3. Isotope ratios in HDO product in the equilibration with DMF using HI/D<sub>2</sub>O.<sup>[a]</sup>

D <sub>n</sub>	<i>m/z</i>	[%] <sup>[b]</sup>
D <sub>5</sub>	119	15.0
D <sub>6</sub>	120	25.5
D <sub>7</sub>	121	29.0
D <sub>8</sub>	122	22.4
D <sub>9</sub>	123	8.0

[a] Reaction conditions: DMF (1 mmol), HI (1.5 mmol), RhCl<sub>3</sub> (0.10 mmol); H<sub>2</sub> (300 psi), D<sub>2</sub>O (2 mL); C<sub>6</sub>D<sub>6</sub> (2 mL) at 140 °C for 12 h. The C<sub>6</sub>D<sub>6</sub> layer was analyzed by GC, GC-MS, and NMR spectroscopy (<sup>1</sup>H and <sup>13</sup>C). [b] Percentages were determined from the integration of peak areas in GC/MS.

was negligible. Broad resonances with a great deal of hyperfine splitting were observed in both the <sup>1</sup>H and <sup>13</sup>C NMR spectra for both the methyl and methylene groups.

Likewise, a large amount of D<sub>3</sub>–D<sub>8</sub> incorporation (GC-MS) was observed for DMF when the molecular ion peak at 96 (D<sub>0</sub>) was examined (Table 4); the amount of D<sub>1</sub>–D<sub>2</sub> products was negligible. Deuterium incorporation was also readily apparent in the <sup>1</sup>H and <sup>13</sup>C NMR spectra.

Table 4. Isotope ratios in DMF product in the equilibration with HDO using HI/D<sub>2</sub>O.<sup>[a]</sup>

D <sub>n</sub>	<i>m/z</i>	[%] <sup>[b]</sup>
D <sub>3</sub>	99	13.5
D <sub>4</sub>	100	24.6
D <sub>5</sub>	101	28.7
D <sub>6</sub>	102	21.5
D <sub>7</sub>	103	9.8
D <sub>8</sub>	104	1.9

[a] Reaction conditions: DMF (1 mmol), HI (1.5 mmol), RhCl<sub>3</sub> (0.10 mmol); H<sub>2</sub> (300 psi), D<sub>2</sub>O (2 mL), C<sub>6</sub>D<sub>6</sub> (2 mL), 140 °C for 12 h. The C<sub>6</sub>D<sub>6</sub> layer was analyzed by GC, GC-MS, and NMR spectroscopy (<sup>1</sup>H and <sup>13</sup>C). [b] Percentages were determined from the integration of peak areas in GC/MS.

These results demonstrated that DMF and HDO are in dynamic equilibrium and the protons in the compounds are readily exchangeable in the acidic environment. Although mechanistic information with respect to hydrogenation could not be determined with this system, due to the high exchange rate of the protons, the deuterium labeling experiments helped to determine the relationships between the major intermediates. The equilibration was also observed when HDO was used as the starting compound and the formation of DMF was observed with extensive deuterium incorporation in both compounds.

Interestingly when DMTHF by itself was heated under the standard reaction conditions using D<sub>2</sub>O as the co-solvent, deuterium incorporation (D<sub>1</sub>, 35%; D<sub>2</sub>, 8%) was observed by GC/MS and the *cis/trans* ratio of the DMTHF diastereomers changed from 1:1 to 1.3:1. Given that the only two acidic protons in DMTHF are in the 2 and 5 positions, the observation that only 1–2 deuteriums were incorporated is not surprising.

**Rhodium-catalyzed conversion of a mixture of DMF/HDO to DMTHF:** Two different routes are possible in the final conversion to DMTHF. The first route involves the direct hydrogenation of DMF (Scheme 5, step (e)), whereas the second route involves the hydrogenation of HDO to 2,5-hexandiol (Scheme 5, step (f)), which then cyclizes to DMTHF in a dehydration step. Bartok has previously shown that different Brønsted- and Lewis acids can be used in catalytic amounts in the cyclodehydration of 2,5-hexandiol to DMTHF in quantitative yields, including the use of HBr and  $\text{RhCl}_3$ .<sup>[22]</sup>

In an attempt to determine which route was predominant, direct hydrogenation of DMF or the hydrogenation–cyclodehydration of HDO, two hydrogenation reactions were attempted using  $\text{RhI}_3$  as the catalyst in the absence of HI. After heating for 30 min at 80 °C, the reactions were stopped and the reaction mixture analyzed by GC. HDO had fully converted after 30 min, whereas only about one third of the DMF had been converted to DMTHF, although full conversion to DMTHF did occur after 3 h of heating. These experiments suggest that, whereas both routes are viable, the route involving HDO is faster and most likely the predominant one in the reaction.

## Conclusion

The combination of HI and a Rh salt serves as dual catalysts in the transformation of fructose to DMTHF, a valuable organic compound and potential gasoline substitute. HI acts as a dehydration agent in converting fructose to HMF. HI also acts as a reducing reagent to convert HMF to MF by reducing conjugated carbinols and generates iodine as a byproduct. It also enables the hydration of DMF to HDO, an important intermediate on route to DMTHF. The Rh catalyzes the conversion of iodine back to HI with hydrogen. The Rh catalyst is also necessary for the hydrogenation of the unsaturated C=C and C=O bonds of the intermediates which lead to the final product DMTHF. The exact identity of the Rh catalyst under the reaction conditions could not be determined, but  $\text{RhI}_3$  was established as the catalyst precursor. The catalyst is stable under optimized reaction conditions and can be recycled repeatedly with an excess of HI at a reaction temperature of 80 °C.

## Experimental Section

**Materials:** Rhodium(III) chloride hydrate was purchased from Pressure Chemical Co., and  $\text{RhI}_3$  was purchased from Strem Chemicals. All of the other chemicals and fructose were purchased either from Sigma–Aldrich or from Alfa Aesar. High pressure hydrogen was obtained from GT&S, Inc. and used without further purification. Toluene and benzene were used as received. Isotopically enriched chemicals such as  $\text{C}_6\text{D}_6$  and  $\text{D}_2\text{O}$  were obtained from Cambridge Isotope Laboratories and used without further purification. ICP-MS analysis was performed by Robertson Microlit Laboratories.

**Analysis methods:** The products were analyzed by  $^1\text{H}$  NMR spectroscopy (Bruker Avance-360 spectrometer equipped with a quad-nuclear probe operating at 360.13 MHz). GC (HP Hewlett Packard-5890 series II with a FID detector; 95% dimethyl/5% diphenyl-polysiloxane column) and GC-MS (Waters GC-TOF with Agilent 6890 GC; 20 meter 150  $\mu\text{m}$  i.d., 0.15  $\mu\text{m}$  95% dimethyl/5% diphenyl-polysiloxane film column; 70 eV electron ionization). The  $^1\text{H}$  NMR spectra and the GC retention times of the products were also compared with authentic samples.

**GC and GC-MS analysis methods:** For GC analysis, the initial oven temperature was 40 °C; the temperature was then ramped at 5 °C  $\text{min}^{-1}$  until 80 °C was reached; after that the temperature was ramped at 10 °C  $\text{min}^{-1}$  until 240 °C. For GC-MS the same method was used. The injector temperature was 290 °C with a split of 20:1. The helium flow rate was 0.5  $\text{mL min}^{-1}$ . The temperature of the transfer line was 220 °C. The mass scan was 35–650  $\text{Da s}^{-1}$ .

**Quantification methods:** Yields of products were determined from  $^1\text{H}$  NMR spectra and GC analysis by using nitromethane as the internal standard. The yields reported were reproduced to within 5%.

**Synthesis of MF from HMF with HI:** HMF (1 mmol, 126 mg), HI (3 mmol, 57 wt% in water, 0.4 mL), nitrogen flushed water (1.8 mL), and  $[\text{D}_6]$ benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with helium, and charged with 300 psi of helium. The bomb was placed in an oil bath and heated to 100 °C for 2.5 h. After the reaction was completed the benzene layer was clear dark-orange whereas the water layer was clear red, and dark brown-black solid had precipitated (humins). The benzene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (47% yield of MF). The intermediate IMF was observed by GC and  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ , 25 °C): 8.97 (s, 1 H, aldehyde proton), 6.19 (d, 1 H,  $J=3.5$  Hz, ring proton), 5.49 (d, 1 H,  $J=3.5$  Hz, ring proton), 3.50 ppm (s, 2 H, iodo-methylene proton).

**Comparison of  $\text{RhI}_3$  versus  $\text{RhCl}_3$  in the conversion of fructose to DMTHF:** *Catalysis by  $\text{RhI}_3$ :* Fructose (1 mmol, 180 mg),  $\text{RhI}_3$  (0.05 mmol, 24.2 mg) HI (1.5 mmol, 57 wt% in water, 0.2 mL), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 125 °C for 11 h. After the reaction was completed the toluene layer was clear and colorless whereas the water layer was clear and yellow with suspended black particles at the solvent interface. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (65% yield of DMTHF).

*Catalysis by  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ :* Fructose (1 mmol, 180 mg),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.05 mmol, 13.2 mg) HI (1.5 mmol, 57 wt% in water, 0.2 mL), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 125 °C for 26 h. After the reaction was completed the toluene layer was clear and colorless while the water layer was clear and yellow with suspended black particles at the solvent interface. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (64% yield of DMTHF).

**Hydrogenation of toluene to methylcyclohexane:** *Comparison of  $\text{RhI}_3$  versus  $\text{RhCl}_3$  using  $\text{RhI}_3$ :*  $\text{RhI}_3$  (0.05 mmol, 24.2 mg), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 2 h. The recovered solution was then analyzed by GC, methylcyclohexane was formed in 0.12% yield. The % yield was computed by taking the area for methylcyclohexane and dividing by the total area (dimethylcyclohexane and toluene).

*Using  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ :*  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.05 mmol, 13.2 mg), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 2 h during which time the pressure dropped to 200 psi. The recovered solution was then analyzed by GC, methylcyclohexane was formed in 65% yield. The % yield was computed

by taking the area for methylcyclohexane and dividing by the total area (methylcyclohexane and toluene).

**Procedures for reactions shown in Scheme 4: Equation (1):**  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.05 mmol, 13.2 mg), water (2 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 2 h. After heating both layers of the recovered solution were clear and colorless with suspended black particles at the solvent interface. Fructose (1 mmol, 180 mg) and HI (1.5 mmol, 57 wt % in water, 0.2 mL) were then added to the reaction mixture. The bomb was recharged with hydrogen (300 psi) and heated at 140 °C for 3.5 h. The recovered toluene layer was orange and clear, and was characterized by GC. DMTHF formation was not observed.

**Equation (2):**  $\text{RhI}_3$  (0.05 mmol, 24.2 mg) water (2 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 125 °C for 2.5 h. After heating, both layers of the recovered solution were clear and colorless with suspended black particles coating the stirrer bar in the water layer. Fructose (1 mmol, 180 mg) and HI (1.5 mmol, 57 wt % in water, 0.2 mL) were then added to the reaction mixture. The bomb was recharged with hydrogen (300 psi) and heated at 125 °C for 16 h. The recovered toluene layer was yellow-orange and slightly cloudy, whereas the water layer was yellow and clear with black solid suspended at the solvent interface. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (40 % yield of DMTHF).

**Equation (3):**  $\text{RhI}_3$  (0.05 mmol, 24.2 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL), toluene (2 mL) and water (1.8 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with helium, and charged with 300 psi of helium. The bomb was placed in an oil bath and heated to 125 °C for 3.5 h. After heating the water solution was cloudy with a brown color whereas the toluene solution was clear and colorless. Fructose (1 mmol, 180 mg) was then added to the reaction mixture. The bomb was recharged with hydrogen (300 psi) and heated at 125 °C for 14 h. The recovered toluene layer was clear and colorless, whereas the water layer was yellow and clear with black solid suspended at the solvent interface. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (82 % yield of DMTHF).

**Equation (4):**  $\text{RhI}_3$  (0.05 mmol, 24.2 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL), toluene (2 mL) and water (1.8 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with hydrogen, and charged with 300 psi of hydrogen. The bomb was placed in an oil bath and heated to 125 °C for 2.5 h. After heating the toluene solution was clear and colorless, whereas the water layer was clear and yellow. Suspended black solid was present at the solvent interface and on the bottom of the water layer. Fructose (1 mmol, 180 mg) was then added to the reaction mixture. The bomb was recharged with hydrogen (300 psi) and heated at 125 °C for 19 h. The recovered toluene layer was slightly cloudy with a green tint, while the water layer was yellow and clear with black solid suspended at the solvent interface. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR (22 % yield of DMTHF).

**Reaction of  $\text{RhI}_3$ , HI, and  $\text{H}_2$  without fructose:**  $\text{RhI}_3$  (0.30 mmol, 145 mg), HI (9 mmol, 57 wt % in water, 1.2 mL), and water (6 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with hydrogen, and charged with 300 psi of hydrogen. The bomb was placed in an oil bath and heated to 125 °C for 2 days. The water was carefully removed by pipette and the suspended black solid was dried in a 100 °C oven for 8 h. The black solid was analyzed by ICP-MS: 78.0 % Rh, 23.0 % I.

**Fructose conversion to DMTHF: Identification of reaction intermediates:** Fructose (1 mmol, 180 mg),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.10 mmol, 26 mg) HI (10 mmol, 57 wt % in water, 1.4 mL), water (3 mL), and toluene (4 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with helium, and charged with 300 psi of helium. The bomb was placed in an oil bath

and heated to 80 °C for 9 h. The toluene layer was then analyzed by GC. The reaction was resumed after charging with 300 psi of  $\text{H}_2$ . After heating at 80 °C for 20 min the toluene layer was re-analyzed by GC. The heating/GC analysis/hydrogen re-charge was repeated after 30, 30, 60, and 120 min. The relative percentages (Table 1) of the intermediates were obtained by taking the area of the intermediate and dividing by the total area of all the intermediates.

**Independent synthesis of DMTHF starting with the major intermediates:**

**General procedure (Scheme 6):** The intermediate (1 mmol),  $\text{RhI}_3$  (0.05 mmol, 24.2 mg) HI (1.5 mmol, 57 wt % in water, 0.2 mL), water (1.8 mL), and toluene or benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 125 °C for 4–12 h. The reaction with MFM was done on a smaller scale to minimize side products from the highly reactive MFM starting material. The toluene layer was characterized and quantified by GC and  $^1\text{H}$  NMR.

**Reaction with HMF:** HMF (1 mmol, 126 mg) was heated for 12 h in benzene/water. DMTHF yield was 54 %.

**Reaction with MF:** MF (1 mmol, 99.5  $\mu\text{L}$ ) was heated for 12 h in toluene/water. DMTHF yield was 100 %.

**Reaction with MFM:** MFM (0.2 mmol, 21  $\mu\text{L}$ ) and HI (0.30 mmol, 57 wt % in water, 40  $\mu\text{L}$ ), was heated for 4 h in benzene/water. DMTHF yield was 41 %, 2'-methylenebis(5-methyl-furan) yield was 18 %, HDO yield was 3 %.

**Reaction with 2,5-DMF:** DMF (1 mmol, 106.5  $\mu\text{L}$ ) was heated for 12 h in toluene/water. DMTHF yield was 95 %.

**Reaction with 2,5-HDO:** HDO (1 mmol, 117  $\mu\text{L}$ ) was heated for 5 h in toluene/water. DMTHF yield was 100 %.

**Reaction with 2,5-hexanediol:** 2,5-hexanediol (1 mmol, 123  $\mu\text{L}$ ) was heated for 4 h in toluene/water. DMTHF yield was 100 %.

**Deuterium labeling experiments: Conversion of Fructose to DMTHF using  $\text{D}_2$ :** Fructose (1 mmol, 180 mg),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.10 mmol, 26 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL), water (1.8 mL), and  $[\text{D}_6]$ benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{D}_2$ , and charged with 60 psi of  $\text{D}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 26 h. After the reaction was complete the benzene layer was dark opaque whereas the water layer was red. The benzene layer was washed with saturated sodium thiosulfate solution (aq), and filtered through glass wool. The benzene layer was analyzed by GC, GC-MS, and NMR spectroscopy ( $^1\text{H}$  and  $^{13}\text{C}$ ).

**Conversion of Fructose to DMTHF using  $\text{D}_1$ :** Fructose (1 mmol, 180 mg),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.05 mmol, 13.2 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL),  $\text{D}_2\text{O}$  (2 mL), and  $[\text{D}_6]$ benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 6 h. After the reaction was complete the benzene was filtered through glass wool to remove suspended particles, washed with saturated sodium thiosulfate solution (aq), and filtered through glass wool. The benzene layer was analyzed by GC, GC-MS, and NMR spectroscopy ( $^1\text{H}$  and  $^{13}\text{C}$ ). See Table 2 for % deuterium incorporation into DMTHF.

**Equilibration of 2,5-DMF and 2,5-HDO with  $\text{D}_1$ :** DMF (1 mmol, 106  $\mu\text{L}$ ),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.10 mmol, 26 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL),  $\text{D}_2\text{O}$  (2 mL), and  $[\text{D}_6]$ benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with  $\text{H}_2$ , and charged with 300 psi of  $\text{H}_2$ . The bomb was placed in an oil bath and heated to 140 °C for 12 h. The recovered benzene solution was clear with a light beige tint while the water layer was still a dark red color. The benzene layer was analyzed by GC, GC-MS, and NMR spectroscopy ( $^1\text{H}$  and  $^{13}\text{C}$ ). See Tables 3 and 4 for % deuterium incorporation of 2,5-DMF and 2,5-HDO.

**Interconversion of cis/trans isomers of DMTHF:** DMTHF (0.83 mmol, 100  $\mu\text{L}$ ),  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  (0.10 mmol, 26 mg), HI (1.5 mmol, 57 wt % in water, 0.2 mL),  $\text{D}_2\text{O}$  (2 mL), and  $[\text{D}_6]$ benzene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure

stainless steel reactor, flushed three times with H<sub>2</sub>, and charged with 300 psi of H<sub>2</sub>. The bomb was placed in an oil bath and heated to 140 °C for 22.5 h. The recovered benzene and water layers were clear and colorless with suspended black particles at the solvent interface. The benzene layer was analyzed by GC and GC/MS. The *cis* and *trans* isomers appear as separate peaks on the GC spectrum, the ratios were calculated by comparing the areas for each isomer. Before heating the ratio was 1.1:1 and after heating the ratio changed to 1.3:1.

**Reactions related to mechanistic elucidation:** Conversion of 2,5-DMF to DMTHF (Scheme 7): DMF (1 mmol, 106 μL), RhCl<sub>3</sub>·3H<sub>2</sub>O (0.077 mmol, 20.3 mg), HI (6 mmol, 57 wt % in water, 0.8 mL), water (1.6 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with helium, and charged with 300 psi of helium. The bomb was placed in an oil bath and heated to 140 °C for 5 h. The recovered solution contained a clear colorless toluene layer with a brownish residue on the side of the liner. The toluene layer was tested by GC which showed a ratio between 2,5-DMF and 2,5-HDO of 1:2.3. The bomb was recharged with helium (300 psi) and heated at 140 °C for an additional 12 h. The toluene layer remained clear and colorless, whereas the water layer had turned clear and orange. The toluene layer was tested again by GC and the DMF/HDO ratio was unchanged. The bomb was recharged with H<sub>2</sub> (300 psi) and heated at 140 °C for an additional 4 h. The toluene layer was clear and colorless whereas the water layer had turned clear and bright red. Analysis by GC showed that complete conversion of DMF and HDO to DMTHF had occurred.

**Hydrogenation of 2,5-DMF to DMTHF:** DMF (1 mmol, 106 μL), RhI<sub>3</sub> (0.05 mmol, 24.2 mg), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with H<sub>2</sub>, and charged with 300 psi of H<sub>2</sub>. The bomb was placed in an oil bath and heated at 80 °C for 30 min. The toluene layer was analyzed by GC, which showed that approximately a third of the DMF had been converted to DMTHF. The bomb was recharged with H<sub>2</sub> (300 psi) and heated at 80 °C for an additional 2 h. The toluene layer was re-analyzed by GC and showed that quantitative conversion to DMTHF had occurred.

**Hydrogenation of 2,5-HDO to DMTHF:** HDO (1 mmol, 117 μL), RhI<sub>3</sub> (0.05 mmol, 24.2 mg), water (1.8 mL), and toluene (2 mL) were added to a glass reactor liner in open air. Then the vial was put into a high pressure stainless steel reactor, flushed three times with H<sub>2</sub>, and charged with 300 psi of H<sub>2</sub>. The bomb was placed in an oil bath and heated at 80 °C for 30 min. The toluene layer was analyzed by GC which showed that quantitative conversion to DMTHF had occurred (nitromethane standard used).

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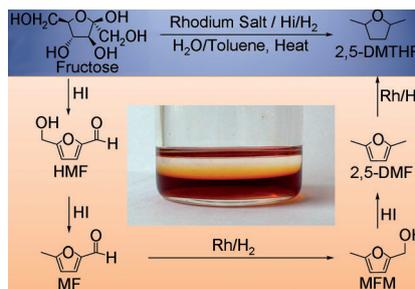
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**Carbohydrates**

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**Mechanistic Study of a One-Step Catalytic Conversion of Fructose to 2,5-Dimethyltetrahydrofuran**



**Sugar to fuel:** Carbohydrates, such as fructose, can be fully dehydroxylated to 2,5-dimethyltetrahydrofuran (DMTHF), a valuable chemical and potential gasoline substitute, by the use of a dual catalytic system consisting of HI and RhX<sub>3</sub> (X = Cl, I; see scheme). A mechanistic study has been carried out to understand the roles that both acid and metal play in the reaction.