Chemical Conversion of Biomass Into New Generations of Renewable Fuels, Polymers, and Value-Added Products

December 28, 2011

Primary sponsor:

Dr. Mark Mascal
Professor
Department of Chemistry
University of California Davis
1 Shields Avenue
Davis, California 95616
Tel: 530-754-5373
Email: mascal@chem.ucdavis.edu

Contact person:

Same as above.

Project title: Chemical Conversion of Biomass Into New Generations of Renewable Fuels, Polymers, and Value-Added Products

Short description of most recent milestone: In 2010, we were granted a US patent. We continue to publish groundbreaking work in this area, and our industrial partners have demonstrated our technology on a multi-kg per day scale, with a 1 ton per week production facility under construction for operation from mid-February. Further, we have enlarged the derivative compass of our cellulose-derived platform chemical into new fuels, plastics, and pharma/agrochemical markets.

Eligibility statement: The technology is nominated by the University of California Davis, and is eligible for the academic award.

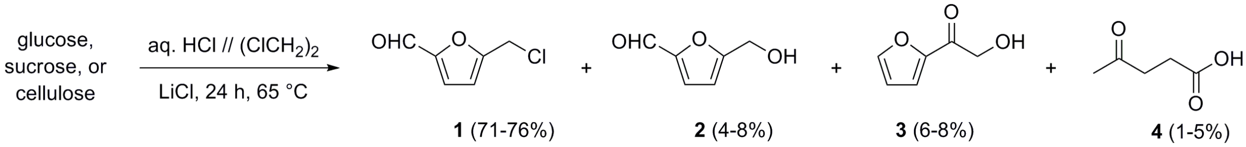
Focus area: The primary focus area is the use of greener synthetic pathways, *i.e.* the use of green feedstocks that are innocuous or renewable (in this case, waste biomass *versus* petroleum). A secondary focus area is the design of greener chemicals, in this case, producing fuels that are less toxic than current products, inherently safer with regard to accident potential, biodegradable, and safer for the atmosphere in the sense that they are carbon-cycle neutral.

Description of the US component: All of the research and development described below occurred within the United States.

Abstract: These are days of extraordinary necessity in bioenergy research. The prevailing, world-wide "petroleum economy" is experiencing a gradual, but inevitable, decline, making way for alternative technologies to fill the void. As such, a variety of schemes for the exploitation of lignocellulose, the most abundant organic material on the planet, have been advanced. While these vary considerably in detail, they all seek to achieve the same basic objective, *i.e.* to cleave the glycan into its monosaccharide components and to derive useful products therefrom, as efficiently and inexpensively as possible. Although new approaches are continually being developed and advanced, ultimately, it will be the "best of the best" which rise to the top, *i.e.* those which **1**) *give the best product yields*, **2**) *minimize capital and operating expenses*, and **3**) *are flexible with respect to feedstock sources*. In 2008 we described a process which actualizes all three of these objectives. The method involves acidic digestion of cellulose in a biphasic acid//solvent reactor to give the novel organic platform chemical 5-(chloromethyl)furfural (CMF), in remarkably high yield. In subsequent work, we determined that the method works equally well on raw biomass, producing not only CMF from the cellulose content of the feedstock, but also furfural itself from the C_5 sugar fraction (hemicellulose), constituting the *total carbohydrate utilization of biomass*. Most recently, we have upgraded the process such that it produces CMF (84%) and the well known carbohydrate breakdown product levulinic acid (LA) (5%) in overall 89% yield from cellulose. Sucrose can be processed in the same way, giving CMF and LA in a remarkable 95% combined yield. The method also works well on oil seed feedstocks, and leads to a 25% increase in biodiesel production from safflower seeds. In short, ***we know of no other process which gives simple organic products directly from cellulosic materials in comparable yield.*** The CMF derivative portfolio includes biofuels, renewable polymers, agrochemicals, and pharmaceuticals, and the technology has now been adopted by the cleantech companies Micromidas and Incitor, with backing from major chemical and energy company partners.

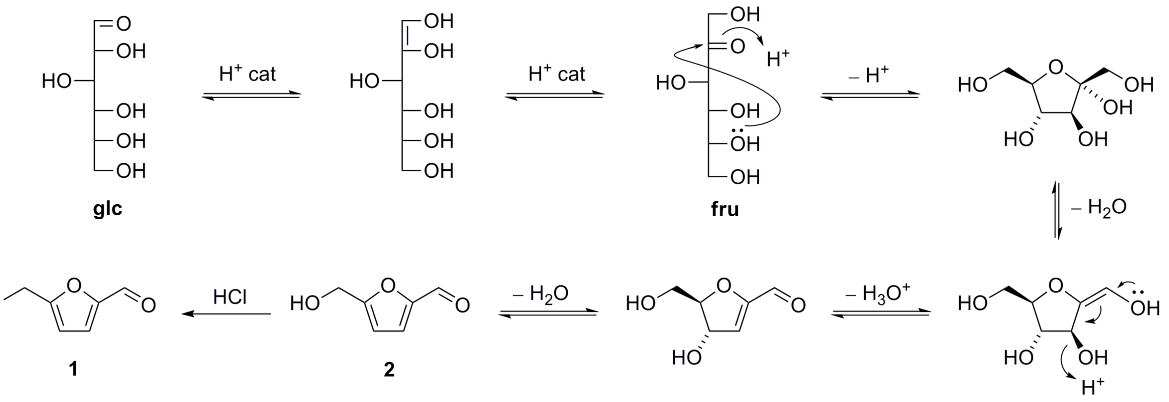
Description of the nominated technology

In 2008, we reported that glucose, sucrose, and microcrystalline cellulose could be converted into a mixture of 5-(chloromethyl)furfural (CMF) **1**, 5-(hydroxymethyl)furfural (HMF) **2**, 2-(2-hydroxyacetyl)furan **3**, and levulinic acid (LA) **4** in combined yields of up to 90% by simple reaction with an aqueous HCl-LiCl solution (Scheme 1).[1] The process involved heating a mixture of the substrate with the HCl-LiCl reagent at 65 °C in a biphasic reactor with continuous circulation of a solvent. The resulting "crude oil" was a mixture of compounds **1**-**4**.



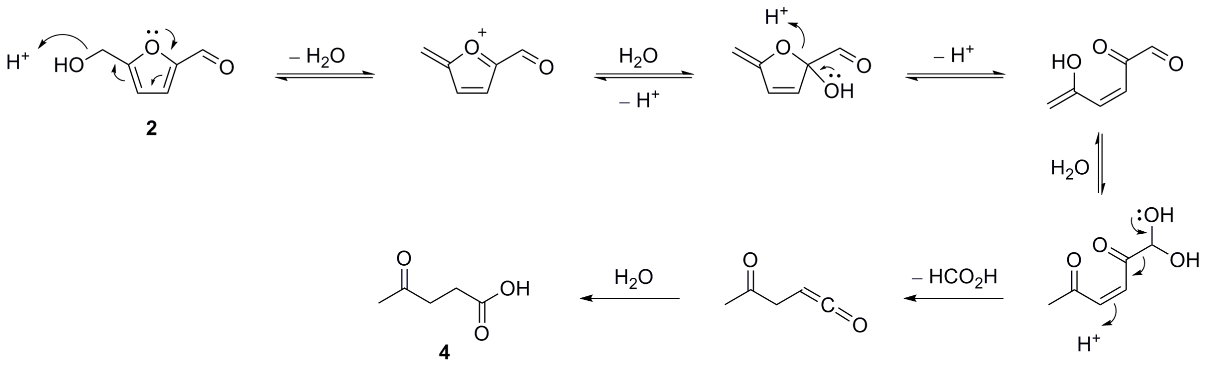
Scheme 1.

Mechanistically, the reaction can be interpreted as shown in Schemes 2 and 3 for the main products of interest in this process, *i.e.* CMF **1**, HMF **2**, and LA **4**. Thus, glucose undergoes an acid-catalyzed isomerization to fructose, which is followed by a series of dehydrations to give HMF **2**. Finally, nucleophilic substitution of the remaining OH group in **2** gives **1**. The reason that the yields of **1** are so high is that it is much more lipophilic than **2** and is swept into the organic phase of the reaction mixture, thereby preventing the degradation reactions that have long plagued the acidic processing of biomass. Nevertheless, a small amount of the HMF **2** does not convert into CMF, and is either isolated in the product mixture, or goes on to give a mixture of formic acid and LA **4** as shown in Scheme 3.



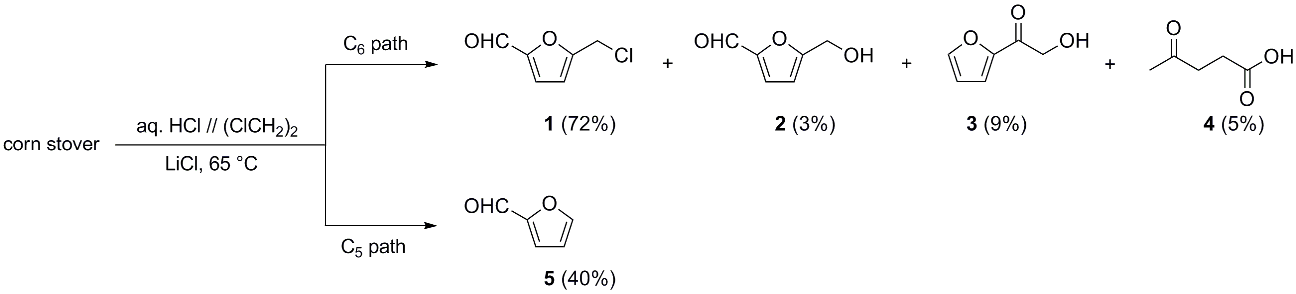
Scheme 2.

The real test of the above process was whether it could also operate on cellulosic waste materials (agricultural, forestry, municipal). We thus subjected cotton, straw, corn stover, newsprint, and wood chips to the same conditions as outlined above for pure cellulose.[2] In each case, we obtained a similar mixture of compounds **1**-**4**. In order to determine the chemical yield, we acquired an analyzed sample of corn stover from the National Renewable Energy Laboratory. Based on the carbohydrate content of the corn stover, the isolated yields of products turned out to be **1**, 72%; **2**, 3%, **3**, 9% and **4**, 5%, for a total of 89%, which is entirely consistent with that of pure cellulose itself. This means that the conversion process was unaffected by the presence of the other components in raw biomass. Lignin, for example, survives the reaction essentially unchanged and can simply be filtered off. Any protein which is present is hydrolyzed and turns up in the aqueous phase as a mixture of amino acid salts (essentially, hydrolyzed vegetable protein).



Scheme 3.

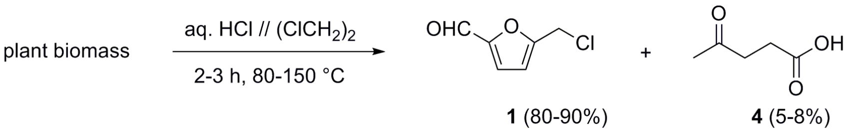
We also isolated furfural **5** from the reaction mixture, which was clearly the result of the same cyclization-dehydration processes operating on the hemicellulose fractions of the feedstocks (Scheme 4). Hemicellulose, which consists mainly of C_5 sugars, is the second most-abundant organic material in nature, typically representing 25–35% of lignocellulose by mass. In mainstream ethanol production, this vast resource typically goes unutilized, because native yeasts do not ferment C_5 sugars. The yield of **5** (40%) is lower than the combined yield of **1**-**4**, but is consistent with reported yields of furfural from biomass in commercial processes, which are typically around 50% of the theoretical. The key point here is that we have accomplished the *total carbohydrate utilization of biomass*, where the cellulose fraction produces mainly CMF **1**, while the hemicellulose fraction gives furfural **5**. Furfural is a chemical commodity which is produced globally as a feedstock for resin manufacture and as a precursor to a range of specialty chemicals, including fuel additives.



Scheme 4.

Another key feature of this process is that only simple mechanical pretreatment of the feedstock is required. In the case of cotton or newspaper, the substrate was shred into small pieces *ca.* 0.5 cm on a side. For straw, corn stover, and wood, the material was milled to a coarse powder. This is significant when one considers the high expense involved in the pretreatment of biomass for enzymatic digestion, which usually involves techniques such as steam, ammonia, or supercritical fluid explosion.

The technology has undergone refinements since it was first reported, and is now best summarized as shown in Scheme 5.[3]

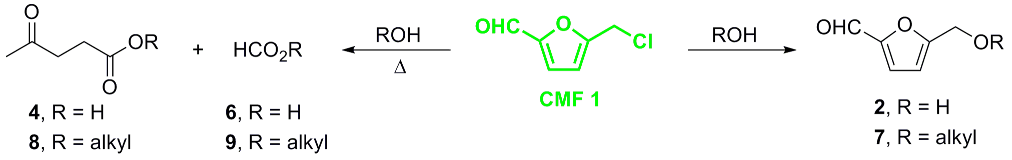


Scheme 5.

The upgrades to the process as summarized in Scheme 5 include the following:

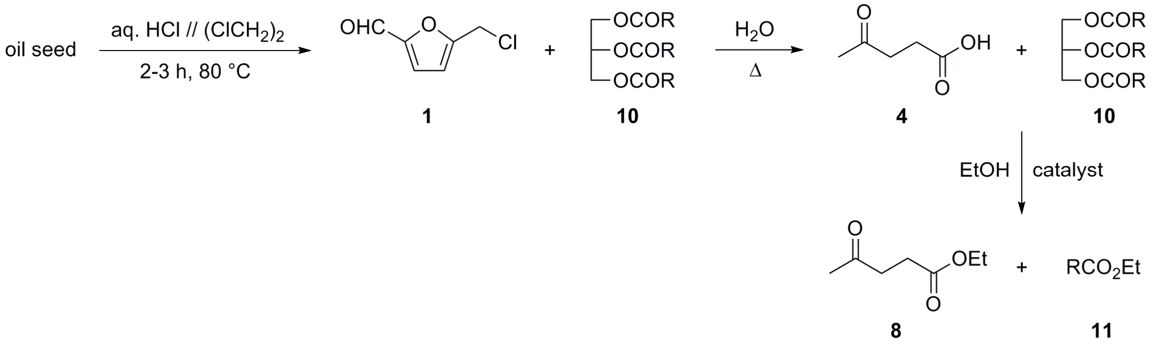
1) *A substantial acceleration of the reaction rate*. Whereas the reaction in Scheme 1 used to take about 24 hours to reach a high yield, it is now complete within 2-3 hours. This was achieved by running the reaction at 80-100 °C (for most feedstocks) and a slight overpressure, generally 40 psi.
2) *A reduction in extraction solvent usage*. We originally described a continuous extraction method which required the circulation of several liters of solvent through the reactor. This has now been replaced with a serial extraction protocol requiring a much smaller solvent loop.
3) *Elimination of the use of the LiCl catalyst*. The improved reactor design and efficiency eliminates the need for this cellulose swelling agent.
4) *Improvement of the yield of CMF **1***. In the upgraded process, there are only two products, CMF **1** and LA **4**. Minor products **2** and **3** from Scheme 1 are no longer observed. Depending on feedstock, CMF yields are between 80-90%, and LA yields are 5-9%. The yield of **1**+**4** from cellulose is 84-89%. Record yields are attained using sucrose as the substrate, which can be as high as 95% of the theoretical.
5) *Extension of the method to chitin as a feedstock*. Chitin, a 1,4-β-linked *N*-acetyl-2-amino-2-deoxy-D-glucan, is best known as the structural component of the exoskeletons of insects and crustaceans, and is second only to lignocellulose in natural abundance. It is a high tonnage waste product of the seafood industry. Chitin is exceptionally insoluble and resistant to hydrolysis, and yet it too can be made to give a mixture of **1**+**4** at higher reaction temperatures (~150 °C).

CMF **1** is a versatile platform chemical from a number of perspectives. It can access two distinct product manifolds – furanic and levulinic. For example, **1** can be converted into HMF **2** by a simple reaction with water. Hydrolysis under more forcing conditions gives a high yield of LA **4** plus formic acid **6** (Scheme 6). LA is has the distinction of appearing on the list of Top Value-Added Chemicals From Biomass published by the US Department of Energy's National Renewable Energy Laboratory (NREL). This list of twelve, mainly sugar-derived products was assembled in order to identify major opportunities for "the production of value-added chemicals from biomass that would economically and technically support the production of fuels and power in an integrated biorefinery, and identify the common challenges and barriers of associated production technologies."[4] In its candidate summary biography, LA is referred to as "one of the more recognized building blocks available from carbohydrates," the derivatives of which "address a number of large volume chemical markets." Reaction of CMF **1** with alcohols gives 5-(alkoxymethyl)furfurals **7**, which are non-toxic, high-energy organic compounds that are being marketed as fuel blending agents.[5] We have measured the energy density of 5-(ethoxymethyl) furfural to be 30.3 MJ L^{-1}, similar to that of gasoline (31.2 MJ L^{-1}) and superior to that of ethanol (23.5 MJ L^{-1}). Reaction with alcohols at higher temperatures leads directly to a mixture of levulinic **8** and formic **9** esters.[6] We have prepared both ethyl and butyl levulinate in this manner. Ethyl levulinate is a non-toxic γ-keto pentanoate ester with boiling point 206 °C and flash point 91 °C. It is has good lubricity and has been tested in blends with petroleum diesel up to 10% with no change in cetane number.[7] Its shorter chain length suggests the potential to favorably impact the cold performance properties of biodiesel (cloud point, pour point, viscosity).



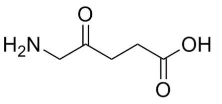
Scheme 6.

We have also integrated the process in Scheme 5 with the extraction of triglycerides from oil crops to produce a hybrid lipidic-cellulosic biodiesel.[8] The basic idea is that the seeds (we have tested camelina, canola, jatropha, safflower, and soybeans) contain not only oils but also significant carbohydrate profiles, in the form of starch, fiber, hemicellulose, and free sugars. When processed under the conditions described above, a mixture of CMF **1** and the triglyceride **10** is obtained (Scheme 7). No hydrolysis of the triglyceride is observed, since the oil is quickly sequestered into the organic phase of the reactor. This mixture can then be heated in water to give a mixture of the unchanged oil **10** and levulinic acid **4**. Under standard conditions for the transesterification of **10**, the **4+10** mixture gives the mixed-source biodiesel blend **8+11**. When safflower was used as the feedstock, sufficient ethyl levulinate **8** was produced by this method to increase the total amount of fuel by 25% over simple transesterification of the oil itself. *We believe this result could have a transformative effect on the biodiesel industry*, producing not only more fuel for the same quantity of feedstock, but also a blend with better cold-flow properties.



Scheme 7. R = long chain fatty acid alkyl group.

Finally, we have recently concluded efficient synthetic routes to δ-aminolevulinic acid (DALA) **12** and ranitidine (Zantac) **13** starting from CMF **1** (Figure 1). DALA is a natural, nontoxic herbicide and is also used in photodynamic cancer therapy. We can make it from corn stover in 4 steps and 55% overall yield.[9] Zantac is one of the blockbuster drugs of all time, and is now sold OTC. Our approach incorporating **1** requires only 3 steps and has an overall 79% yield.[10] This work marks the beginnings of a green agrochem-pharma market sourced by **1**.



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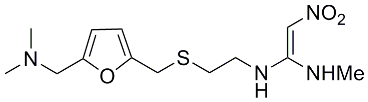

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Figure 1. Structures of DALA **12** and ranitidine **13**.

An overall summary of the opportunities around CMF is shown in Figure 2. Of particular note also are the polymer targets that can be pursued. For example, furan-2,5-dicarboxylic acid (see plastics box in Figure 2) is being adopted by the Coca-Cola company as a renewable replacement for polyethylene terephthalate (PET).[11] It is obtainable from CMF in a single step by oxidation in aqueous solution. Another drop-in fuel molecule of exceptional promise, 3-ethyl-4-methyl heptane (fuels box), is also a CMF derivative.[12] In the pharma and agrochem box, alongside DALA and Zantac, we also include a pyrethroid insecticide derivative of CMF.

To date, the above technology has been described by seven journal publications[1,2,3,6,8,9,10] and a US patent.[13] We are currently partnered with two green tech startup companies: Micromidas, a

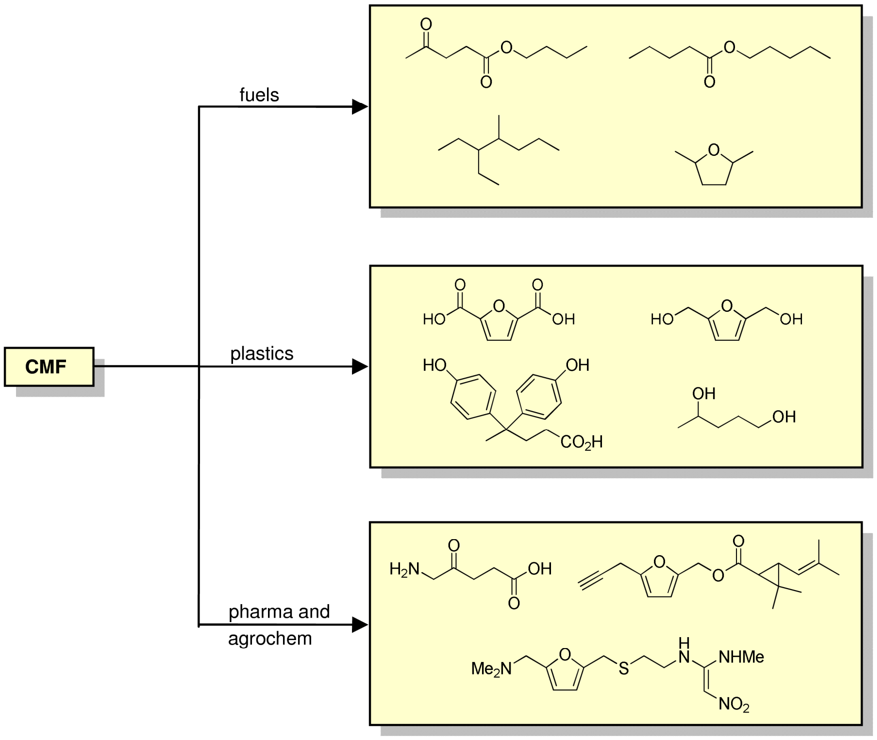

Figure 2. Markets addressed by CMF.

Sacramento-based wastewater valorization company and winner of the 2009 National Cleantech Open Competition, and Incitor, an Albuquerque, NM based company formed entirely around CMF-based products. Both Micromidas and Incitor are currently producing CMF on the multiple kg per day scale.

Micromidas has a 1 ton per week CMF production facility under construction for operation from mid-February 2012. The identity of the commercial product being targeted by Micromidas is confidential, but it is a petrochemical derivative with a vast global market, and can be produced in excellent yield from CMF. They are being backed in this effort by mainstream chemical companies, the identity of which also cannot be disclosed before the formal announcement.

Incitor produces a renewable fuel called Alestron™ in a single step from CMF, and plan a 1 million gallon/year facility within a *ca.*18-24 month timeframe. Working together with the Army Corps of Engineers, Incitor has submitted diesel-Alestron™ blends to testing by the US Army Tank, Automotive Research, Development and Engineering Center (TARDEC) and the results were highly encouraging. With a target price of $2 per gallon, biomass-derived Alestron™ is positioned to become one of the first commercial, eco-friendly diesel blending agents.

Green relevance and comparison with competing technologies

First, it is important to note that the biomass-to-CMF reaction produces *no* waste stream. For every molar equivalent of cellulose, one molecule of water is consumed to give glucose. In the ensuing formation of CMF **1**, one molecule of HCl is used and four molecules of water are produced. Then, in the production of the derivatives such as those in Scheme 6, one molecule of water or alcohol is consumed and the molecule of HCl is returned. Thus, the only non-organic product is water. The method does require the use of an extraction solvent; in Schemes 1, 4, 5, and 7 that solvent was ethylene chloride but, in principle, any polar hydrophobic solvent could be used with appropriate modifications to the reactor, and in any case, the solvent is employed in a closed extraction loop and is thus recycled. We consider the potential disadvantage of the use of a solvent in this process to be greatly outweighed by the advantages of displacing petroleum from the global carbon cycle.

The environmental burden of petroleum use is well understood. Highly efficient, carbon-cycle neutral, renewable energy technologies such as described here will be central to the mitigation of greenhouse gas emissions and the remediation of urban smog issues in US metropolises. This nomination addresses key green challenges on two vast fronts: automotive fuels and intermediates for the preparation of organic materials (plastics, textiles, and specialty chemicals). If plant-based feedstocks for these purposes can be sourced, whether green waste or "energy crops," we could displace petroleum as the basis of major sectors of our economy. Of course, our technology will not do it alone, but it has the potential to contribute in a major way towards the realization of this goal and all of its implications for the environmental, political, and economic health of the planet.

This technology may be compared in some ways to the "BioForming Process," in which sugars and hydrogen react to directly give hydrocarbons. The main advantage of BioForming, now being developed by Virent Energy Systems, is that the product hydrocarbons are already well integrated as fuels in the current automotive infrastructure. The disadvantages, relative to our process, are that 1) complex, expensive metal catalysts, high temperatures, and high pressures are required; 2) the overall yield of useable hydrocarbon products ($\geq C_8$) is modest, with substantial quantities of carbon being stripped out in the reforming process as CO_2; 3) the method operates only on simple sugars, not directly on cellulose or cellulosic biomass, and 4) despite the attention it has received, it is unlikely to ever be the basis an economically viable business, being ultimately displaced by technologies that can produce new generations of biofuels at a fraction of the cost.

Another related technology is the Biofine process, which converts cellulosic biomass directly into LA **4**. Biofine has been known since the 1980s and has been piloted at more than one site, but *no industrial production facility has been built to date*. The approach similarly involves the acidic processing of feedstocks, but employs very high processing temperatures and pressures, which translates into high capital and operating expenses. It also uses sulfuric acid, leading to a waste stream. The yields are said to be in the 70-80% range, whereas our much milder process gives >80% overall LA yield from biomass. Another key difference between Biofine and our technology is that Biofine only allows access to levulinate products, whereas we can access both the furan *and* levulinate manifolds to give a much broader range of commercial derivatives.

1 Mascal, M.; Nikitin, E. B. *Angewandte Chem. Int. Ed.* **2008**, *47*, 7924.

2 Mascal, M.; Nikitin, E. B. *ChemSusChem* **2009**, *2*, 423.

3 Mascal, M.; Nikitin, E. B. *ChemSusChem* **2009**, *2*, 859.

4 "Top Value Added Chemicals From Biomass. Volume I," PNNL and the National Renewable Energy Laboratory (http://www1.eere.energy.gov/biomass/pdfs/35523.pdf).

5 http://www.avantium.com/news-events/press-releases/2007-2/avantium-steps-ahead-with-its-biofuels-program/

6 Mascal, M.; Nikitin, E. B. *Green Chemistry*, **2010**, *12*, 370.

7 B. McCormick, National Renewable Energy Laboratory (http://www1.eere.energy.gov/vehiclesandfuels/pdfs/deer_2002/session4/2002_deer_mccormick.pdf).

8 Mascal, M.; Nikitin, E. B. *Energy & Fuels* **2010**, *24*, 2170.

9 Mascal, M.; Dutta, S. *Green Chem.* **2011**, *13*, 40.

10 Mascal, M.; Dutta, S. *Green Chem.* **2011**, *13*, 3101.

11 Press release: Will your Coca Cola bottle be made from PEF soon? (http://www.yxy.com/Avantium-and-The-Coca-Cola-Company-sign-partnership-agreement-to-develop-next-generation-100-plant-based-plastic-PEF/).

12 The chemistry leading to this cellulosic gasoline molecule cannot be disclosed at this time due to pending IP; we anticipate publication of this work in early 2012.

13 Mascal, M. *U.S. Patent* 7,829,732, **2010**.