

Unleashing Biocatalysis/Chemical Catalysis Synergies for Efficient Biomass Conversion

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Biomass conversion to useful fuels and chemicals is not a new field of endeavor; however, the bright spotlight currently publicizing the field has inspired creative new approaches. These new conversion approaches, although seemingly residing independently in the realm of either biocatalysis or chemical catalysis, likely will necessitate some form of integration between the two areas of technology. For example, the tremendous amount of ongoing work in biocatalytic lignocellulose deconstruction to sugars is commonly tied to fermentation of these sugars to ethanol. An alternative path, where the biocatalytically released sugars are converted chemically to an alternate fuel, dimethylfuran (DMF) (1), can be constructed from the combined results of two recent papers. Zhang and colleagues (2) demonstrate the selective dehydration of glucose to hydroxymethylfurfural (HMF) by using a metal chloride catalyst in an ionic liquid. The Dumesic laboratory (3) reports the application of a copper-based catalyst for efficient hydrogenolysis of HMF to DMF. Biocatalysis of plant biomass followed by a series of chemical catalysts illustrates the potential of an integrated approach.

For chemical catalysts to play their role in the conversion of biomass-derived molecules, catalytic materials and reaction systems must be designed that can address the challenges associated with selectively converting these substrates, which contain multiple reactive functional groups. To overcome this hurdle, the chemical catalyst sys-

tem must have tight control over the active site as well as the reaction environment around the site. Advances in the synthesis of nanostructured materials provide the opportunity for unprecedented control over the chemistry of the catalytic active site. In addition, the reaction environment can now be modified by the design of the scaffold or ligands around the catalytic site and/or through the selection of the solvent.

The substantial yield of HMF from glucose reported by Zhang and colleagues (2) is an example of a chemical catalyst reaction system that invokes design elements needed for selective conversion of biomass-derived substrates. They used 1-ethyl-3-methylimidazolium chloride to solubilize the glucose, and the result was solvated glucose in the α -anomer form. Introduction of either a chromium chloride or copper chloride catalyst led to mutarotation of this anomer to an equilibrium mixture of α - and β -anomers. This mutarotation created the conditions for isomerization to fructose, which was speculated to be through hydride transfer. The fructose intermediate was then dehydrated to HMF by the chromium chloride in the ionic liquid solvent. It is interesting that the copper chloride catalyst, although effective for the mutarotation reaction, did not give selective dehydration to HMF. The successful coupling of specific catalytic site chemistry and solvent effects clearly demonstrates the need for complete reaction environment control for the efficient conversion of these highly functionalized substrates.

ABSTRACT The goal of incorporating renewable carbon into the fuel and chemical enterprise will most likely be successful when combined systems of biocatalysts and chemical catalysts are exploited. Significant efforts in the biocatalytic release of sugars from biomass are being pursued for subsequent use in fermentation. Two recent papers demonstrate an alternative approach to converting these sugars to a liquid fuel by using chemical catalysts.

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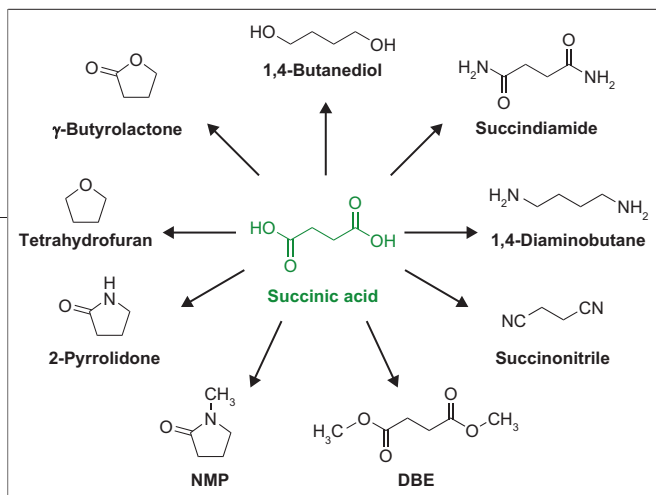


Figure 1. Chemicals that could be produced from a succinic acid platform (adapted from ref 8). NMP = *n*-methyl pyrrolidinone, DBE = dibasic ester.

In the synthesis of DMF, the Dumesic laboratory (4, 5) built on its prior work in the biphasic selective dehydration of fructose to HMF. In their most recent work, HMF was selectively converted to DMF with a copper chromite catalyst. This specificity for C-O bond hydrogenolysis was achieved without concomitant hydrogenation of the furan ring. In contrast, ruthenium supported on carbon was found to primarily hydrogenate the furan ring, even though this metal is known to be effective for C-O and C-C hydrogenolysis of polyols. The unique C-O bond reactivity with copper was further demonstrated through a carbon-supported bimetallic copper/ruthenium catalyst. Because the copper partitions preferentially to the surface, the bimetallic catalyst gave selectivity similar to that of the CuCrO_4 catalyst, whereas the ruthenium imparted tolerance for reaction impurities.

DMF synthesis through dehydration and hydrogenolysis of glucose provides an example of how chemical catalyst reaction systems can be designed to selectively convert biomass-derived molecules. The chemical catalytic conversion of glucose may seem unrelated to biocatalysis; however, generating glucose on the scale needed for significant fuel production will most likely necessitate the use of biocatalysis for lignocellulose deconstruction. Although biocatalysis (6) and chemical catalysis (7) each have significant potential to contribute to biomass conversion, a more direct coupling between biocatalysis and chemical catalysis can be readily imagined that will signifi-

cantly broaden the possible transformations to fuels and chemicals. One model for synergy between biocatalysis and chemical catalysis is the “platform” chemical approach. In this model, a chemical intermediate is produced that can be subsequently converted to a range of useful chemicals. From an industrial chemical perspective, this model is analogous to the current petrochemical industry, which is primarily based on ethylene, propylene, and benzene building blocks. The efficiency of this approach is only achieved if the platform chemicals can be readily produced. Using the platform chemical model as a basis, Werpy and Peterson (8) have evaluated which biomass-based chemicals are the most promising platform chemical candidates. It is important that most of the building block chemicals they identified would be produced biocatalytically and that most of the chemicals then produced from these building blocks would utilize chemical catalytic transformations.

The intersection of catalytic technologies in biomass conversions is nicely demonstrated by considering the emerging example of succinic acid as a platform chemical (9). The chemicals that could potentially be produced from succinic acid are shown in Figure 1 (8). In this chemical tree, succinic acid is produced *via* fermentation and then is converted to a range of chemical products through chemical catalysis. The succinic acid product tree can be viable only if an efficient fermentative route to succinic acid is developed. Although the fermentative production of succinic acid is not new, it suffers from the common challenges associated with biocatalytic synthesis for many fuels and chemicals: high selectivity and high productivity for the desired molecule.

Recently, San and colleagues (10) reported the metabolic engineering of *Escherichia coli* to create a new pathway design that offers superior succinate yield and productivity.

The central anaerobic metabolic pathway they engineered is shown in Figure 2. Under anaerobic conditions, a maximum of 1 mol of succinate per mole of glucose can normally be achieved because of the NADH requirement. This NADH limitation was overcome by increasing succinate synthesis through the glyoxylate pathway, which requires less NADH than the fermentative pathway, and by knocking out the NADH-consuming lactate and ethanol pathways. Increased flux through the glyoxylate pathway was achieved by deletion of *iclR* to enhance the flow of acetyl-coenzyme A (CoA) through the desired pathway and knockout of the ethanol and acetate pathways by *adhE* and *ack-pta* deletions to diminish competing acetyl-CoA utilization. Finally, heterologous overexpression of pyruvate carboxylase was used to increase flux through both the fermentative and glyoxylate pathways. After these changes were incorporated, the engineered *E. coli* was found to yield almost 1.6 mol of succinate per mole of glucose and was able to ferment high glucose concentrations. By knocking out byproduct pathways and increasing the carbon flux to succinate, the engineered biocatalyst addresses both high selectivity and high productivity for this fermentative system.

Increased efficiency of succinate production opens up the possibility of exploiting succinic acid conversions, as shown in Figure 1. Varadarajan and Miller (11) have given an overview of some succinic acid reactions with chemical catalysts. Through acid-catalyzed esterification, alkyl mono- or diesters can be formed that can be used as solvents or as intermediates for polybutylene succinate polymers. It is interesting that copper chromite, as also used in the Dumesic work, has been reported as an effective catalyst for succinic acid hydrogenation

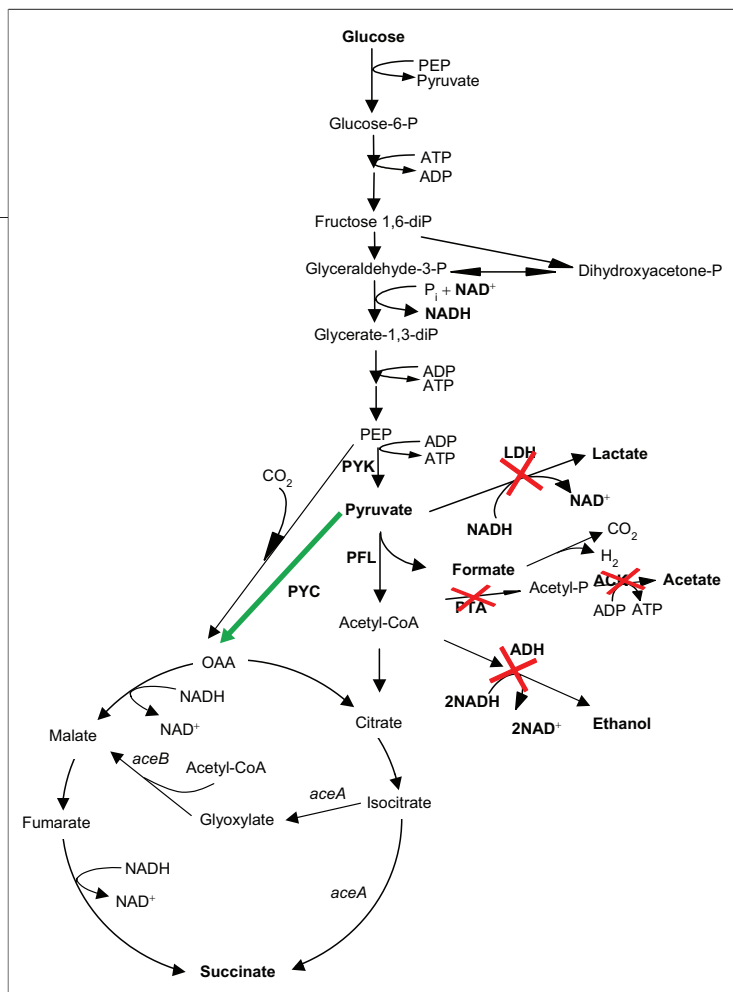


Figure 2. Central anaerobic metabolic pathway of *E. coli* engineered to enhance succinic acid production. Shown are knockouts of the NADH competing pathways and acetate pathway, activation of the glyoxylate pathway, and overexpression of pyruvate carboxylase. Courtesy of K. Y. San, Rice University.

tion to either 1,4-butanediol or tetrahydrofuran, with appropriate selection of reaction conditions favoring one hydrogenation product over the other. 2-Pyrrolidinone can be synthesized by reacting succinic acid with hydrogen and ammonia over a ruthenium, rhodium, or palladium catalyst. For each of these reaction systems, higher efficiencies could be achieved if further improvements were made in the chemical catalysts.

The chemistry required to produce fuels and industrial chemicals is often deceptively simple. A challenge in this area is the ability to create highly efficient transformations where product yield is high and the desired product is separated easily from the overall reaction effluent stream. Therefore, the goal of merely producing a desired product is inadequate. Ethanol and butanol are very good examples that delineate the challenge.

As a transportation fuel within the current infrastructure, butanol has properties superior to those of ethanol, with higher energy content and considerably lower solubility with water. Despite these clear advantages, ethanol is the current alcohol of choice because it is fermentatively produced in high yield without significant byproducts. In contrast, butanol, which is a product of the acetone-butanol-ethanol fermentation, is encumbered with high levels of byproducts.

Beyond transformation efficiency, fuel and chemical production from biomass also requires determination of the optimal synthesis path from multiple options. In the case of chemicals, these multiple pathways conclude with a target molecule, but for fuels, multiple synthesis pathways and possible end products exist. This broad array of potential transformations creates a wealth of opportunities for both biocatalysis and

chemical catalysis research. Furthermore, creative coupling of the catalyst technologies has not been extensively explored. The required efficient synthesis pathways place quite exacting standards on the production scheme, which necessitates consideration of the full range of biocatalytic and chemical catalytic options as well as their synergistic combination.

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