APPLICATION OF HIGH THROUGHPUT EXPERIMENTATION TO THE PRODUCTION OF COMMODITY CHEMICALS FROM RENEWABLE FEEDSTOCKS

Gary M. Diamond*, Vince Murphy and Thomas R. Boussie

Rennovia, Inc., Menlo Park, California, USA

Abstract: Rennovia is employing cutting-edge technology to adapt chemical catalytic processes, already proven to be scalable and efficient in the refining and chemical industries, for the conversion of biorenewable feedstocks to existing major-market chemicals. This chapter outlines Rennovia’s general approach to the cost-advantaged production of renewable chemicals, and describes the scale-up of Rennovia’s bio-based adipic acid process and how it offers the potential for significant commercial and environmental advantages over the current petrochemical process.

Keywords: Bio-based, renewable, biorenewable, sustainable, chemical, adipic acid, glucaric acid, hexamethylenediamine, HMD, HMDA, life cycle assessment, LCA, carbon footprint, low carbon footprint, carbon footprint reduction, bio-based chemical, renewable chemical, biorenewable chemical, sustainable chemical, 100% bio-based, 100% renewable, 100% biorenewable, nylon-6,6, nylon-66, polyamide, polyamide-6,6, polyamide-66, high-throughput screening, catalyst synthesis, catalyst screening, oxidation, reduction, hydrodeoxygenation, optimization, process, scale-up, Rennovia.

INTRODUCTION

The rapid increase in petroleum and petrochemical feedstock prices over the last decade has renewed interest in the production of current petroleum-derived chemicals from renewable feedstocks [1-5]. The U.S. chemical industry contributes $770 billion to the U.S. economy (about 5% of GDP), including $188 billion in exports, and provides 780,000 direct jobs and over 6 million indirect jobs [6]. However, the U.S. chemical industry has suffered from declines both in terms of total number of jobs and global market share, due to increasing competition from low-wage countries in Asia, as well as petroleum feedstock-advantaged regions such as the Middle East.

*Address correspondence to Gary M. Diamond: Rennovia Inc., 1080 Hamilton Ave., Menlo Park, California 94025, USA; Tel: +1-650-804-7400; Fax: +1-650-804-7499; E-mail: gdiamond@rennovia.com
Bio-based chemicals production, exploiting America’s advantaged agricultural and forestry infrastructure, offers the opportunity for the U.S. to regain leadership in the global chemical industry. Compared with bio-fuels, bio-chemicals production provides higher value products, at smaller scale, with lower capital investment required. A number of commodity-scale chemicals can potentially be produced from biomass at costs lower than current petrochemical processes [4,5]. To date, the U.S. and other governments have focused alternative feedstock funding almost exclusively on fuels, yet bio-based chemicals are inherently better positioned to become commercially viable well before biofuels.

In recent years many companies, including both multinational chemical companies and new “startup” companies, have investigated the application of biotechnology and fermentation for the production of chemicals and materials from renewable resources [3-5]. However, a bio-based chemicals industry does not necessarily imply a reliance on industrial biotechnology [2]. Catalysis plays a key role in the U.S. and global chemical industry, and is used in 90% of chemical manufacturing processes. Worldwide, catalysts are estimated to add $2,400 billion of value by converting raw materials to higher value chemical products. In the U.S., over 20% of industrial products, worth over $500 billion, rely on catalytic processes [7]. Rennovia is building on the success of these proven, scalable, and efficient technologies by developing advanced chemical catalytic processes for the conversion of bio-based, renewable feedstocks into major-market chemical products [8]. Fig. 1 illustrates how this is incorporated into Rennovia’s strategy for risk reduction in renewable chemicals production by: (i) minimizing supply chain risk by employing existing renewable raw materials available at multi-billion lb/year scale, (ii) producing existing large-volume products, and (iii) minimizing conversion risk by utilizing proven, scalable chemical-catalytic process technology.

![Figure 1: Rennovia Strategy for Risk Reduction in Renewable Chemicals Production.](image-url)
It is expected that Rennovia’s bio-based chemical processes will initially utilize conventional carbohydrates, e.g., glucose from corn starch, which is available today at a multi-billion lb/yr (pounds per year) scale from corn wet milling in the U.S. [9], and from a variety of other crops globally. Today, most corn-derived glucose is converted to high-fructose corn syrup, but this market is declining in the U.S., and corn wet millers are looking for alternative, higher value applications, including bio-based chemicals [10]. There has been an extensive “Food vs. Fuel” debate in recent years, on the use of conventional carbohydrates as feedstocks for biofuels [11]. The much smaller scale of even commodity chemical production compared to fuels production means that any impact of bio-based chemicals production will be marginal. However, as Fig. 2 illustrates, Rennovia is also preparing to utilize non-food based lignocellulosic carbohydrates as they become available at commercial scale. When fully developed and scaled, lignocellulosic-derived sugars will add to the global supply of glucose, further strengthening the cost advantage vs. petroleum, and potentially providing further reductions in environmental impact [12].

Figure 2: Rennovia Feedstock Strategy: initially leverage existing carbohydrate supply chain, while ensuring technology is forward-compatible with emerging feedstocks.

Rennovia’s first commercial target is adipic acid, which is produced today in a multi-step process from benzene [13]. Adipic acid is widely used in the
production of nylon resins and fibers, as well as polyurethanes and non-phthalate plasticizers, and has a global market of over 6 billion lbs/yr [14]. The dominant petrochemical route to adipic acid, shown in Fig. 3, begins with hydrogenation of benzene to cyclohexane, followed by oxidation of cyclohexane to a mixture of cyclohexanone and cyclohexanol, known as “KA Oil”, as shown in Fig. 3. The final step requires the use of nitric acid for the oxidation of the KA Oil to adipic acid [15]. This final step produces the powerful greenhouse gas N₂O as a by-product, which has a Global Warming Potential (GWP) approximately 300 times that of CO₂, contributing significantly to the high “carbon footprint” (kgCO₂ equivalent per kg product) of the overall process [16].

![Figure 3: The Dominant Petrochemical Route to Adipic Acid.](image)

While several companies are investigating fermentation routes to adipic acid from renewable feedstocks, Rennovia is developing a chemical catalytic process [17]. As illustrated in Fig. 4, Rennovia has employed its high-throughput catalyst synthesis and screening technology infrastructure to identify new heterogeneous catalysts for producing adipic acid in two steps from glucose: (i) a selective catalytic oxidation of glucose to glucaric acid, followed by (ii) a selective catalytic hydrodeoxyxygenation of glucaric acid to adipic acid [18].

![Figure 4: Rennovia’s Two Step Process for Production of Bio-based Adipic Acid from Glucose](image)

This chapter will outline Rennovia’s general approach to the cost-advantaged production of renewable chemicals, and describe the scale-up of Rennovia’s renewable adipic acid process and how it offers potential for significant
commercial and environmental advantages compared to the current petrochemical process.

**HIGH-THROUGHPUT SCREENING AT RENNOVIA**

Since the late 1990s, the field of catalyst and materials synthesis and testing has begun to adopt “High-Throughput Screening” (HTS) technology for accelerated discovery and development in industrially important research [19]. Rennovia was established with the mission to apply HTS technology to the discovery and development of new catalysts and catalytic processes in the emerging area of bio-based chemicals production [8,17]. Since late 2009, Rennovia has put in place a world-class high-throughput catalyst R&D infrastructure, employing: (i) robotics for micro-scale automated catalyst synthesis and processing in “library” (array) formats, (ii) multi-channel batch reactors for parallel catalyst testing, (iii) high-throughput automated analytical assays (including mass spectrometry, liquid chromatography, gas chromatography, ion chromatography, and other techniques), (iv) software for library design, automated synthesis, screening reactions, and data collection, and (v) an extensive archive of catalysts and commercially relevant catalyst supports, as illustrated below in Fig. 5.

![Catalyst Archive](image)

**Figure 5:** High-Throughput Catalyst Synthesis & Screening Process at Rennovia.

The most promising catalyst “hits” from this first round of HTS are scaled up and tested under continuous flow conditions in multi-channel fixed-bed reactors.
These fully-automated reactors are used for optimization of lead catalysts for activity, selectivity, lifetime, and initial optimization of continuous process conditions. It is at this scale that the catalysts identified in parallel batch reactor screening are formulated onto shaped supports and extrudates for testing in larger-scale fixed bed reactors. As well as acting as a “bridge” between the high-throughput batch reactors and lab pilot scale continuous reactors, the information generated in the multi-channel fixed-bed reactors is fed back to improve the parallel batch reactor micro-scale catalyst synthesis and screening.

In addition to screening catalysts and reaction conditions for aggregate substrate-to-product transformations, the HTS infrastructure can also be employed to probe individual reaction steps in multi-step chemical transformations. An example of this capability is shown in Fig. 6, which illustrates the parallel quantification of multiple reaction components (Reaction Components 1-6), as a function of the ratio of three metals (M1, M2, M3) in a ternary catalyst system. The lowest concentrations are shown as blue, and the highest concentrations are shown as red.

Fig. 7 illustrates how multiple information feedback loops are created, both within and between the different scales of HTS, to enable the very rapid optimization of newly discovered catalysts and processes.

The most promising “lead” catalysts and conditions from the continuous flow multi-channel fixed-bed reactor testing are scaled up and taken forward to Rennovia’s lab pilot scale reactors for further catalyst and process optimization. At the lab pilot scale the catalysts are synthesized at kg scale on shaped supports and extrudates, and tested under continuous flow conditions at production rates on the order of kilos per day. The two primary deliverables of the lab pilot scale work are: (i) optimized catalysts and process conditions for pilot scale production, and (ii) production of material for product separation and purification studies, and for initial downstream product qualification.

As illustrated above in Fig. 4, the first step in Rennovia’s process for production of bio-based adipic acid is the selective oxidation glucose to glucaric acid. In addition to being the key intermediate in Rennovia’s adipic acid process, glucaric
Figure 6: Parallel Multi-Component Concentration Profile as a Function of the Ratio of Three Metals in a Ternary Catalyst System.
acid and its derivatives also have a number of potential applications of commercial significance, especially as an alternative to fermentation-derived citric acid [20] and gluconic acid [21]. Examples include both food applications (*e.g.* use as acidulant and/or fortifier in formulated food and drinks), and non-food applications including use as a strong chelator in detergent builder, corrosion inhibitor, and water treatment applications, and also in cement and concrete admixtures, personal care, and other applications [22].

The catalytic oxidation of glucose to glucaric acid has been demonstrated previously, *e.g.* using a platinum catalyst in the presence of oxygen under basic conditions [23]. Glucaric acid can also be produced from the oxidation of glucose using nitric acid [24] or other oxidants [25]. However, these processes have historically suffered from economic shortcomings, and none of these processes are used for the selective oxidation of glucose to glucaric acid at an industrial scale.

**Figure 7:** Catalyst Development Workflow at Rennovia.
Rennovia has successfully employed its high-throughput catalyst discovery and optimization infrastructure to develop new, industrially scalable catalysts and processes for the selective conversion of glucose to glucaric acid. This selective catalytic oxidation, shown in Fig. 8, employs water as a solvent and air as the oxidant, occurs at native pH, and is proposed to proceed through a multi-step pathway. High selectivity must be achieved in each step to avoid the production of undesired off-pathway products. It should be noted that in aqueous solution, the open-chain form of glucaric acid is in equilibrium with mono-lactone and di-lactone species [26], but for simplicity only the open-chain structure is shown.

![Figure 8: Selective Catalytic Oxidation of Glucose to Glucaric Acid.](image)

The discovery process began with the synthesis and screening of thousands of diverse heterogeneous catalysts, using the micro-scale workflow described above. A wide range of catalyst were synthesized by combining a diverse set of supports, metal loadings and metal combinations, and employing a range of catalyst synthesis, processing and activation methods. The catalyst screening conditions were also varied, testing a range of substrates, temperatures, oxygen or air pressures, reaction times, etc. This broad-based screening led to the discovery of many new catalysts for the selective oxidation of glucose to glucaric acid [27]. The initial optimization of these catalysts was achieved using the same mg-scale catalyst synthesis and screening workflow, but focusing on the most promising regions of the metal / support / condition multi-dimensional landscape. The most promising metal combinations were optimized using higher resolution multi-metal combinations, and also through modification of the supports [28].

The most promising “lead” catalysts from this high-throughput screening have been scaled up and transferred to shaped supports and extrudates, and tested under continuous flow conditions in multi-channel fixed-bed reactors, and then
continuous lab pilot (kilo scale) reactors for further catalyst and process optimization, in preparation for a commercial demonstration plant and eventual commercialization. The large scale use of glucaric acid and its derivatives has been limited to date, due to the lack of a commercially viable industrial synthetic process. Rennovia’s new selective catalytic oxidation route is expected to produce glucaric acid with a cost of production significantly below that of fermentation-derived citric acid [29], which should allow for the widespread adoption of glucaric acid for a range of applications [22].

One of the major challenges for converting biorenewable resources such as carbohydrates (e.g. glucose), to current commodity petrochemicals, is the selective removal of oxygen atoms from the carbohydrate. Approaches are known for converting carbon-oxygen single bonds to carbon-hydrogen bonds [30]. However, each of these known approaches suffers from various limitations. Thus, there remains a need for new, industrially scalable methods for the selective and commercially-meaningful conversion of carbon-oxygen single bonds to carbon-hydrogen bonds, especially as applied in connection with the production of important petrochemical intermediates from biomass.

As with the conversion of glucose to glucaric acid, Rennovia has successfully employed its high-throughput catalyst discovery and optimization infrastructure to develop new, industrially-scalable catalysts and processes for the selective conversion of glucaric acid to adipic acid, in a multi-step selective catalytic reduction [31]. The overall process is shown in Fig. 9.

![Figure 9: Selective Catalytic Reduction (Hydrodeoxygenation) of Glucaric Acid to Adipic Acid.](image-url)
unprecedented, a very broad range of catalyst formulations were synthesized and screened under diverse reaction conditions. A rapid (< 30 seconds per sample), semi-quantitative analytical method was developed to enable an initial survey of many thousands of catalytic experiments, and identified a number of systems demonstrating proof-of-principle performance. The results of the first several thousand experiments are shown in Fig. 10.

**Figure 10:** Reduction of Glucaric Acid to Adipic Acid: Rapid Analytical Results for First Several Thousand Parallel Batch Reactor Experiments.

Optimization of initial catalyst “hits” was performed using the same micro-scale catalyst synthesis and screening workflow, but focusing on the most promising regions of the multi-dimensional metal / support / promoter / reaction-condition landscape. The most promising metal combinations were optimized using higher resolution binary and ternary metal combinations, and through modification of the supports. An example of this optimization is shown in Fig. 11, which illustrates the profound effect of the catalyst support on adipic acid yield for four, otherwise identical, ternary catalyst systems with the same three metals (M1, M2, M3) and composition ranges.
PROCESS SCALE UP

As with the glucose to glucaric acid step, the most promising “lead” catalysts and conditions from the HTS for the glucaric acid to adipic acid step have been scaled up and transferred to shaped supports and extrudates, and tested under continuous flow conditions for further catalyst and process optimization. The process information generated has been used to construct detailed engineering models to compare Rennovia’s renewable adipic acid process with the conventional petrochemical route to adipic acid via cyclohexane oxidation.

ESTIMATION OF COST OF PRODUCTION

Engineering process simulation software was used to create “side-by-side” models employing the same equipment and other capital project costs, manufacturing expense calculations, etc. and was performed by the same personnel, to ensure an “apples-to-apples” comparison. The results indicate that at current crude oil and carbohydrate prices, the Rennovia process is predicted to have robust advantages
in both capital and operating expenses, including lower capital, lower raw materials costs, lower utilities, and lower manufacturing costs. The relative total variable costs, manufacturing costs and depreciation costs, which together make up the relative total cost of production (e.g. in $ per kg), are illustrated in Fig. 12.

Figure 12: Comparison of Relative Cost of Production of Adipic Acid for the Dominant Petroleum-Based Process vs. Rennovia’s Bio-Based Process.

Additionally, the Rennovia process has recently been identified in an independent report by IHS Chemical as the leading prospect for cost-advantaged bio-based adipic acid production vs. conventional petroleum-based processes based on oxidation of cyclohexane, and more recently described processes employing fermentation. While noting that the Rennovia process has yet to be scaled to commercial plants, which introduces some inherent uncertainties in the technical and economic analyses, the IHS Chemical Process Economics Program (PEP) Report #284 Bio-Based Adipic Acid concluded that Rennovia’s process offers lower projected cash and full production costs than the current, dominant petroleum-based process, and potential fermentation processes proposed to be under development [32].

REDUCTION OF ENVIRONMENTAL IMPACT

A second driver towards bio-based chemicals, in addition to the potential for cost advantage, is the potential for reduced environmental impact, including
greenhouse gas emissions [4]. The environmental impacts of products and processes are typically quantified and compared through the application of Life Cycle Assessment (LCA) [33]. A properly performed LCA identifies the material, energy and waste flows associated with a product over its entire life cycle to determine environmental impacts and potential improvements. Reduction in eco-footprint is becoming increasingly important in many markets, and many companies are requiring a reliable LCA for new project and product proposals.

A detailed comparative Life Cycle Assessment was performed comparing Rennovia’s adipic acid process with the petroleum-based process, using commercial LCA databases and software [34]. Since the product use and end-of-life disposal or recycle was assumed to be the same for the petro-based and bio-based adipic acid, a “cradle-to-factory gate” comparative analysis was performed using established and accepted methodologies [16,33,34]. The petrochemical
process produces the powerful greenhouse gas nitrous oxide (N\textsubscript{2}O) as a by-product, contributing to a high “carbon footprint”. The global warming potential (GWP) of N\textsubscript{2}O is about 300 times that of CO\textsubscript{2}, and in recent decades petrochemical adipic acid plants in the U.S. and Europe have added extensive emissions reduction technology to greatly reduce N\textsubscript{2}O emissions [16]. A state-of-the-art adipic acid plant in Europe was used as a baseline for the petrochemical process, with 98% N\textsubscript{2}O abatement. Even with this very high level of N\textsubscript{2}O abatement, the petrochemical process still has a high “carbon footprint”, compared to many other petrochemical intermediates [4]. Through a combination of renewable feedstock, lower energy usage, and avoidance of N\textsubscript{2}O by-product, Rennovia’s target process is predicted to reduce the “carbon footprint” (kg CO\textsubscript{2}-equivalent per kg adipic acid) by as much as 85%, compared to a state-of-the-art petrochemical process (Fig. 13), and even greater reductions compared to a typical plant in China with lower emissions abatement (and utilities heavily dependent on coal). Significant reductions were also predicted for other environmental impacts on human health, ecosystem quality, and resource depletion (Eco-indicator 99 (H/A) method, cradle-to-gate) [34].

CONCLUDING REMARKS

Rennovia is developing advanced chemical catalytic processes for the conversion of bio-derived, renewable feedstocks to major-market chemical products. These processes are designed to be readily scalable and to employ standard chemical production process technologies. Rennovia’s first product, adipic acid, is a monomer widely used in the production of nylon resins and fibers as well as an important component of polyurethane resins and foams, and non-phthalate plasticizers. High-throughput catalyst synthesis and screening at Rennovia has enabled identification of proprietary catalyst formulations, and an intimate understanding of the reaction pathway. Scale up of the catalysts and processes has proceeded through multi-channel fixed bed reactors to kilo-scale continuous lab pilot production, with further scale-up to demonstration plant and commercial production to follow in the next few years. Compared to the incumbent petrochemical processes, Rennovia’s renewable adipic acid process offers significant potential for reductions in both cost of production and environmental impact.
Rennovia is using its world-class catalyst discovery and development capabilities to create a pipeline of additional bio-based chemicals. Most recently, Rennovia has announced that it has successfully demonstrated production of hexamethylenediamine (HMD) from widely available, renewable feedstocks [35]. Coupled with Rennovia’s renewable adipic acid, this enables for the first time the production of 100% bio-based nylon-6,6 from monomers derived from bio-renewable feedstocks, using chemical catalytic technology [36].

ACKNOWLEDGEMENTS

The authors would like to acknowledge the contributions of all their colleagues at Rennovia to the successful development of Rennovia’s catalyst and process technologies.

CONFLICT OF INTEREST

The authors confirm that this chapter content has no conflict of interest.

REFERENCES


[5] Hackett, M., Chemical Building Blocks from Renewables (Safe & Sustainable Chemicals Report), SRI Consulting (now IHS Chemical), Menlo Park, California, USA, 2011.


[17] Hackett, M. Adipic Acid and Other Nylon Intermediates, in Chemical Building Blocks from Renewables (Safe & Sustainable Chemicals Report), SRI Consulting (now IHS Chemical), Menlo Park, California, USA, 2011, pp. 124-130.


