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Bridging the Chemical and Biological Catalysis Gap: Challenges and Outlooks for Producing Sustainable Chemicals

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ABSTRACT: Recent advances in metabolic engineering have allowed for the production of a wide array of molecules via biocatalytic routes. The high selectivity of biocatalysis to remove functionality from biomass can be used to produce platform molecules that are suitable for subsequent upgrading over heterogeneous catalysts. Accordingly, the more robust continuous processing allowed by chemical catalysis could be leveraged to upgrade biologically derived platform molecules to produce direct or functional replacements for petroleum products. Herein, we highlight recent results that utilize a combination of chemical and biological catalysis, and using the perspective of heterogeneous chemical catalysis, we identify challenges that need to be addressed to bridge the gap between the two catalytic approaches. Specifically, studies are required to address the effects on catalyst performance of impurities that originate during bioprocessing. In addition, new generations of heterogeneous catalysts are required for stable operation under liquid phase reaction conditions in the presence of biogenic impurities. Finally, the design and syntheses of new catalysts are required to tailor the active sites and the environment around these sites to achieve selective conversion of the functional groups present in biologically derived platform molecules.

KEYWORDS: *heterogeneous catalysis, biocatalysis, biomass, biogenic impurities, catalyst stability, active site design, biorenewable chemicals*

INTRODUCTION

Continued utilization of fossil-based resources is raising concerns related to environmental and economic sustainability, such as the combination of increased costs to procure additional resources and process them sustainably coupled with rising demand for these resources in an ever more globalized economy. Accordingly, significant attention over recent decades has addressed renewable and sustainable replacements for fossil-based resources. Of particular interest has been the utilization of biomass because it represents a carbon-neutral and sustainable option to supplement or replace fossil-based resources. Methods for utilizing atmospheric carbon sources (i.e., CO_2) have also received increasing interest,[1] but the current state of technology likely precludes this carbon source from being economically viable in the near term.

The general approaches for upgrading biomass to fuels and chemicals have typically fallen into two categories. One category is thermochemical conversion and upgrading (i.e., pyrolysis or gasification), which has been extensively reviewed[2,3] and will not be discussed here. The second category encompasses biomass deconstruction to yield sugars, followed by either biological or catalytic upgrading.[4−7] These upgraded sugars can be either functional or direct "drop-in" replacements for petroleum products.

Although the subject of fuels production has received considerable attention since the turn of the 21st century, the inherent value of chemicals suggests that they may be an attractive use of biomass.[8] Further, it has been suggested that production of fuels from biomass can be augmented by the coproduction of chemicals in an integrated biorefinery.[9] Because a substantial infrastructure for chemicals production and utilization is already in place, successful biomass-derived products will likely need to target replacing a petroleum-derived analogue. This approach can take the form of direct replacements (e.g., biomass-derived terephthalic acid) or functional replacements that may have different chemical structures but similar properties (e.g., furandicarboxylic acid). The latter approach allows for the interchangeability of, for example, furandicarboxylic acid and terephthalic acid as monomers for use in consumer products, such as plastic bottles (see Figure 1).

To date, the catalytic conversion of biomass to chemicals has focused primarily on dehydration processes to yield either hydroxymethylfurfural (HMF) from cellulose-derived C_6 sugars or furfural from hemicellulose-derived C_5 sugars, both of which

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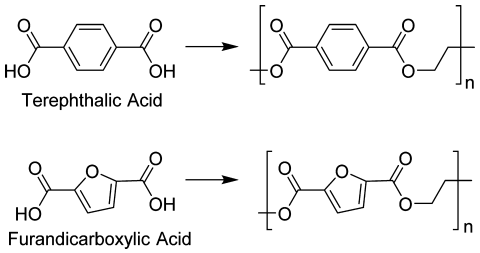

Figure 1. Illustration of the distinction between a direct replacement (biomass-derived terephthalic acid, top) and a functional replacement (furandicarboxylic acid, bottom).

have been suggested as platform chemicals. HMF can be used to produce a variety of species, including dimethylfuran[10] (which can be upgraded to make renewable *p*-xylene[11,12]), furandicarboxylic acid,[13,14] and levulinic acid.[15,16] Furfural and its partially hydrogenated product furfuryl alcohol are already used extensively as solvents for resins and polymers.[17,18] Hydrogenation of furfural to furfuryl alcohol allows for the subsequent production of levulinic acid,[19,20] which is on the original DOE "Top 10" list[21] as well as its more recent update (see Figure 2),[18] providing interesting process synergies with promising C_6 strategies.[22]

Because all common sugars obtained from biomass have either five or six carbon atoms, dehydration of these species leads to products that are inherently five or six carbons long,[23] often in relatively modest yields because of the difficulty of selectively reducing the oxygen content of such highly functionalized substrates. Alternatively, biocatalysis allows for the production of variable carbon-number molecules while selectively retaining some of the functionality natively present in biomass. This approach can thus circumvent some of the limitations of a purely chemical catalytic approach. Historically, the application of biocatalysis has focused on utilization of naturally occurring enzymes (e.g., cellulase enzymes for cellulose depolymerization[24]) and enhanced or modified metabolic processes (e.g., fermentation to yield citric, lactic, and succinic acids,[25] etc.). Recent advances in metabolic engineering have allowed for the production of a wider array of molecules via biocatalytic routes,[6] notable examples being the polyketide and fatty acid biosynthesis pathways. Both of these biosynthesis pathways produce long-chain molecules by condensation of molecular building blocks (e.g., acetyl-coenzyme A (CoA) or malonyl-CoA).[26,27] This approach allows for production of molecules with limited functionality (similar to those traditionally obtained from petroleum) that could be further converted using chemical catalysis, especially alkanes,[28] long-chain fatty alcohols,[29,30] or long-chain α-olefins.[31] At present, there are few examples of processes that use biocatalysis alone to produce drop-in replacements for use in existing chemical processes.

The identification of strategies to bridge the gap between chemical and biological catalysis could help overcome the shortfalls of either a purely chemical or purely biological approach for producing high-value chemicals from biomass. Conceptually, the superior ability of biocatalysis to selectively remove functionality from biomass could be used to produce platform molecules that are suitable for catalytic upgrading, and the more robust continuous processing allowed by chemical catalysis could be leveraged to upgrade these biologically derived platform molecules into either direct or functional replacements for petroleum products. Such a strategy, illustrated in Figure 3, is supported by the diversity of potential platform molecules that have so far been described. For example, half of the chemicals reviewed by the DOE[21] and others[18] are of biological origin (see Figure 2). This approach would be congruent with other strategies that have recently been suggested[32−34] and can be thought of as the logical extension of earlier ideas about cascade synthesis schemes for various organic compounds.[35−37]

Herein, we highlight recent results that utilize a combination of chemical and biological catalysis, using the perspective of heterogeneous chemical catalysis to identify challenges that need to be addressed to bridge the gap between the two catalytic approaches.

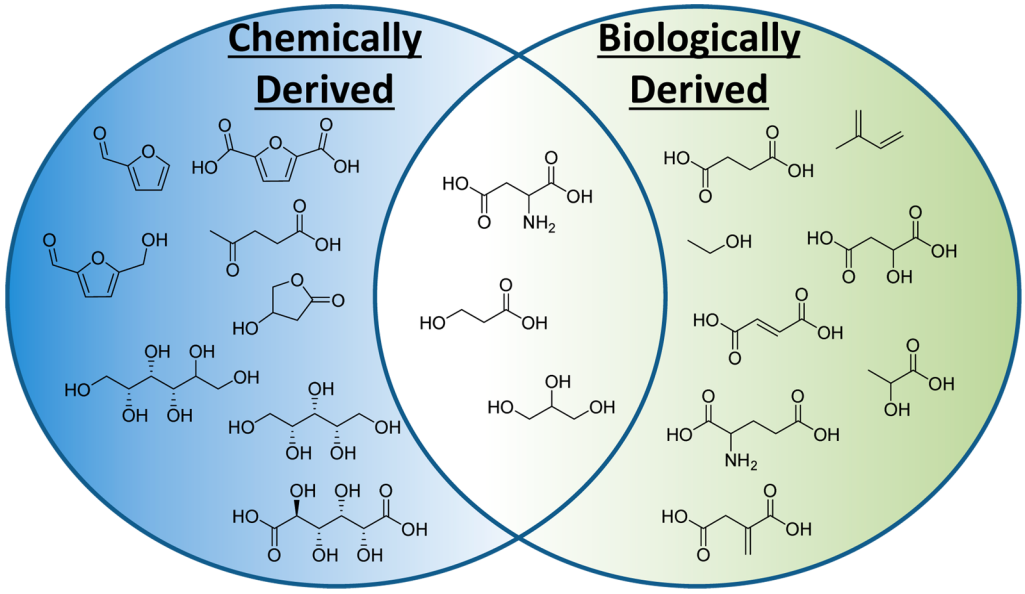

Figure 2. Top biorenewable chemicals divided into those species that can be produced via chemical processes, biological processes, or both (from the DOE "Top 10" list[21] and its update[18]).

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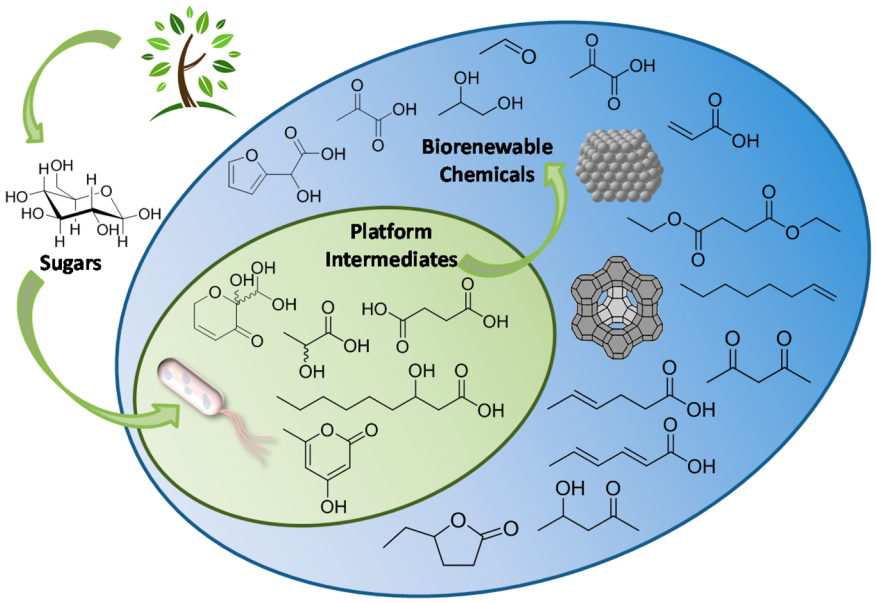


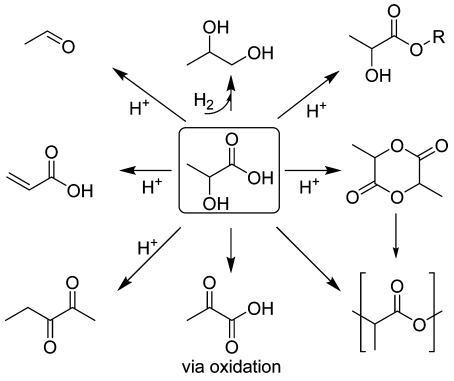
Figure 3. Overview of the coupling of chemical and biological catalysis for production of biorenewable chemicals.

BIOBASED PLATFORMS

Production of biofuels has dominated the biorenewables literature for most of the past 2 decades. An interesting example of fuels production via combined chemical and biological processing is the alkylation of the products of acetone−butanol−ethanol (ABE) fermentation to yield C_5- through C_{11}-range alkanes.[38] In this process, acetone, *n*-butyl alcohol, and ethanol are extracted from spent fermentation media. A Pd/C catalyst with K_3PO_4 was used for alkylation of the two alcohols with acetone, yielding a mixture of C_5−C_{11} ketones that are amenable to deoxygenation to alkanes. Although this approach is an intriguing utilization of the products of ABE fermentation, technical challenges remain, especially with regard to catalyst stability. Furthermore, because of the low margins involved in fuel production and the inherently high cost of producing fermentable sugars from biomass,[39] any economically viable process for the production of fuels from biomass will necessitate minimal additional cost from processing. Thus, it does not seem likely that fuels will be an attractive target for production by combining chemical and biological catalysis, and there are few additional examples of such conversion strategies.

Lactic acid is a biobased platform chemical that has developed a large market. It is now in commercial-scale production, with about 260 000 tons produced per year as of late 2012.[40] Much of the global capacity is used to supply the production of poly(lactic acid), a biorenewable and biodegradable alternative to petroleum-derived plastics.[41] Because of its reactive nature, lactic acid has the potential for conversion to an array of C_3 chemical building blocks via heterogeneous chemical catalysis.[42] It is a promising platform molecule (see Scheme 1) because it can be reduced to 1,2-propanediol[43−45] or oxidized to pyruvic acid over a variety of metal oxide and reduced metal catalysts.[42] It can also be either dehydrated[46,47] or esterified[48] via solid acid catalysts. Unfortunately, when studies are performed with real, biologically derived feedstocks, especially those using reduced metals, catalytic activity can suffer, suggesting that stable catalysts still need to be developed.

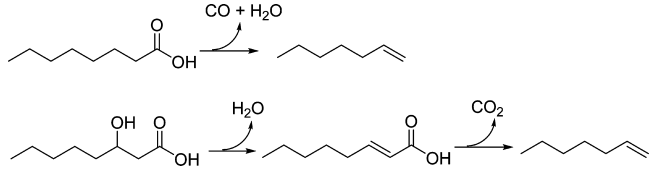
Scheme 1. Use of Lactic Acid As a Platform Chemical[a]



[a]Adapted from Dusselier and coworkers with permission of The Royal Society of Chemistry.[42]

In general, carboxylic acids are attractive platforms that are often natural microbial products.[25] These compounds can take the form of short-chain acids produced via mixed culture fermentation,[49] or long-chain fatty acids produced via fatty acid biosynthesis.[27] Short-chain carboxylic acids can be converted to a variety of industrially relevant[50] ketones using chemical catalysis.[51] Long-chain fatty acids are an attractive feedstock because they can be produced in varying carbon chain lengths.[52] As shown in Scheme 2, decarbonylation of such molecules can produce olefins, which are valuable industrial chemicals, especially when the carbon=carbon double bond is

Scheme 2. Conversion of Carboxylic Acids to α-Olefins via Metal-Catalyzed Decarbonylation (top) or Acid-Catalyzed Decarboxylation (bottom)



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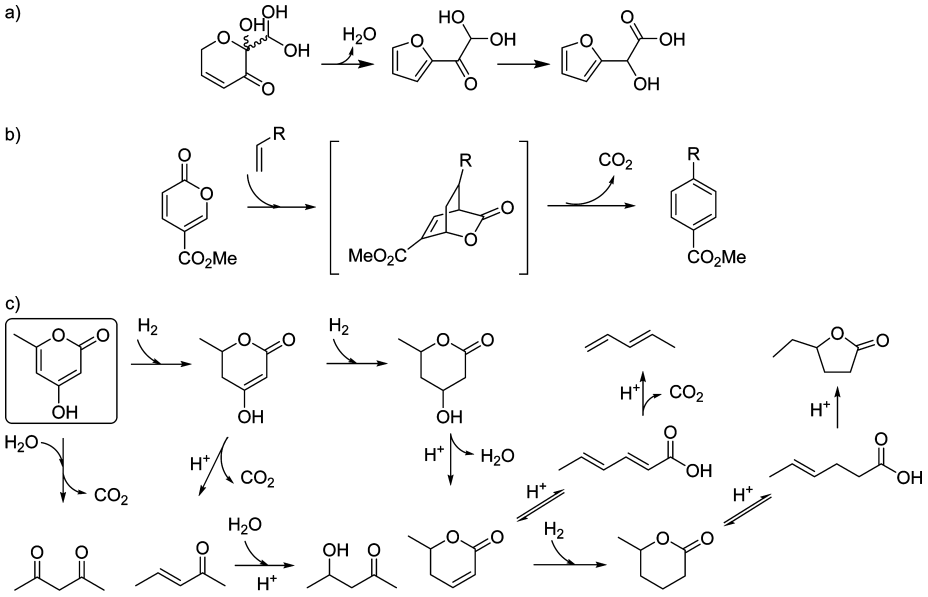
Scheme 3[a]



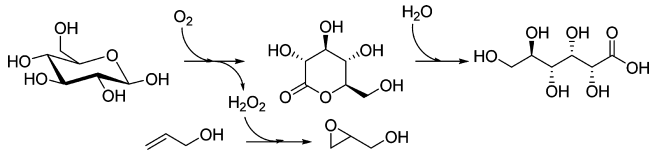
[a](a) Conversion of cortalcerone to furylglycolic acid (adapted from Schwartz et al.).[57] (b) Diels–Alder reaction of methyl coumalate to terephthalic acid derivatives (adapted from Kraus et al. with permission of the Royal Society of Chemistry).[60] (c) Reactions of triacetic acid lactone (reproduced from Chia et al. with permission of the Royal Society of Chemistry).[61]

retained in the terminal position (i.e., the α-olefin).[53] The appropriate choice of catalyst can improve selectivity to α-olefins, with Pt- and Pd-based catalysts being particularly active and Pt being especially favorable for decarbonylation.[54,55] When β-oxidation of fatty acids is reversed in *Escherichia coli*, it can be used to generate functionalized fatty acids,[29] which opens a possible route for the highly selective production of α-olefins using metal-free catalysts (see Scheme 2).[56] Two important challenges are that metal-catalyzed decarbonylation is only selective at low conversion and that, using the metal-free route, selectivity decreases for the conversion of higher carbon number substrates. In addition, supported metal catalysts may not be stable under liquid phase conditions. Thus, further advances will be needed in the design of both stable and highly active and selective active sites.

Chemical conversion of multiply functionalized, biologically derived molecules can be employed to yield attractive end products. For example, cortalcerone (see Scheme 3a), which is derived enzymatically from glucose and contains five distinct functional groups, can be upgraded to yield furylglycolic acid, a potential comonomer for poly(lactic acid).[57] Somewhat more moderately functionalized molecules such as 2-pyrones are also promising platform chemicals. Coumalic acid and methyl coumalate are examples of 2-pyrones that can be produced chemically from malic acid,[58] which itself can be derived biologically.[21] These pyrones can, as shown in Scheme 3b, act as dienes in Diels–Alder reactions, yielding aromatic species such as terephthalic acid.[59,60] In this case, many end products are available, depending on the choice of dienophile. Triacetic acid lactone (TAL), also known as 4-hydroxy-6-methyl-2-pyrone, is another 2-pyone that has been shown to be suitable as a platform chemical, as shown in Scheme 3c.[61] Using an array of different catalysts, it is possible to produce various bifunctional ketones, lactones, and unsaturated acids, all of which have value as commodity or specialty chemicals. Molecules such as TAL are highly reactive and can readily undergo sometimes undesired reactions, such as decarboxylation at low temperature in water,[62] leading to the necessity to operate at relatively mild conditions and requiring a well-designed active site.

In a variation on the biological-followed-by-chemical catalysis sequence, Van Wouwe and co-workers showed that it is possible to achieve ~93% enantioselectivity of L-lactic acid using a combination of tin catalysts followed by enzyme catalysts.[63] In particular, racemic mixtures of lactic acid or alkyl lactate can be produced from sugars using Al- or Sn-containing chemical catalysts,[64,65] and this mixture can then be hydrolyzed using *Candida rugosa* lipase to yield the enantiomerically pure product. Heterogeneous catalysis can also be applied in the same pot as enzymatic catalysis. Notably, oxidation of glucose using glucose oxidase suffers from deactivation by H_2O_2, which is a byproduct of that reaction. Vennestrøm et al. demonstrated that the peroxide can be consumed in situ by oxidizing allyl alcohol to acrylic acid using titanium silicalite (see Scheme 4).[66]

Scheme 4. Coupled Enzymatic Oxidation of Glucose and Heterogeneously Catalyzed Oxidation of Allyl Alcohol[a]



[a]Adapted from Vennestrøm et al.[66]

This has the benefit of improving the glucose oxidation yield by preventing deactivation of the enzyme while also producing a valuable commodity chemical. Although such one-pot strategies are attractive, the range of operating conditions for these processes is narrow. In addition, long-term stability of these oxide catalysts in the liquid phase still needs to be demonstrated.

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From these examples of biologically derived chemical platforms, three principal challenges become apparent for producing biorenewable chemicals via heterogeneous catalytic upgrading of biological feedstocks. First, because many studies have used model compounds, substantial advances must be made in the use of real, biologically derived feedstocks, and understanding is needed about how these real feeds affect catalyst activity, selectivity, and stability. Second, most reactions occur in the liquid (often aqueous) phase, which is a significant challenge for heterogeneous catalysts, especially related to catalyst stability under reaction conditions. Finally, new heterogeneous catalysts are required to achieve high selectivity for the conversion of biologically derived feedstocks because of the complex nature of these platform molecules.

CHALLENGES AND OPPORTUNITIES

An important challenge to be addressed in the catalytic conversion of biologically derived molecules is the nature of impurities present in the feedstock. Such feedstocks can contain a collection of impurities originating from additives to the fermentation or reaction media, and there have been few systematic studies of the effects of these compounds. In contrast, the effects of biomass impurities on microbial systems are well reviewed, especially in the context of fuel ethanol production by *E. coli*,[67] and these effects will not be discussed here. Biological upgrading of biomass-derived sugars will, by necessity, require either cleanup of the sugars[68−71] or a sugar-production method that yields naturally clean feedstocks.[72] Several studies have been performed that indicate the presence of residual biogenic compounds from fermentation processes can have a substantial impact on catalyst activity.[73−75] Other studies have utilized real feedstocks but have not examined in detail catalyst stability in the presence of biogenic impurities.[76] Thus, it will be important to understand the fundamental impact of biogenic impurities on catalyst performance because this information is needed to guide both catalyst and process design for upgrading biologically derived intermediates.

The successful handoff from biological to chemical catalysis has been demonstrated in the literature for enzymatically derived intermediates. A notable early example is the one-pot, cascade synthesis of 4-deoxy-D-glucose derivatives by Schoevaart and Kieboom.[77] Here, D-galactose was enzymatically oxidized via D-galactose oxidase (in the presence of catalase), which was subsequently dehydrated with L-proline and hydrogenated over Pd/C in consecutive steps without any intermediate purification. The use of real feedstocks in this case was possible because water was used as the solvent in all three cases. In general, the simplicity of the reaction media in enzymatic processes makes such products attractive for heterogeneous catalytic upgrading. For example, the in situ, synergistic coupling of heterogeneously catalyzed alcohol oxidation chemistry with enzymatically catalyzed glucose oxidation[66] would not have been possible if impurities in the reaction media substantially inhibited the titanium silicalite. Similarly, production of furylglycolic acid[57] was carried out using enzymatically derived cortalcerone. In this case, glucose was oxidized and dehydrated enzymatically, and the only impurity in the enzyme reaction media was a small amount of phosphate buffer, which did not have a significant impact on the zeolites under study.

In contrast, metabolic processes are performed in whole cells, requiring conditions suitable for cell growth.[78] This approach requires nutrients that are supplied in the form of fermentation medium, the composition of which ranges in complexity. A simple example would be a synthetic medium such as Synthetic Defined Minimal (SD Minimal) medium, containing only glucose, ammonium sulfate, and yeast nitrogen base (YNB). YNB finds application in different types of culture media, and represents a minimal set of vitamins, salts, and trace metals needed for cell growth (see Table 1). Synthetic medium can be supplemented with various amino acids as needed by the microbes. At the other end of the spectrum are the "complex" media, including the common Lysogeny Broth (also known as Luria Broth and LB medium) and yeast−peptone−dextrose (YPD) medium. Nutrients in these media come from hydrolyzed protein (either tryptone or peptone) as well as yeast-extract. Because these media rely on hydrolyzates of natural products, it is difficult to determine their exact composition. Consequently, these solutions are also referred to as "undefined" media.

Table 1. Composition of Yeast Nitrogen Base[a]

component	mass per liter
ammonium sulfate	5 g
biotin	2 μg
calcium pantothenate	400 μg
folic acid	2 μg
inositol	2 mg
nicotinic acid	400 μg
p-aminobenzoic acid	200 μg
pyridoxine HCl	400 μg
riboflavin	200 μg
thiamine HCl	400 μg
citric acid	100 mg
boric acid	500 μg
copper sulfate	40 μg
potassium iodide	100 μg
ferric chloride	200 μg
manganese sulfate	400 μg
sodium molybdate	200 μg
zinc sulfate	400 μg
potassium phosphate monobasic	1 g
magnesium sulfate	0.5 g
sodium chloride	0.1 g
calcium chloride	0.1 g

[a]Sigma-Aldrich Catalog no. Y0626; "Yeast Nitrogen Base Without Amino Acids".

Few studies have focused on the impact on heterogeneous catalysts of the biogenic impurities that originate from fermentation media. Perhaps one of the most complete studies is that by Miller et al.[73] In this work, the authors note substantial loss of activity for Ru-catalyzed hydrogenation of lactic acid when fermentation-derived lactic acid was used as a feedstock. These authors studied the effects of organic acids, sugars, inorganic salts, amino acids, and proteins, and they determined that amino acids and proteins caused the most extensive catalyst deactivation. Alanine, which possesses only a methyl side chain, resulted in reversible deactivation, whereas cysteine and methionine, both possessing sulfur-containing side chains, caused irreversible catalyst deactivation.

Recent studies have also addressed the performance of solid acid catalysts in the presence of biogenic impurities. For example, succinic acid has been targeted for esterification because the diester can be used in polymer synthesis. Luque

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and co-workers[79] used sulfonic acid-containing carbon catalysts for the esterification of succinic acid, and they noted a decrease in activity when using succinic acid that was recovered from fermentation broth. The loss of activity was attributed to adsorption of organic species on the catalyst. Similar observations of deactivation were made by Delhomme and co-workers[74] using dodecylbenzenesulfonic acid, Nafion NR-50, and *Candida antarctica* lipase B. This study revealed that activity loss in the presence of real succinic acid feed was similar to that in the presence of phosphates (Na_2HPO_4, KH_2PO_4, and $(NH_4)_2HPO_4$).

Another important challenge for production of biorenewable chemicals is the stability of the catalyst under high-temperature liquid phase reaction conditions. Similar to the influence of biogenic impurities, there is limited information in the literature regarding catalyst stability and regenerability for liquid phase reactions, in which both sintering and leaching may be enhanced by the presence of a solvent (with the latter only occurring in the liquid phase). For example, the reactants, intermediates, products, and impurities present in biomass conversion processes may enhance leaching by serving as ligands for leached metal species, although this effect is not often studied. Furthermore, many studies of biologically derived feeds are performed in batch reactors. In such cases, stability is often evaluated by catalyst recovery/reuse cycles, and product yield or reactant conversion at long reaction times is used as an indicator of stability. This approach can be potentially misleading, as noted by Davis,[80] because measurement of reactant conversion or product yield at long times can mask catalyst deactivation, whereas measurements at shorter times and lower conversions are more sensitive indicators of catalyst performance, as illustrated in Figure 4. Evaluating stability in a kinetically controlled regime is also critical for continuous flow experiments. Conversely, it should be noted that evaluation of stability of heterogeneous catalysts against leaching must be done at long times or with many recycles because only catalysts with high dispersions will show clear changes in activity at short times. In addition, determinations of stability against leaching should be paired with direct measurements of the remaining active material recovered after continuous flow reactions, or if batch reactions are necessary, after hot-filtration recovery whenever possible.

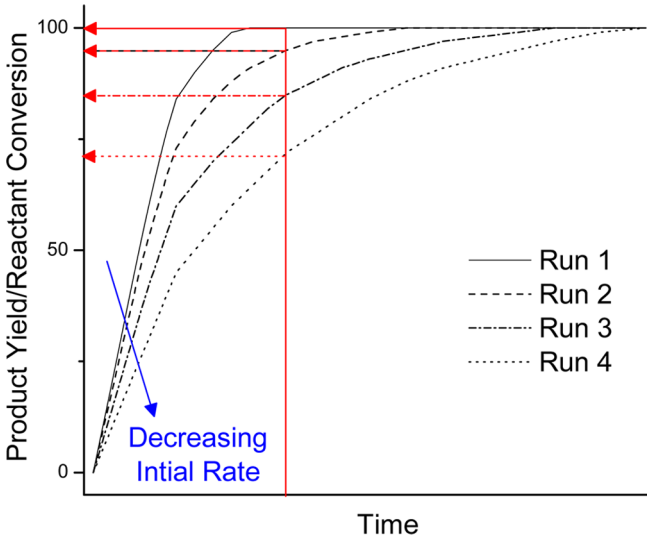

Figure 4. Representative reaction profiles as would be obtained from recovery/reuse batch recycle experiments, demonstrating the importance of assessing catalyst stability at short reaction times (adapted from ref 80 under a Creative Commons Attribution-Non Commercial-Share Alike 3.0 Germany (cc by-nc-sa 3.0) License).

A simple strategy for engineering a stable catalyst includes the use of high loadings of the active metal to reduce the impact of sintering and leaching by starting from low dispersion materials. This strategy is not feasible for expensive catalysts, such as precious metal hydrogenation catalysts, or in situations when environmental regulations prevent the discharge of leached heavy metals. Other approaches to synthesize stable catalysts include inducing strong metal support interactions to anchor the active phase in place,[81−83] coprecipitation methods to create robust bulk materials,[84] and silica sol−gel and encapsulation techniques to protect the active phase.[85,86] Many of these techniques have shown promise for imparting stability to catalysts for gas phase reactions. However, the effectiveness of these techniques has not been assessed extensively for liquid phase reactions.

Recent studies have examined the mechanisms of sintering, which may be facilitated in the liquid phase, and the role of the porous support in preventing particle agglomeration[87] as well as the role of reactants in facilitating particle transport.[88] In addition, advances in environmental microscopy have contributed to the understanding of the mechanisms of carbonaceous species deposition on catalysts.[89] These experimental studies have been supplemented with improved theoretical understanding of the mechanisms of carbon deposition, sintering, and leaching.[90] An important challenge for the future is to use these developments in mechanistic insight to design catalytic systems that can better withstand deactivation under the conditions demanded by upgrading biologically derived species, such as high-temperature reactions carried out in the liquid phase.

One area that has seen recent improvement is the development of more robust oxide catalysts and support materials that can withstand hydrothermal processing conditions. Loss of crystallinity in alumina supports[91,92] and the hydrolysis of Si−O linkages in silica supports[93] are causes of deactivation of catalysts that utilize these common support systems. Carbon-based supports are more stable in liquid (especially aqueous) environments, but carbon-supported metal catalysts are prone to sintering and low dispersion due to a weaker interaction between the support and the active phase.[83] Hydrothermal synthesis methods,[94] as well as the addition of stabilizing agents to prevent support rearrangement,[94,95] can lead to increased hydrothermal stability of support materials and the supported metal nanoparticles.[95,96] An interesting alternative for support stabilization is the coating of the support material. For example, it has been shown that coating mesoporous silica materials with carbon can lead to enhancement in hydrothermal stability as well as modification and control of surface interactions between the support and the active phase, which can affect catalytic activity and selectivity.[95] Similarly, the deposition of niobia onto mesoporous silica by atomic layer deposition (ALD) had the effect of stabilizing both the silica support material as well as the deposited niobia material,[97] and ALD of alumina on titania prevented its rearrangement from anatase to rutile.[98]

In recent work, it has been shown that the sites responsible for leaching and sintering of metal nanoparticles, leading to catalyst deactivation, can be selectively armored by ALD. For

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example, porous alumina overcoats were synthesized to provide resistance to sintering for platinum nanoparticles by decomposing layers of aluminum alkoxide deposited by molecular layer deposition (MLD).[99] This idea was extended by applying ALD of alumina films to palladium to eliminate sintering and reduce carbonaceous deposits.[100−102] This stabilization was achieved by pairing the mechanistic insight that sintering and coking originate from high energy, low coordination sites on the surface of metal nanoparticles, with the observation that species deposited by atomic layer deposition preferentially bind to these same sites, effectively protecting them from deactivation. The selective armoring can be achieved through the synthesis of multiple layer films followed by pore opening,[100] or by the selective nature of ALD to deposit submonolayer films onto the high energy, low coordination surface sites.[101,102] Interestingly, this technique can be extended to base metals, such as copper, which are inherently less stable, and whose effective commercial use can be limited by their tendency to deactivate irreversibly. In particular, a copper catalyst was stabilized against both sintering and leaching under both organic and aqueous liquid phase conditions by overcoating the catalyst with alumina by ALD, leading to selective armoring of the copper nanoparticles, an important advance for the application of these catalysts to upgrade biologically derived substrates.[98]

Another important challenge for applying heterogeneous catalysis to the upgrading of biologically derived intermediates is the design of highly selective active sites. In this respect, important advances have recently occurred in the synthesis and understanding of bifunctional, bimetallic nanoparticles. Using ALD, it is now possible to synthesize highly dispersed nanoparticle catalysts that are uniform in size and composition.[103] Furthermore, due to the self-limiting nature of ALD, the nanoparticles are tunable in composition and structure (i.e., mixed alloy, core−shell, near surface alloy, etc.). The importance of this control is illustrated by a RhRe/C catalyst that exhibits high selectivity in C−O hydrogenolysis reactions.[104] The origins of the unique catalytic properties of this catalyst were elucidated using in situ and operando X-ray absorption spectroscopy, scanning transmission electron microscopy/energy dispersive spectroscopy, and density functional theory. The active sites consist of highly reduced, undercoordinated Re on the surface of Rh−rich particles. Water is activated on these sites by interaction with undercoordinated Re atoms to create Brønsted acidity, and the nearby Rh surface species perform hydrogenation and maintain the Re in a highly reduced state.[105] The importance of this structural motif in imparting the high selectivity to the catalyst was confirmed by manipulating the catalyst structure via the pretreatment conditions. Atomic level control of the catalyst structure was essential for maximizing activity, which suggests that precise synthesis techniques, such as ALD or other surface limited reactions, have the potential to create new highly active and selective materials. Further advances in the understanding of the nature of such active sites will be essential for guiding such syntheses and for achieving efficient conversion of reactive and functionalized biologically derived molecules.

Atomic-level control of active sites can also be achieved in zeolite synthesis. Tin-containing beta zeolites (Sn-BEA) are water-tolerant Lewis acids that can catalyze reaction pathways analogous to those of metalloenzymes.[106] These zeolites have been used for a myriad of liquid phase reactions, ranging from Baeyer−Villiger oxidations[107] to Meerwin−Ponndorf−Verley−Oppenauer reactions,[108] including many examples in biorenewables,[109,110] and there have been reports of Sn-BEA being used in approaches that combine chemical and biological catalysis.[57,63] Tin resides in a precise framework position,[111] which has been shown to be necessary for catalyst performance because extraframework tin is typically unselective or unreactive.[112]

The local environment around an active site is also important in determining the activity and selectivity of the active site. In this respect, conversion of reactive and highly functionalized molecules can be influenced by the liquid solvent surrounding the active site. Because biologically derived intermediates are typically formed in the aqueous phase, water should be an ideal solvent for upgrading such species. However, water can have deleterious effects on the catalyst and the reaction pathways. For example, as discussed above, TAL undergoes decarboxylation in water,[62] making it necessary to carry out hydrogenation of TAL in organic solvents. Water can also competitively inhibit active sites or result in degradation of highly reactive species, as in the case of Meerwin−Ponndorf−Verley−Openauer reactions of triose sugars, in which the use of methanol precludes significant catalyst deactivation caused by the formation of carbonaceous residues for reactions in water.[112]

Water has also been shown to be less favorable for use as a solvent in recent studies of sugar dehydration reactions, which have employed polar, aprotic solvents such as tetrahydrofuran,[113] dimethyl sulfoxide,[114,115] and γ-valerolactone.[116,117] Importantly, it has been demonstrated that these organic solvents decrease the amount of degradation products formed. Applications of such solvent effects could have the potential to mirror the well-studied effects of ligands in homogeneous catalysis, which simultaneously solvate both the active site and entering/exiting species.[118] However, to date, the role of solvent in controlling activity and selectivity is not fully understood, and a fundamental framework is needed to allow for the rational optimization of solvent choice. Accordingly, future studies for upgrading biologically derived feeds should consider the choice of solvent as an integral part of developing new processing strategies.

Recent studies have shown that beneficial solvents effects can be built into a heterogeneous catalyst by forming a tailored microenvironment around the active sites, thereby creating a "nanoreactor" that incorporates localized solvent effects.[119] In this case, solid-state NMR demonstrated that the cross-linking of poly(vinylpyrrolidone) (PVP) inside the pores of an SBA-15 catalyst could mimic the effects of polar, aprotic solvents, which induce the tautomerization of fructose to its more reactive furanose form. This example demonstrates that it is possible to control the environment inside the catalyst pores and around the active site as a means to improve selectivity. Such an approach has the potential to selectively stabilize highly reactive, functional intermediates that are the product of biological processes, for example, by inducing structural changes in the bioderived substrate.

Another approach to tailor the active sites is to use a protecting overcoat to modify the environment immediately around the active site. Strong metal support interactions could be considered an early example, in which the oxide support material modifies the chemisorption behavior and reactivity of metal-catalyzed reactions.[81] More sophisticated attempts to utilize this approach include the nanoreactor concept proposed by Somorjai to increase the active sites at the interface of

Pt/CoO catalysts.[120] ALD may represent another approach to modify active sites through overcoating materials. In addition to the stabilizing effect discussed previously, ALD can be used to selectively expose specific facets of nanoparticles[98,100] and impart size selectivity to catalysts.[121] Further modification of the overcoats by the introduction of hydrophobicity through MLD (e.g., overcoat with alucone rather than alumina), the addition of a different element during ALD to decrease side reactions (e.g., Mg to reduce acidity of the oxide overcoat), or the introduction of a bifunctional layer to perform tandem catalysis are interesting catalytic architectures made available by the atomic level control of ALD/MLD. Importantly, ALD and MLD provide spatial control over the location of a second active site and provide pores that can be filled with solid polymer "solvents", making biomimetic functionalities a realistic option, as illustrated in Figure 5. Progress in this last

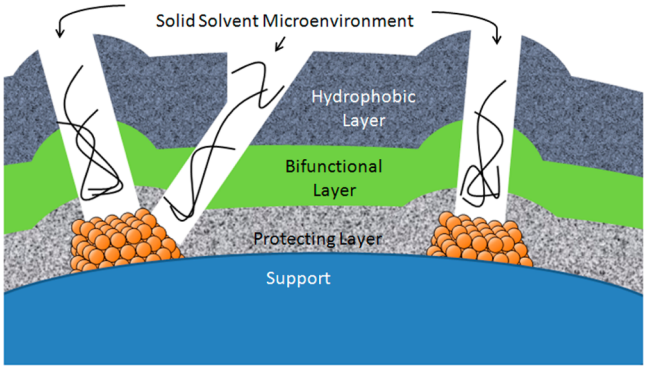

Figure 5. An example of the potential for a tailored active site surrounded by a microenvironment that could be created with the combination ALD/MLD and polymer overcoating.

challenge has been made by the introduction of acidity via NbO_x with an AlO_x overcoat on Cu nanoparticles to pair the hydrogenation of furfural to furfuryl alcohol with the etherification to furfuryl ether.[122]

OUTLOOK

The combination of chemical and biological catalysis offers new opportunities to upgrade biomass to produce chemicals from biorenewable feedstocks. Current research has focused on the necessary elucidation of new chemistries required for these processes. In this paper, we have identified three challenges that should be addressed in future research. Specifically, real biologically derived feedstocks must be investigated because impurities that originate during bioprocessing are significantly different from those present in traditional petroleum or even biomass feeds. Furthermore, the nature of bioprocessing dictates that catalytic reactions frequently must be performed in the liquid phase, and new generations of heterogeneous catalysts are required for stable operation under these conditions. Finally, biologically derived molecules often possess a high degree of functionality, and the design and syntheses of new catalysts are required to tailor the active sites and the environment around these sites to achieve selective conversion of specific functional groups.

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Notes

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