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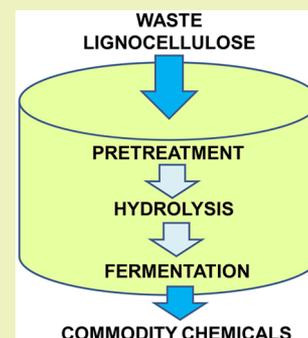
# The Road to Biorenewables: Carbohydrates to Commodity Chemicals

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**ABSTRACT:** The pressing need for climate change mitigation has focused attention on reducing global emissions of carbon dioxide by effectuating the transition from fossil-based chemicals manufacture to a carbon neutral alternative based on lignocellulosic waste. The first step involves fractionation of the lignocellulose into cellulose, hemicellulose, and lignin. Subsequently, a cellulase enzyme cocktail is used to catalyze the hydrolysis of the polysaccharides into their constituent sugars. This is followed by selective conversion of the carbohydrates into commodity chemicals using a variety of sustainable bio- and chemocatalytic methodologies. These include, inter alia, fermentative production of alcohols, diols, and carboxylic acids and a variety of chemocatalytic reductions and oxidations. Hence, the transition from fossil feedstocks to lignocellulose represents a switch from hydrocarbons to carbohydrates as the primary basic chemicals. To compare these renewable biomass-based routes with their petrochemical equivalents, it is necessary to develop reliable sustainability metrics.

**KEYWORDS:** Lignocellulose, Renewable biomass, Lignin, Carbohydrates, Magnetic enzymes, Enzyme immobilization, Sustainability metrics, Ethanol equivalent



## INTRODUCTION: TRANSITION TO A BIOBASED ECONOMY

It has become increasingly clear in recent years that society at large and the chemical and allied industries in particular are currently in a transition<sup>1</sup> from an unsustainable, linear economy based on finite fossil resources (oil, coal, and natural gas) to a sustainable, circular economy based on the utilization of solar energy. This can be achieved either directly via solar hydrogen generation<sup>2</sup> or indirectly via the conversion of biomass in a so-called biobased economy.<sup>3</sup> It forms the basis for a new industrial revolution as embodied in the Sustainable Process Industry through Resource and Energy Efficiency (SPIRE) Roadmap.<sup>4</sup> It is driven by the need, on the one hand, to conserve the earth's fossil resources for future generations and, on the other hand, to mitigate anthropogenic global warming by reducing carbon dioxide emissions to the atmosphere.

Resource depletion and ecological degradation are two sides of the same coin, but the latter probably constitutes the more acute threat to humanity. Thus, in a business-as-usual scenario, with a world population increasing from the current 7.3 billion to about 11.2 billion by the end of the century, economically recoverable coal, oil, and natural gas reserves will be depleted in less than a hundred years.<sup>5</sup> However, before this happens, increasing carbon dioxide levels in the atmosphere will almost certainly precipitate extensive ecological destruction. This will not signal the end of the world, but it could very well herald the demise of humankind. On the other hand, if we look at it from the planet's point of view, it is more a question of good riddance to bad rubbish. *Homo sapiens* will have been a mere blip on the 3.8 billion year timeline of life on planet Earth.<sup>6</sup> It would be a field day for rats and cockroaches.<sup>7</sup> The conclusion is clear: it is essential to improve energy efficiency and, above

all, to switch to renewable energies before fossil fuel shortages lead to economic and political crises and even armed conflicts.

The global primary energy consumption (PEC) is currently estimated to be 600 EJ (exa joules,  $10^{18}$  joules) per annum, corresponding to 82 GJ (giga joules,  $10^9$  joules) or 2 toe (tonne oil equivalents) per capita per annum.<sup>5</sup> Fossil resources currently dominate the energy mix with a contribution of ca. 80%. Renewable biomass currently contributes 10% (ca. 62 EJ) to the PEC, but it is worth reflecting on the fact that only 200 years ago, the energy supply consisted almost entirely of renewables, mainly in the form of biomass.<sup>8</sup> Renewable energy as a whole and biomass in particular will certainly play an important role in the future energy mix, but it should be seen as *part* of the energy solution, not *the* solution. Moreover, in a world without fossil resources, the only sources of carbon are biomass and carbon dioxide, and the latter is ultimately derived from biomass. As such, biomass is indispensable, not only for the production of food and feed but also for the manufacture of all carbon products, including biofuels.<sup>5</sup>

The biomass contribution of 62 EJ to the energy mix is a little more than 1% of the global production of biomass that is estimated to be ca. 200 billion tonnes dry weight per annum, equivalent to 4500 EJ per annum.<sup>8</sup> However, only ca. 3% of the global biomass, that is ca. 6 billion tonnes, consists of cultivated plant material, comprising roughly one-third of wood, one-third of grain, and one-third of oil seeds, sugar cane, sugar beet, fruits, etc.<sup>9</sup> The future contribution of biomass energy will certainly increase, but there is no consensus on how much it will be, and data are being continually revised and challenged.<sup>8</sup>

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Numerous options are being investigated for the transportation sector, but liquid biofuels, either neat or blended, are probably the best alternative to fossil fuels in the short to medium term. This will mainly consist of bioethanol and biodiesel for road transportation. By analogy with petrochemical refineries, the comanufacture of biofuels and commodity chemicals in integrated biorefineries is envisaged. Indeed, bioethanol is not only a biofuel but can also serve as a potential source of many platform chemicals. It has even been suggested that the optimal use of bioethanol could well be as a platform chemical rather than as a biofuel.<sup>10</sup> The major producers are the United States and Brazil with 56 billion and 30 billion liters (ca. 43 and 24 million tonnes), respectively, in 2014.<sup>11,12</sup> This is expected to increase substantially in the near future with the Asia-Pacific as a region with considerable growth potential. Bio-*n*-butanol and bioisobutanol also have important potential but are viewed more as longer term options.<sup>13</sup>

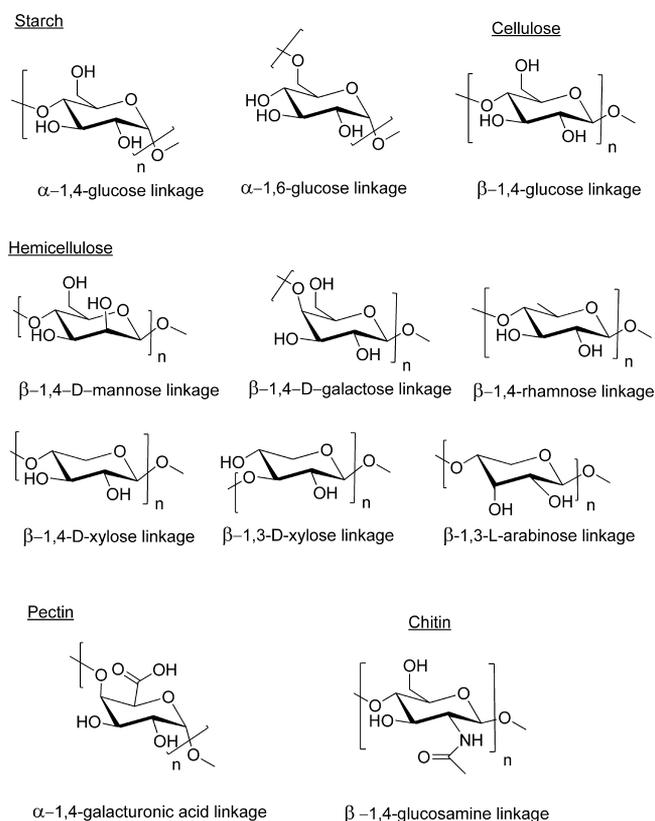
Biomass consists primarily of carbohydrates, which can be divided into storage polysaccharides, e.g starch and inulin, and the disaccharide, sucrose, and structural polysaccharides such as cellulose, hemicelluloses, pectin, and chitin. In particular, lignocellulose, the fibrous material that constitutes the cell walls of plants, is available in very large quantities. In addition, aquatic carbohydrates derived from micro- and macroalgae, comprising a variety of polysaccharides that differ in structure from those of terrestrial biomass, are potential feedstocks for third generation biorefineries.<sup>14</sup> The remainder of biomass comprises triglycerides (from fats and oils), proteins, and terpene hydrocarbons. The carbohydrate (sugar) constituents of polysaccharides form the basis for the production of biofuels and commodity chemicals in biorefineries just as simple hydrocarbons (alkanes, alkenes, and aromatics) derived from oil and natural gas are the cornerstone of petrochemical refineries. Hence, a transition from a fossil-based to a renewable biomass-based chemical industry will mean a switch from hydrocarbons to carbohydrates as the key basic chemicals. As discussed later, further processing of the carbohydrates can be via initial conversion to the hydrocarbon feedstocks of the petrochemical industry or via direct conversion to oxygen-containing commodity chemicals.

The structures of many of the C<sub>6</sub> and C<sub>5</sub> sugar building blocks of starch and the various structural polysaccharides are shown in Figure 1. Starch consists of  $\alpha$ -1,4- and  $\alpha$ -1,6-linked D-glucose units, while cellulose is a linear polymer of  $\beta$ -1,4-linked D-glucose units. Hemicellulose, in contrast, is a complex mixture of linear and branched polymers derived from a variety of C<sub>6</sub> and C<sub>5</sub> sugars, including D-glucose, D-mannose, D-galactose, D-xylose, D-rhamnose, D-arabinose, and small amounts of some L-isomers, mostly linked by 1,4-glycoside bonds. For example, D-mannose is an important building block of soft wood hemicellulose that consists primarily of a linear mannan backbone with D-galactose side chains. Some of the hydroxyl groups in hemicelluloses are acylated; that is, they are esters of acetic, ferulic, and *p*-coumaric acids.

The sugar building blocks of pectin and chitin differ from those of cellulose and chitin. Pectin is a heteropolysaccharide block copolymer comprising 1,4- $\alpha$ -linked galacturonic acid, and chitin is a polymer of 1,4- $\beta$ -linked 2-acetamido-2-deoxy- $\beta$ -D-glucose units.

## ■ FEEDSTOCK OPTIONS FOR BIOREFINERIES

The use of first generation (1G) biomass feedstocks, comprising sucrose from sugar cane and beet or starch from



**Figure 1.** Building blocks of polysaccharides.

corn and wheat and triglycerides from edible oil seeds, is not perceived as a sustainable option in the longer term because it competes, directly or indirectly, with food production.<sup>15</sup> This food vs fuel debate is a nonissue in parts of the world, e.g. Brazil,<sup>16</sup> that have more than enough arable land to produce all the food and fuel that is consumed, but is the subject of an ongoing discussion, in the context of fossil-based fuels vs biofuels, in the United States and the EU. Rosillo-Calle<sup>8</sup> summed it up as follows: "The debate has been for most parts, sterile, driven by moral/ethical, policy concerns, vested interest, and generally, a negative press, rather than by science. The movement towards pragmatism is welcome." Hence, there is a tendency toward recognizing that a "food and biofuel" scenario can contribute to energy security and socioeconomic development without affecting food security.

Second generation (2G) feedstocks, in contrast, comprise lignocellulose and triglycerides produced by the deliberate cultivation of fast-growing, nonedible energy crops or, preferably, by the valorization of waste triglycerides (oils and fats) and, in particular, the enormous amounts of waste lignocellulose generated in the harvesting and processing of agricultural products. Waste is the key word; waste that is essentially unavoidable in agricultural production of primarily food and beverages but also nonfood crops such as cotton.<sup>17</sup> Examples of such agricultural waste include sugar cane bagasse, sugar beet pulp, corn stover, wheat straw, rice straw, and orange peel.<sup>18,19</sup>

Food supply chain waste (FSCW) is produced along the whole supply chain from farms through processing, manufacturing and distribution, to consumption.<sup>20,21</sup> According to a report<sup>22</sup> of the Food and Agriculture Organization (FAO) of the United Nations, roughly one-third of all food produced

globally ends up as waste, amounting to 1.3 billion tonnes per annum, representing a carbon footprint of 3.3 billion tonnes of CO<sub>2</sub> equivalents, economic costs of \$750 billion and 1.8 billion hectares of land (28% of the world's agricultural land mass). Similarly, a recent EU survey<sup>23</sup> concluded that some 88 million tonnes of food waste are produced yearly in the EU (173 kg per capita) with associated costs estimated at 143 billion euro. Generation of FSCW not only results in the loss of valuable and often scarce resources such as water, soil, and energy but also significantly contributes to global warming. Driven by the need to avoid waste and find new sources of renewable biomass for fuels and chemicals, attention has recently focused on the use of FSCW as a feedstock for biorefineries.<sup>24–29</sup>

An illustrative example of valorization of waste derived from food processing is provided by whey, the liquid effluent of cheese and yoghurt manufacture. Hundreds of millions of tons of whey are produced annually on a global basis, making it one of the most abundant food supply chain wastes. High value-added whey proteins are separated by ultrafiltration to leave a whey permeate containing substantial amounts of lactose, for which there is only a limited market. Hence, there is a clear need to upgrade it to more valuable products. Ravasio and coworkers<sup>30</sup> described a one-pot conversion of lactose, involving a cascade of hydrolysis and hydrogenation over a Cu/SiO<sub>2</sub> catalyst, to an equimolar mixture of sorbitol and dulcitol that is readily separated. Sorbitol has many commercial applications, and dulcitol has potential value-added applications, e.g. as a precursor of the sweetener D-tagatose.

Similarly, biorefineries are envisaged based on various polysaccharide waste streams generated in the production of foods and beverages. These include pectin from the processing of citrus fruits,<sup>24,31,32</sup> coffee beans<sup>33</sup> and sugar beet pulp<sup>34</sup> and chitin from crustacean shell waste.<sup>35</sup> As noted earlier, the building blocks of pectin and chitin differ from those of cellulose and hemicellulose (Figure 1) and can, therefore, be converted to other platform chemicals. Chitin and its deacetylated counterpart, chitosan, are widely applied as such, e.g. in biomedical applications. Similarly, pectin finds many applications in foods and pharma. Conversion of these polymers to commodity chemicals, on the other hand, is still largely unexplored.

## PRIMARY CONVERSION OF POLYSACCHARIDE FEEDSTOCKS

Irrespective of whether the final product is a liquid fuel or a platform chemical, the first step is the depolymerization of the polysaccharide feedstock: starch or second generation waste biomass comprising lignocellulose, pectin, and chitin. Lignocellulose is much more difficult to process than the first generation renewable feedstocks such as sugars, starches, and vegetable oils. It consists of roughly 65% polysaccharides (40% cellulose and 25% hemicellulose), 25% lignin, and 10% other minor components. Lignin is a three-dimensional polyphenolic biopolymer having a nonuniform structure that imparts rigidity and recalcitrance to plant cell walls. It is in volume the second largest biopolymer after cellulose and the only one composed entirely of aromatic subunits.

There are basically two ways to depolymerize lignocellulose: hydrolytic and thermochemical (Figure 2).<sup>36</sup> Thermochemical processing involves pyrolysis to a mixture of charcoal and pyrolysis oil or gasification to afford syn gas (a mixture of carbon monoxide and hydrogen), analogous to syn gas from coal gasification<sup>37</sup> that was developed following the first oil

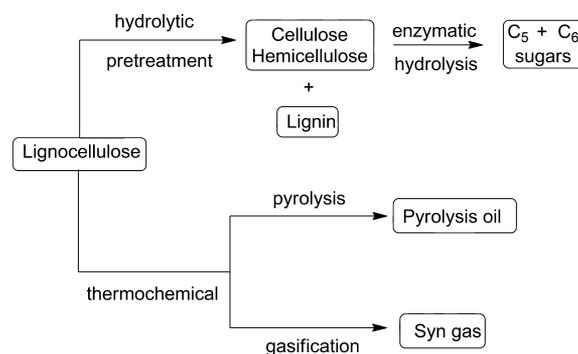


Figure 2. Methods for lignocellulose conversion.

crisis in 1974. The syn gas can be subsequently converted to liquid fuels or platform chemicals using established technologies such as the well-known Fischer–Tropsch process or methanol synthesis, respectively. More recently, processes have been commercialized for the fermentation of syn gas or mixtures of carbon dioxide and hydrogen to biofuels and platform chemicals.<sup>38,39</sup> It is interesting to note, in this context, that the companies developing this technology are mainly targeting the waste “syn gas” that is available in large quantities, e.g. from steel manufacture.

Alternatively, lignocellulose can be converted to a mixture of lignin, cellulose, and hemicellulose. Further hydrolysis of the polysaccharides affords their C<sub>6</sub> and C<sub>5</sub> monosaccharide building blocks. In this scenario, the lignin fraction is separated from the other components and, for commercial viability, it should preferably be valorized.

## HYDROLYSIS (SACCHARIFICATION) OF POLYSACCHARIDES

Hydrolysis of lignocellulose is catalyzed by dilute mineral acids at elevated temperatures. Unfortunately, this results in the formation of copious amounts of inorganic salts as waste, resulting from subsequent neutralization of the dilute mineral acid. Consequently, attention is being focused on the design of solid acid catalysts for the conversion of biomass<sup>40,41</sup> by analogy with the processing of crude oil fractions in the petrochemical industry. An interesting recent development<sup>42</sup> is the combination of mechanical processing with acid catalysis to afford mechanocatalytic dissolution and subsequent hydrolysis of lignocellulose at 140 °C. However, the method of choice is currently the milder enzymatic hydrolysis of the cellulose and hemicellulose to their constituent sugars, in a process referred to as saccharification.<sup>43</sup>

**Pretreatment of Lignocellulose.** Some form of pretreatment such as a steam explosion, ammonia fiber expansion (AFEX), or lime treatment is necessary to open up the recalcitrant lignocellulose structure and render the targeted glycoside (ether) and ester bonds accessible to the enzyme cocktails.<sup>44–46</sup> Indeed, the pretreatment generally accounts for a substantial fraction of the total energy requirements<sup>47</sup> and up to 20% of the capital and operating costs<sup>48</sup> of lignocellulose processing, and has, therefore, been a significant barrier to commercialization of lignocellulosic bioethanol.<sup>49</sup> However, process improvements continue to be made. For example, a modified AFEX process using dilute aqueous ammonia solution is simpler and less expensive than the original process.<sup>50</sup>

Pretreatment is generally conducted in water, in which the cellulose, hemicellulose, and lignin are present as suspended

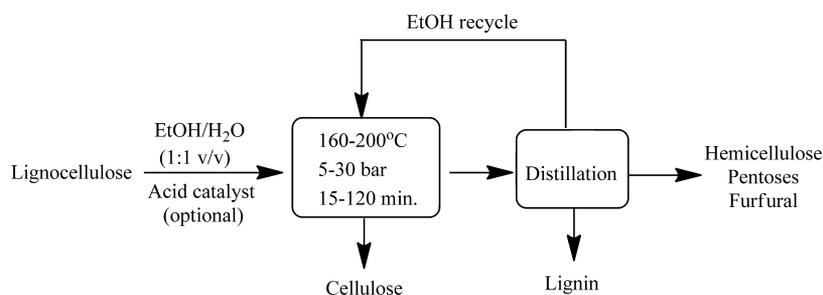


Figure 3. Organosolv pretreatment of lignocellulose with ethanol.

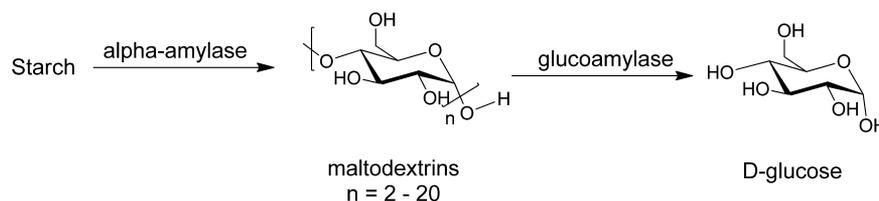


Figure 4. Enzymatic hydrolysis of starch.

solids. The use of alternative reaction media that (partially) dissolve these polymeric substrates could have processing advantages. However, to be economically and environmentally viable, the solvent should be inexpensive, nontoxic, biodegradable, recyclable, and preferably derived from renewable resources. In the Organosolv process (Figure 3), for example, lignocellulose is subjected to elevated temperatures (185–210 °C) in water/organic solvent (e.g., ethanol) mixtures.<sup>51,52</sup> Organic acids formed in situ are able to catalyze the cleavage of the lignin–polysaccharide complex. Alternatively, the process can be conducted at lower temperatures (e.g., 140–160 °C) by adding a mineral acid catalyst, generally resulting in higher selectivities.<sup>53</sup> Cellulose is removed by filtration and the ethanol (for recycling) is distilled, resulting in precipitation of the lignin to leave a filtrate containing hemicellulose and/or the hydrolysis products. Alternatively, in the Glycell process developed by Green Leaf Technologies, crude glycerol/water mixtures are used to pretreat the lignocellulose, affording a mixture of sugars at under \$50 per tonne and recovering the glycerol in high purity.<sup>54</sup>

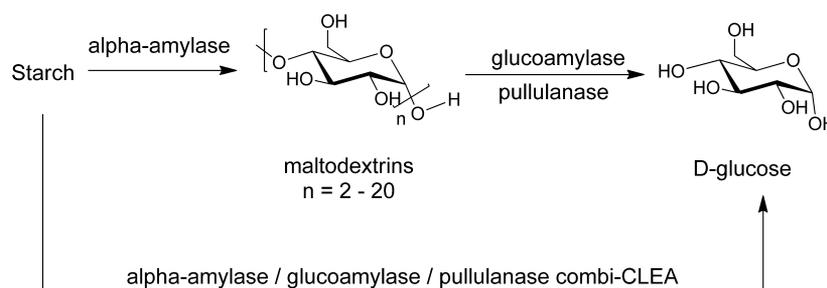
Ionic liquids (ILs) are known to dissolve polysaccharides and are being considered as alternative reaction media for saccharification of lignocellulosic biomass.<sup>55,56</sup> A potentially interesting goal is an integrated process for IL pretreatment of the lignocellulose and enzymatic hydrolysis with efficient recycling of both the IL and the (immobilized) enzyme.<sup>57</sup> Basically, two strategies have been followed for IL pretreatment. The first one involves the complete dissolution of the lignocellulose in the IL and is determined largely by the ability of the anion to disrupt the stabilizing network of hydrogen bonds. Carboxylate and halide ions are particularly effective in this respect, and 1-ethyl-3-methylimidazolium acetate, [Emim]-[OAc], has been extensively studied. However, such dialkylimidazolium carboxylates suffer from various drawbacks: high cost, relatively low thermal stabilities,<sup>58</sup> and low tolerance to water. The second approach involves the use of much less expensive protic ionic liquids (PILs), readily prepared by mixing commodity amines with mineral acids such as sulfuric acid.<sup>59,60</sup> For example, the cost-price of triethylammonium (TEA) hydrogen sulfate, [Et<sub>3</sub>NH][HSO<sub>4</sub>], is estimated<sup>61</sup> to be as little as ca. \$1/kg. In this approach, the lignocellulose is

heated with a PIL/water mixture whereby the lignin and the hemicellulose dissolve and the cellulose remains as a filterable solid. For example, Hallett and coworkers<sup>62</sup> investigated the fractionation of *Miscanthus giganteus* (switchgrass), using a TEA-HSO<sub>4</sub>/water (80/20) mixture at 120 °C for 8 h, into a cellulose-rich pulp, lignin, and a hemicellulose-derived distillate comprising the constituent sugars in which pentoses were partially converted to furfural. The PIL was recycled 4 times with 99% recovery in each recycle. A techno-economic analysis predicted that capital and operating costs are lower than the benchmark dilute acid pretreatment.

Polysaccharides such as lignocellulose<sup>63</sup> and chitin<sup>64</sup> also dissolve in deep eutectic solvents (DESs), formed by mixing a salt with a hydrogen bond donor and gently heating. Most DESs tested exhibit high lignin solubilities combined with negligible solubility for cellulose and, hence, are potential candidates for lignocellulose fractionation and saccharification. For example, mixtures of choline chloride and a variety of hydrogen bond donors, together with water, were shown to be effective reaction media for the pretreatment and saccharification of lignocellulose from energy crops or agricultural residues.<sup>65–67</sup>

**Enzymatic Hydrolysis of Starch.** Although lignocellulosic biofuels are seen as the long-term option, in the short term, biofuels consist primarily of bioethanol from corn starch or sucrose. This involves initial  $\alpha$ -amylase catalyzed hydrolysis of starch to a mixture of maltodextrins (oligomers of glucose comprising 2–20 glucose units) followed by glucoamylase-catalyzed hydrolysis of  $\alpha$ -(1,4) and  $\alpha$ -(1,6) glycosidic bonds in the latter, affording glucose (Figure 4). The glucose is subsequently fermented to produce bioethanol. The overall process can be conducted in a separate hydrolysis and fermentation (SHF) mode or in a more cost-effective simultaneous saccharification and fermentation (SSF) process.<sup>68</sup> An SSF process has the advantage that the glucose is immediately consumed by the fermenting organism, thus circumventing possible inhibition by increasing concentrations of glucose.

**Enzyme Immobilization.** The enzyme(s) used in the hydrolysis step are dissolved in the aqueous reaction medium and, consequently, are discarded with the wash water; that is,



**Figure 5.** One-pot starch hydrolysis with a combi-CLEA (adapted with permission from Figure 24 in ref 201, Copyright 2018 American Chemical Society).

they are employed on a single use, throw-away basis. Enzyme manufacturers have been able to substantially reduce the enzyme cost contribution by optimizing the production of the enzymes involved. Further reduction of the enzyme cost contribution and environmental footprint, thereby improving competitiveness and sustainability, can be achieved by their immobilization as readily recoverable free-flowing solids to enable multiple recycling. A further benefit is increased operational stability resulting from decreased flexibility of the enzymes, thereby suppressing their propensity to unfold (denature) under the influence of heat or organic solvents.

Immobilization typically involves binding the enzyme to a prefabricated carrier (support) such as an organic resin, silica, or a biopolymer,<sup>69</sup> but this inevitably leads to substantial “dilution” of activity and, hence, lower space-time yields and catalyst productivities.<sup>70</sup> The extra costs of a carrier and accompanying lower productivities can be avoided by cross-linking the enzyme molecules together by reaction with a bifunctional reagent such as glutaraldehyde to afford an insoluble powder. For example, cross-linked enzyme aggregates (CLEAs) are formed by precipitation of the enzyme from aqueous buffer, as physical aggregates held together by noncovalent bonding without perturbation of their tertiary structure, followed by cross-linking.<sup>71</sup> The method does not require highly pure enzymes and is, therefore, simple and inexpensive. Selective precipitation with ammonium sulfate is commonly used to purify enzymes and, hence, the CLEA methodology combines purification and immobilization into a single unit operation. The technology has been successfully applied to the immobilization of a broad spectrum of enzymes.<sup>72–76</sup>

Coprecipitation of two or more enzymes, e.g. from crude enzyme extracts, affords combi-CLEAs that can be used to catalyze two or more reactions in parallel<sup>77</sup> or in tandem; that is, in multienzyme cascade processes. These have many advantages compared with classical multistep syntheses: fewer unit operations, less solvent and reactor volume, shorter cycle times, higher space-time yields, and less waste formation. Furthermore, coupling of reactions can be used to drive equilibria toward product, thus avoiding the need for excess reagents. Because biocatalytic processes generally proceed under roughly the same conditions (in water at ambient temperature and pressure), they can be readily integrated into cascade processes. These have become a focus of attention in recent years, largely motivated by the envisaged environmental and economic benefits.<sup>78</sup>

Combi-CLEAs have been widely used in carbohydrate conversions. A pertinent example is the coimmobilization of glucoamylase and pullulanase (E.C. 3.2.1.41). The latter enzyme is added to increase the rate of hydrolysis of the  $\alpha$ -

(1,6) branches in starch, which is relatively slow with glucoamylase alone. Coimmobilization of the two enzymes in a combi-CLEA produced a shift in optimum pH (from 5 to 7) and temperature (from 60 to 70 °C).<sup>79</sup> The combi-CLEA afforded 100% hydrolysis after 3 h compared with 30% with the free enzyme and 80% with a physical mixture of the two separate CLEAs. The retained activities of the glucoamylase and pullulanase in the combi-CLEA after 8 cycles were 90 and 85%, respectively. The same group prepared a trienzyme combi-CLEA containing  $\alpha$ -amylase, glucoamylase, and pullulanase from a commercially available mixture.<sup>80</sup> In a one-pot batch hydrolysis (Figure 5), 100% conversion was observed with the combi-CLEA, compared with 60% with a mixture of the separate CLEAs and 40% with a physical mixture of the three enzymes. Moreover, the thermal stability of all three enzymes was improved, and the catalytic performance was maintained for up to five cycles.

#### Enzymatic Hydrolysis of Cellulose and Hemicellulose.

Apart from the extra pretreatment step, the conversion of lignocellulose to biofuels and commodity chemicals is analogous to that of starch: enzymatic hydrolysis of the polysaccharides cellulose and hemicellulose to fermentable sugars is followed by fermentation, e.g. to ethanol or lactic acid. These can be carried out separately in an SHF process or simultaneously as an SSF process. Alternatively, in so-called consolidated bioprocessing (CBP) cellulolytic enzyme producing microbes (bacteria, fungi, or yeasts) mediate the conversion of the cellulose and hemicellulose in which three consecutive steps (enzyme production, enzymatic hydrolysis, and fermentation) proceed simultaneously.<sup>81</sup> Although CBP is potentially very attractive, productivities need to be further improved for commercial viability.

Hydrolysis of cellulose and hemicellulose to fermentable sugars requires the involvement of a complex cocktail of cellulolytic and hemicellulolytic enzymes.<sup>43,82</sup> The hydrolysis of cellulose involves catalysis by at least five enzymes: exo-1,4- $\beta$ -glucanase (EC 3.2.1.91), endo-1,4- $\beta$ -glucanase (EC 3.2.1.4), cellobiohydrolase (EC 3.2.1.176),  $\beta$ -glucosidase (EC 3.2.1.21), and the more recently discovered, copper-dependent lytic polysaccharide monooxygenase (LPMO)<sup>83</sup> that catalyze the oxidative cleavage of glycosidic linkages in polysaccharides. Hemicellulose has a more complicated structure than cellulose and requires another complex enzyme cocktail to affect its hydrolysis to its constituent sugars, mainly xylose and mannose. This comprises both core enzymes that catalyze cleavage of the polysaccharide backbone and ancillary enzymes that mediate the removal of functional groups. Examples of core enzymes are endo- $\beta$ -1,4-xylanase (EC 3.2.1.8), xylan-1,4- $\beta$ -xylosidase (EC 3.2.1.37), endo-1,4- $\beta$ -mannanase (EC 3.2.1.78), and  $\beta$ -1,4-mannosidase (EC 3.2.1.25). Ancillary enzymes include  $\beta$ -

glucuronidase (EC 3.2.1.139), acetylxyylan esterase (EC 3.2.1.55), ferulic acid esterase (EC 3.1.1.73), and *p*-coumaric acid esterase (EC 3.1.1.-).

In vivo, these enzymes are contained in multienzyme complexes, so-called cellulosomes,<sup>84</sup> produced by many cellulolytic fungi and bacteria. Compared to simple mixtures of the free enzymes, cellulosomes have the advantage of close proximity of the enzymes. This advantageous close proximity of the individual enzymes is also mimicked in combi-CLEAs.

#### Magnetic Separation of Immobilized Enzymes.

Applications of immobilized enzymes in processes involving suspensions of other water insoluble solids such as fibers and/or yeasts in SSF conversions of 1G and 2G biomass is challenging. However, industrially viable separation on a large scale, using standard commercial equipment, can be readily achieved with enzyme-ferromagnetic particle composites. The magnetic separation of ferromagnetic heterogeneous catalysts such as Raney nickel is a well-established technology<sup>85</sup> practiced on an industrial scale. More recently, increasing attention has been devoted to the design of magnetically recoverable catalysts based on ferromagnetic magnetite (Fe<sub>3</sub>O<sub>4</sub>) or maghemite ( $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) (nano)particles in both chemo-catalytic<sup>86,87</sup> and biocatalytic<sup>88,89</sup> processes. In combination with commercially available magnetic separation equipment (e.g., see [www.eclipsemagnetics.com](http://www.eclipsemagnetics.com)), very high recoveries can be obtained at industrially acceptable flow rates. Magnetic separation also provides a solution to a basic problem of heterogeneous catalysis: how to combine the high activity of small particles with the ease of processing of large particles.

Similarly, smart ferromagnetic CLEAs (mCLEAs) have been prepared by conducting the cross-linking in the presence of ferromagnetic (nano)particles.<sup>90</sup> Preparation following the optimized methodology<sup>91</sup> adds little cost to regular CLEAs, and recyclable mCLEAs are expected to find applications in a variety of processes, including 1G and 2G biofuels.

mCLEAs have been prepared from a variety of enzymes, including lipases<sup>92</sup> and carbohydrases. An example of the latter is provided by the preparation of mCLEAs of  $\alpha$ -amylase<sup>93</sup> with an activity recovery of 100%, improved thermal and storage stability, and complete activity retention after 6 recycles. A mCLEA of  $\alpha$ -amylase prepared using pectin dialdehyde as the cross-linker exhibited 95% activity recovery compared to 85% using glutaraldehyde.<sup>94</sup> The higher activity recovery was attributed to better mass transfer of macromolecular substrates in the more open porous structure. Similarly, mCLEAs of glucoamylase from *Aspergillus niger* exhibited 93% activity recovery combined with enhanced thermal and storage stability and reusability.<sup>95</sup>

Immobilization of the cellulase enzyme cocktail on prefabricated magnetic carriers<sup>96–99</sup> or as magnetic CLEAs<sup>100,101</sup> has been extensively investigated. However, activities were generally measured in the hydrolysis of the water-soluble carboxymethylcellulose as a model for the complex mixture derived from lignocellulose. It may not be essential to immobilize all of the enzymes in the cellulase cocktail to achieve substantial cost reductions. For example,  $\beta$ -glucosidase, one of the key enzymes contained in the cellulase cocktail, has been successfully immobilized on magnetic silica-based particles.<sup>102</sup> Similarly, Bhattachariya and Pletschke<sup>103</sup> prepared mCLEAs of a bacterial xylanase and observed that incorporation of Ca<sup>2+</sup> ions in the CLEA led to increased thermal stability. Interestingly, Illias and coworkers<sup>104</sup> prepared mCLEAs of a recombinant xylanase from *Trichoderma reesei*

using maghemite ( $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) rather than the more usual magnetite (Fe<sub>3</sub>O<sub>4</sub>) nanoparticles.

#### ■ SUGARS TO COMMODITY CHEMICALS

To have any impact on the economics of biorefineries, the chemicals produced should be largely restricted to high-volume commodities such as the raw materials for industrial polymers. Indeed, there is increasing pressure to substitute oil-based polymers with more sustainable renewable alternatives. Ease of recyclability and/or biodegradability are important from the viewpoint of sustainability, but substitution will only be possible if the biobased polymers can compete on price and have equivalent or better properties than the products they replace. Different scenarios are envisaged. First, production of existing industrial monomers that are subsequently converted, using existing technology, to the corresponding polymers, e.g. bioethylene to biopolyethylene. Second, conversion to new monomers that are subsequently polymerized. This involves a time-consuming market introduction of a new product. Third, the biomass is converted directly into a polymer which has to compete with an existing oil-based polymer, e.g. carbon fibers from lignin.

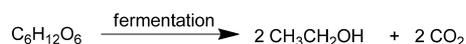
Two scenarios are envisaged for carbohydrates processing in a biorefinery:

- (i) Conversion to “drop-in” petroleum hydrocarbons (lower olefins and aromatics) that form the cornerstone of the petrochemical industry. The oxygen atoms of the carbohydrates are removed as water in an overall process that requires a reducing agent such as hydrogen. The main advantage of this scenario is that established petrochemical technologies and facilities can be used in the further conversion of the hydrocarbons to commodity chemicals.
- (ii) Direct conversion to oxygenates as platform chemicals. Many commodity chemicals are oxygenates, and their production in an oil refinery involves the introduction of an oxygen functionality into petroleum hydrocarbons, usually by catalytic aerobic oxidation. In contrast, the C<sub>6</sub> and C<sub>5</sub> sugars derived from cellulose and hemicellulose already contain multiple oxygen-containing functionalities and, according to the concept of redox economy, it is energetically more economical to avoid changes in oxidation state during a multistep process. Hence, removal of all the oxygens to generate hydrocarbons followed by reintroduction of oxygen functionalities by oxidation is to be avoided.

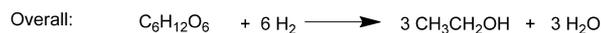
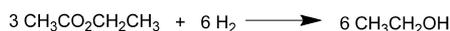
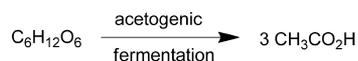
**Direct Conversion of Sugars to Oxygenates.** Direct conversion of lignocellulose derived sugars to commodity platform chemicals can be conducted using chemical<sup>105–110</sup> or biological catalysis<sup>111</sup> or combinations thereof.<sup>112,113</sup>

**Fermentation Processes.** Thanks to the significant advances in metabolic engineering and synthetic biology in the last two decades,<sup>114–116</sup> a wide variety of oxygenates, including lower alcohols, diols, and mono- and dicarboxylic acids, can be produced directly in a redox economic and cost-effective manner by fermentation. The most well-known and well-investigated is undoubtedly ethanol, which is produced by yeast fermentation of glucose according to the stoichiometry shown in Figure 6a. In this process, one molecule of glucose is converted to two molecules of ethanol and two molecules of carbon dioxide. From an environmental viewpoint, it would be interesting if all of the glucose could be converted to product,

## a. Yeast fermentation



## b. Acetogenic fermentation

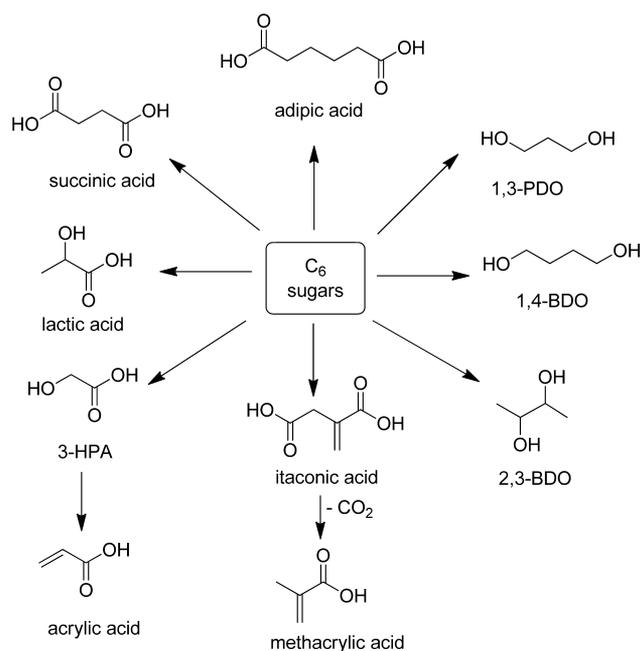


**Figure 6.** Glucose to ethanol via yeast (a) and acetogenic (b) fermentation.

as is the case when the fermentation is mediated by acetogens, a group of anaerobic bacteria found, for example, in the digestive tract of termites (Figure 6b).

In this so-called acetogenic fermentation process, developed commercially by the company Zechem,<sup>117</sup> three molecules of acetic acid are formed from one molecule of glucose. The acetic acid is converted to ethyl acetate by reaction with ethanol, and subsequent catalytic hydrogenation of the ethyl acetate affords two molecules of ethanol, resulting in the overall production of three molecules of ethanol and three molecules of hydrogen from one molecule of glucose. In Zechem's lignocellulosic bioethanol process, the required hydrogen is produced by gasification of the lignin fraction. The Zechem process is an example of a hybrid hydrolytic-thermochemical conversion.

In addition to bioethanol, other lower alcohols can be produced cost-effectively on an industrial scale by fermentation (Figure 7). For example, 1-butanol and isobutanol can be produced efficiently by fermentation,<sup>13,118–120</sup> and various companies, including Butamax Advanced Technologies, Green Biologics, Gevo and Cobalt Technologies, are commercializing microbial production of biobutanol and/or bioisobutanol as



**Figure 7.** Commodity chemicals by fermentation of biomass derived sugars.

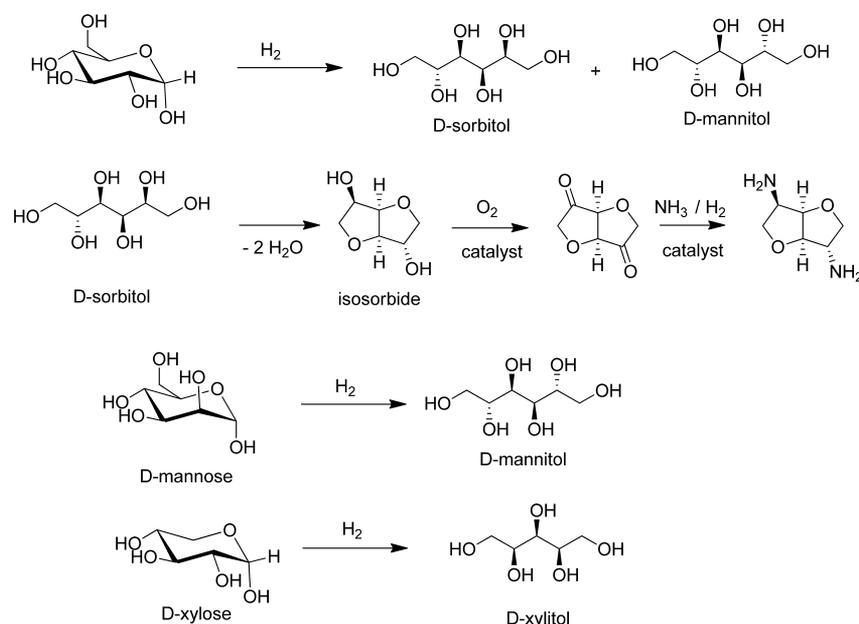
biofuels and commodity chemicals. Initially developed processes were not cost-effective owing to the low product concentrations obtained, resulting in challenging product recovery. However, as a result of the extensive application of advanced metabolic pathway engineering techniques, product concentrations and productivities and carbon efficiencies have been substantially improved. It seems likely, therefore, that cost-effective fermentative production of 1-butanol and isobutanol will be forthcoming in the near future. Similarly, 1-propanol and isopropanol can be produced by fermentation,<sup>121</sup> but yields and productivities are not yet sufficient to compete with chemical processes.

Four commercially important diols: 1,3-propanediol (1,3-PDO), 1,2-propanediol (1,2-PDO), 2,3-butanediol (2,3-BDO), and 1,4-butanediol (1,4-BDO) can be produced on an industrial scale by fermentation<sup>122</sup> and may be considered as green platform chemicals. Indeed, the development of the microbial production of 1,3-PDO in a recombinant *Escherichia coli* strain by DuPont was a milestone in the application of modern biotechnology in commodity chemicals production.<sup>123,124</sup> PDO is a raw material for the polyester polytrimethylene terephthalate (PTT), which is used in fibers, plastics, films, and coatings. More recently, the microbial production of 1,4-butane diol (1,4-BDO), a raw material for polybutylene terephthalate (PBT) and other polyesters, has been commercialized.<sup>125</sup> Although 1,2-PDO can be produced by fermentation, chemocatalytic production by hydrogenation of glucose may be more cost-effective (see later).

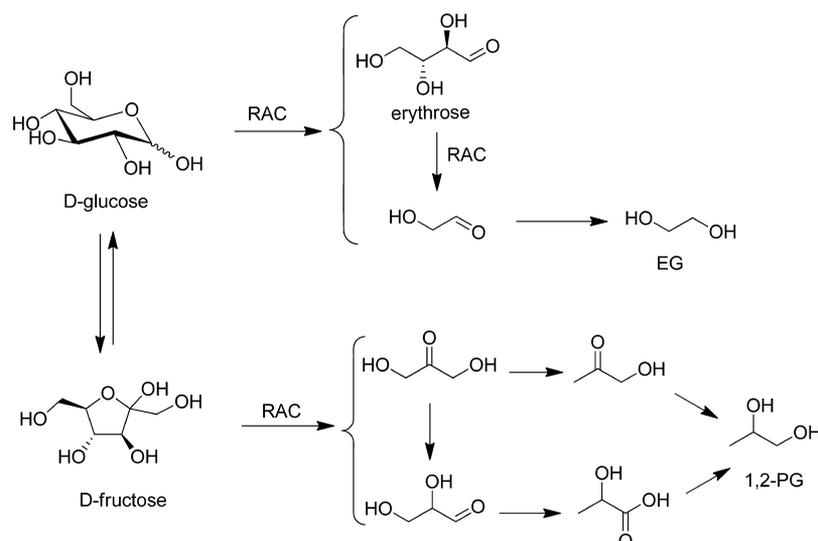
Lactic acid is a good example of a product that has been traditionally produced by fermentation because it is more cost-effective and more environmentally attractive than the chemical process.<sup>126</sup> The rapidly increasing market for the biodegradable polylactate (PLA) as a green and sustainable alternative to petroleum-derived plastics has significantly increased the global consumption and, hence, production of lactic acid. Citric acid is another example of a first generation, large volume commodity chemical that is produced by fermentation. More recently, itaconic acid has been targeted for microbial production.<sup>127</sup> It is the raw material for a variety of renewable polyesters<sup>128</sup> and decarboxylation over noble metal catalysts affords biomethacrylic acid.<sup>129</sup> Similarly, succinic acid<sup>130</sup> has attracted considerable attention because of potentially large volume applications in polyesters and polyamides, and microbial production is being developed by several companies: Myriant Technologies, Reverdia, Bioamber, and Purac.

Bioacrylic acid is available via microbial production of 3-hydroxypropionic acid (3-HPA) and subsequent dehydration<sup>131</sup> but has to compete with production from cheap propylene from propane dehydrogenation. Several companies are actively pursuing biorenewable routes to adipic acid.<sup>132</sup> Verdezyne, for example, has employed metabolic pathway engineering to afford a feedstock agnostic process that accepts carbohydrates, vegetable oils, or alkanes.<sup>133</sup>

**Chemocatalytic Conversion of Carbohydrates.** Chemocatalytic conversion of carbohydrates into commodity chemicals generally involves either reduction or oxidation. For example, catalytic hydrogenation of the C<sub>6</sub> and C<sub>5</sub> sugars derived from lignocellulose affords the corresponding sugar alcohols (Figure 8).<sup>134</sup> Thus, D-glucose is converted to a mixture of D-sorbitol and D-mannitol. The former has a global market of ca. 2 million tonnes per annum and has applications in food, pharmaceuticals, and chemical industries. Acid-catalyzed dehydration of sorbitol affords isosorbide, a raw



**Figure 8.** Catalytic hydrogenation of sugars from lignocellulose.



**Figure 9.** Pathways for hydrogenation of glucose to EG and 1,2-PG.

material for biobased polyesters. Interestingly, cellulose can be directly converted into isosorbide (Figure 8) using a hydrogenation catalyst in combination with  $\text{ZnCl}_2 \cdot 3\text{H}_2\text{O}$  as both a Lewis acid catalyst and a molten salt reaction medium.<sup>135</sup> Catalytic aerobic oxidation of isosorbide, in the presence of acetylamin-TEMPO/ $\text{HNO}_3$ <sup>136</sup> or Laccase/TEMPO<sup>137</sup> as a chemo- or biocatalyst, respectively, affords the corresponding diketone. The latter can be subsequently converted to the diamine, which can be used to produce biobased polyamides. Similarly, D-mannose and D-xylose, derived from the hemicellulose fraction of lignocellulose, are converted to D-mannitol and D-xylitol, respectively. The latter has important applications in food and pharma.

From the viewpoint of commodity chemicals, however, the 1,2-diols, ethylene glycol (EG), and propylene glycol (1,2-PG), with global productions of 23 and 2 mio tonnes per annum, respectively, are more important than the above-mentioned sugar alcohols. To convert cellulose to EG and 1,2-PG via

hydrogenation of glucose, carbon–carbon bonds must be broken. This is achieved via retro-aldol condensations (RACs) that are catalyzed by, inter alia, tungsten-based catalysts (Figure 9). Hence, yields of up to 72–76% EG are obtained by hydrogenation of cellulose over a Ni–W carbide-on charcoal catalyst.<sup>138</sup> Small amounts of 1,2-PG are formed as byproducts.

The formation of 1,2-PG involves initial isomerization of the glucose to fructose followed by RAC, affording two  $\text{C}_3$  units that are, inter alia, hydrogenated to mixtures of 1,2-PG and glycerol. When Cu–W or Pd–W based catalysts are used, 1,2-PG becomes the major product in yields up to 61%. Preliminary studies indicate that lignocellulose can also be used as the feedstock, but the lignin has to be first separated and conversion of the hemicellulose has to be optimized. Perhaps the process could be conducted in conjunction with Ionosolv fractionation of the lignocellulose (see earlier).

Acid catalyzed dehydration of the  $\text{C}_6$  and  $\text{C}_5$  sugars derived from lignocellulose affords 5-hydroxymethylfurfural (HMF)<sup>139</sup>

and furfural,<sup>139,140</sup> respectively. The latter is already an important commodity chemical, and the former has enormous potential<sup>141</sup> as a raw material for the production of chemicals, polymers, and biofuels. However, its cost-effective industrial production remains a significant challenge, mainly owing to its unstable nature toward conversion to levulinic acid under the acidic reaction conditions (see below). The conversion of D-glucose to HMF involves its initial isomerization to D-fructose, a reaction catalyzed by the enzyme, glucose isomerase, bases, and Lewis acids.<sup>142,143</sup> This is followed by the Brønsted acid catalyzed removal of three molecules of water (Figure 10). The

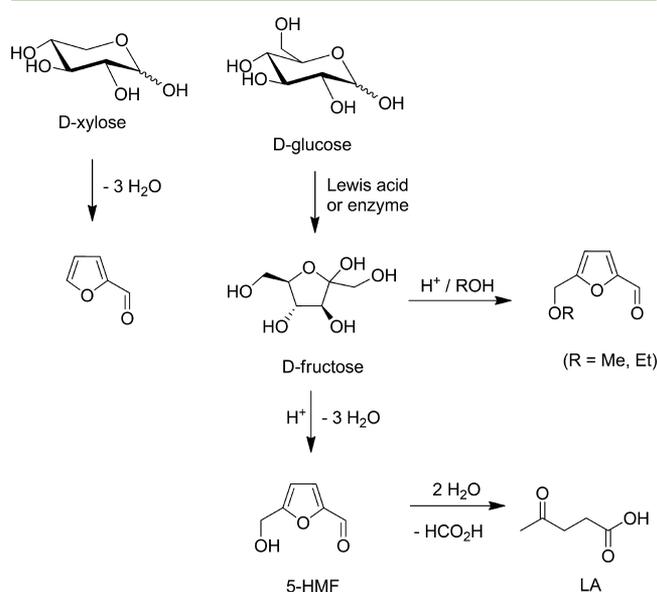


Figure 10. Acid catalyzed dehydration of C<sub>6</sub> and C<sub>5</sub> sugars to furans.

use of an aqueous/organic biphasic system such as water/ $\gamma$ -valerolactone (GVL) can improve yields by removing the sensitive HMF from the aqueous acidic phase.<sup>144</sup> Nonetheless, the maximum yields of HMF obtained from glucose are ca. 60% together with ca. 20% levulinic acid (LA) as a valuable byproduct. Alternatively, undesirable byproduct formation can be suppressed by conducting the reaction in the presence of an alcohol such as methanol or ethanol to afford more stable HMF ethers, although it is not clear that this leads to higher yields.<sup>145,146</sup>

HMF can be converted to 2,5-diformylfuran (DFF) and further to furan-2,5-dicarboxylic acid (FDCA) by aerobic oxidation<sup>147</sup> over supported noble metal catalysts<sup>148–152</sup> in aqueous media (Figure 11). Alternatively, the aerobic oxidation of aqueous HMF to FDCA in which all three individual oxidation steps were catalyzed by the same flavin-dependent HMF oxidase has also been reported.<sup>153</sup> FDCA is the key raw material for polyethylene furandicarboxylate (PEF), developed by Avantium as a biobased plastic to replace fossil-based polyethylene terephthalate (PET). PEF is being commercialized by Synvina, a joint venture of Avantium and BASF.<sup>154</sup>

A cradle-to-grave comparison<sup>155</sup> of corn-based PEF with fossil-based PET concluded that PEF production would reduce the nonrenewable energy use by 40–50% and the greenhouse gas (GHG) emissions by 45–55%. A further reduction of GHG emissions could be obtained by switching from corn to waste lignocellulose as the feedstock. Furthermore, PEF bottles have superior properties to PET bottles.<sup>156</sup> For example, they have

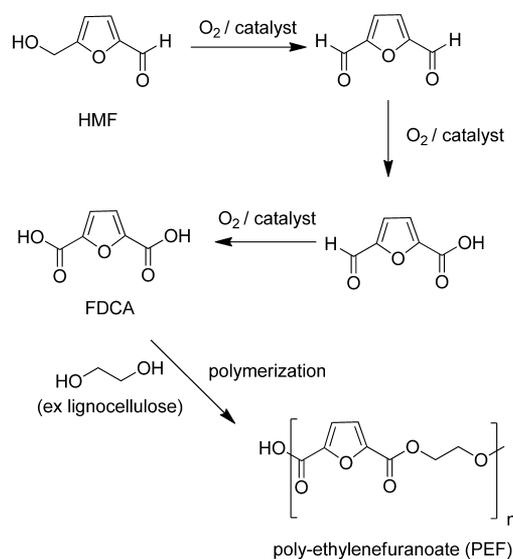


Figure 11. Oxidation of 5-HMF to FDCA and subsequent polymerization to PEF.

better permeability of oxygen, carbon dioxide, and water, providing for longer-lasting carbonated drinks. PEF also has a more attractive glass transition temperature and melting point and, hence, a better ability to withstand heat and be processed at lower temperatures. Both PET and PEF exhibit poor biodegradability but, on the other hand, this is not really a problem as they are easy to recycle.

Reaction of HMF with water, under acidic conditions, affords levulinic acid (LA) with elimination of formic acid (Figure 12).

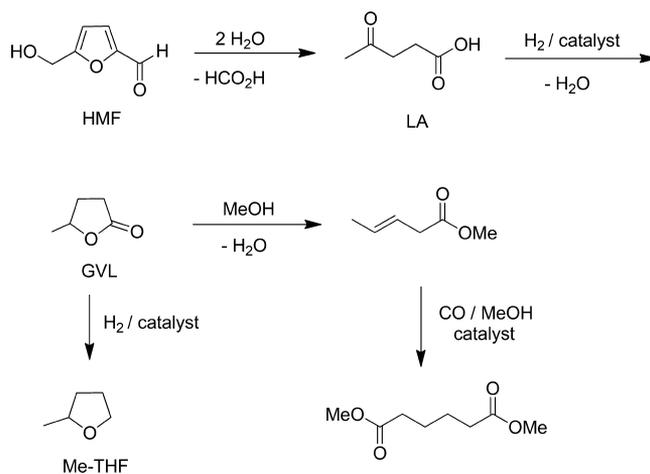
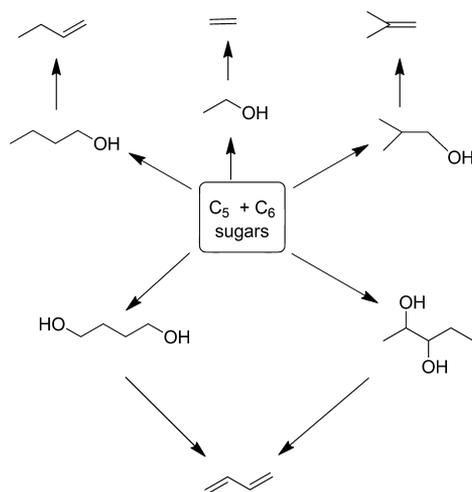


Figure 12. Conversion of HMF to LA and GVL.

LA and its esters are precursors of various polymers and the biobased solvent, methyl tetrahydrofuran. Hydrogenation of aqueous LA over a ruthenium catalyst in supercritical carbon dioxide affords  $\gamma$ -valerolactone (GVL) in 100% selectivity.<sup>157</sup> The LA partitions into the aqueous phase and the GVL into the carbon dioxide phase. Similarly, highly selective hydrogenation of LA to GVL was observed with a Ru/Sn-on-C catalyst.<sup>158</sup> Alternatively, the formic acid generated as the coproduct in the formation of LA from HMF can be used as the reductant.<sup>159</sup> GVL has been proposed as both a sustainable liquid fuel<sup>160</sup> and a platform chemical.<sup>161,162</sup> Ring opening with methanol followed by dehydration, for example, affords methyl

pentenoate, a potential precursor of dimethyl adipate and, hence, a nylon-6,6 intermediate.<sup>163</sup> Interestingly, GVL has even been used as a solvent for the direct mineral acid-catalyzed saccharification of lignocellulose through complete dissolution of the biomass, including the lignin.<sup>164</sup>

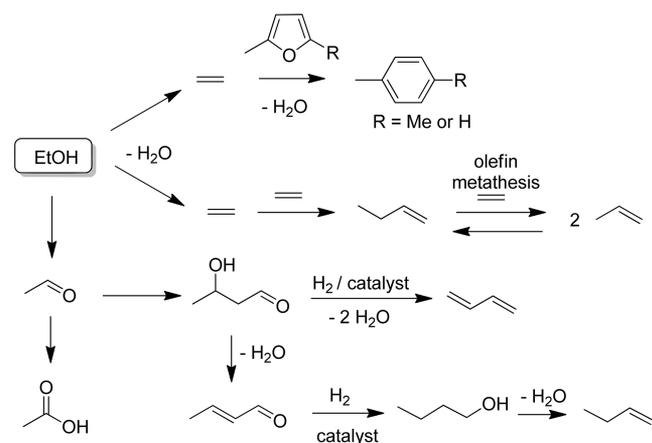
**Conversion of Carbohydrates to Hydrocarbons.** There are various chemo- and biocatalytic strategies for the conversion of C<sub>6</sub> and C<sub>5</sub> sugars to hydrocarbons, providing a direct link into existing petrochemical supply chains. One approach is to produce lower alcohols (ethanol, propanol, and butanols) and diols by fermentation and dehydrate them to the corresponding olefins (Figure 13). 1-Butanol and isobutanol



**Figure 13.** Carbohydrates to hydrocarbons via lower alcohols and diols.

can be produced efficiently by fermentation (see earlier) and dehydrated to 1-butene and isobutene, respectively. Similarly, 2,3-butane diol and 1,4-butane diol can also be produced by fermentation and can be dehydrated to butadiene.

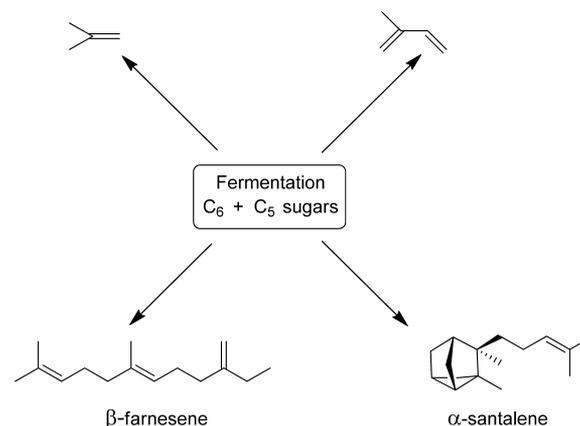
In Brazil, the bioethanol production (mainly from sucrose) substantially exceeds its consumption as a fuel and, hence, there is an incentive to find other large volume outlets. It can be readily converted to drop-in petroleum hydrocarbons such as ethylene, propylene, 1-butene, and butadiene (Figure 14),<sup>165,166</sup> thus completing the C<sub>2</sub>, C<sub>3</sub>, and C<sub>4</sub> triad that forms the basis of the petrochemical industry. Alternatively, ethanol can be



**Figure 14.** Conversion of bioethanol to commodity chemicals.

converted to propylene in 62% yield over a scandium modified indium oxide catalyst at 550 °C, but improvements are needed for commercial viability.<sup>167</sup> Ethylene can also be converted to toluene and *p*-xylene by Diels–Alder reaction and in situ dehydration with 2-methylfuran and 2,5-dimethylfuran, respectively.<sup>168,169</sup>

Alternatively, hydrocarbons can be produced directly by fermentation,<sup>170</sup> thereby circumventing the energy intensive separation of water miscible lower alcohols from the aqueous fermentation medium. Metabolic engineering is being used to re-engineer the isoprenoid pathway or fatty acid biosynthesis, in bacteria or yeast, to directly yield hydrocarbons (Figure 15).



**Figure 15.** Hydrocarbons directly from fermentation.

For example, direct production of isobutene by fermentation<sup>171</sup> has recently been commercialized by Global Bioenergies.<sup>172</sup> Isoprene can also be produced by fermentation.<sup>173,174</sup> Similarly, various terpenes such as the sesquiterpenes  $\beta$ -farnesene and santalene can be produced by fermentation with genetically modified yeast.<sup>175</sup> The former has applications ranging from jet fuel to cosmetic ingredients and has been commercialized by Amyris.<sup>176</sup>

A third approach to hydrocarbons from carbohydrates is to employ chemocatalytic conversion by so-called aqueous phase reforming (APR).<sup>177</sup> APR was originally developed as a method to produce renewable hydrogen by treating carbohydrate feedstocks with supported Pt or Pt–Re catalysts.<sup>178</sup> Subsequent combination with the dehydration of carbohydrates over solid acid catalysts affords a mixture of mainly C<sub>4</sub>–C<sub>6</sub> alkanes.<sup>179,180</sup> The latter can be further upgraded over heterogeneous noble metal catalysts and/or solid acids to mixtures of gasoline, diesel, and kerosene range alkanes or the mixture of benzene, toluene, and xylenes (BTX) that is produced in oil refineries. Alternatively, diesel and jet fuel range (C<sub>9</sub>–C<sub>12</sub>) alkanes<sup>181</sup> can be produced by the solid-base-catalyzed aldol condensation of furfural with 2-pentanone and 2-heptanone, followed by hydrodeoxygenation over Pd-on-solid acid catalysts. 2-Pentanone and 2-heptanone are available from base-catalyzed condensation of acetone-*n*-butanol fermentation products.

## ■ LIGNIN VALORIZATION: THE FINAL CHALLENGE

Lignin, the inevitable coproduct of the conversion of lignocellulosic biomass to fermentable sugars, comprises 20–30% by weight but accounts for 37% of the carbon content of lignocellulose. Hence, valorization of the lignin fraction represents a vital contribution to the cost-effective conversion of lignocellulose to biofuels and commodity chemicals. The

global pulp and paper industry alone produces more than 50 million tonnes per annum of lignin waste, most of which is used as a low-grade solid fuel to power the operation.<sup>182</sup> The development of biorefineries based on lignocellulosic waste as the feedstock is expected to generate several hundred million tonnes per annum of lignin waste, and less than 40% of this would be enough to power the operation.<sup>183</sup> It is not surprising, therefore, that the valorization of lignin is currently the focus of much attention.<sup>184</sup>

Lignin is an amorphous, highly branched aromatic polymer, the biosynthesis of which involves the copolymerization of three primary monolignols: *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol. Lignins have structures that are random with regard to the degree of polymerization, branching, and monomer composition. Moreover, the fact that the structure is dependent on both the source of the lignocellulose and the method of pretreatment used presents an extra challenge. These problems can be circumvented by conversion of the lignin to syn gas (mixtures of carbon monoxide and hydrogen) in a process that is analogous to coal gasification.<sup>185</sup> The syn gas can be further converted to commodity chemicals or biofuels using established technologies. In the earlier described Zechem process for bioethanol, the syn gas is used as a source of the hydrogen needed to hydrogenate the initially formed ethyl acetate.

Alternatively, the lignin can be converted to commodity aromatic chemicals via chemo- and/or biocatalytic processes, the effectiveness of which can be improved by appropriate bioengineering *in vivo* to afford lignins with more readily cleavable linkages.<sup>183,184</sup> Lignin is an obvious source of aromatic hydrocarbons or phenols that can be produced by appropriate catalytic (partial) hydrodeoxygenation. Yet another alternative is to convert the lignin directly to a biomaterial exemplified by the production of high-value carbon fiber from Organosolv lignins.<sup>186</sup>

## METRICS OF SUSTAINABLE PRODUCTION OF CHEMICALS FROM RENEWABLE BIOMASS

To compare lignocellulose-based with fossil-based routes to commodity chemicals, reliable sustainability metrics are essential.<sup>187</sup> A variety of metrics has been used to measure the sustainability of renewable transportation fuels,<sup>188</sup> but much less attention has been devoted to assessing that of biobased commodity chemicals. First, the suitability of different waste lignocellulosic feedstocks has to be compared. To this end, Girio and coworkers<sup>189</sup> developed a Biotechnological Valorization Potential Indicator (BVPI) based on biological, physicochemical, technological, economic, and geographical factors. Using the BVPI, several lignocellulosic waste streams from the Portuguese agroindustrial sector, e.g. rice husks and tomato pomace, with high valorization potential were identified.

Patel and coworkers,<sup>190</sup> building on earlier work of Sugiyama and coworkers,<sup>191</sup> described a methodology for relatively quick, preliminary assessment of the sustainability of processes in the laboratory phase based on (i) ratio of raw materials costs to value of the product and coproduct(s), (ii) environmental impact of raw materials, (iii) costs and environmental impact of the conversion, (iv) environmental, health, and safety (EHS) index, and (v) risk assessment (e.g., feedstock availability and supply).

The method was used to compare biobased vs naphtha-based butadiene and was later extended to other early stage biobased

vs petroleum-based products.<sup>192,193</sup> A more comprehensive study of biobased vs naphtha-based butadiene, using a simplified life cycle approach based on five indicators (cumulative energy demand, carbon footprint, water usage, and an economic index) was subsequently reported by Cavani and coworkers.<sup>194</sup> They concluded that the direct conversion of (bio)ethanol to butadiene has a lower environmental burden than the naphtha-based route and that future efforts should be focused on this route.

In another study, four criteria were used for a relatively quick cradle to gate comparison of fossil- vs biobased routes to commodity chemicals:<sup>195</sup> (i) material efficiency = mass of useful products/mass of useful products + waste, (ii) energy efficiency = caloric value of useful products/caloric value of fossil and renewable energy inputs, (iii) land use per tonne product, (iv) raw material and capital costs.

Seven commodity chemicals were chosen for the study: lactic acid, acrylonitrile, 1-butanol, 1,2-propane diol, succinic acid, isoprene, and methionine. It was concluded that some chemicals, e.g. lactic acid, can already be produced from biomass with less energy input and even at lower cost compared to established petrochemical routes, while others are currently more expensive and less energy efficient. For the latter, such concise metrics are useful in identifying bottlenecks and providing a basis for planning further optimization. When the relevant processes have been demonstrated at an industrial scale, full-blown sustainability assessments can be used to compare different process strategies.<sup>196</sup>

Horvath and coworkers<sup>197</sup> recently described a novel set of metrics for evaluating the sustainability of biomass-based carbon chemicals that address the two key issues of sustainability: resource depletion and the fate of waste. To be sustainable, a technology must fulfill two conditions: (i) natural resources should not be consumed at rates that are higher than the rate that they can be replaced naturally and (ii) wastes should not be generated faster than the rate of their remediation.<sup>197,198</sup> The metrics are based on the ethanol equivalent (EE) as the common currency for assessing the sustainability of biomass-based routes to fuels and chemicals.<sup>199</sup> An EE is defined as the mass of ethanol required to deliver the equivalent amount of energy from a given feedstock using energy equivalency or produce the equivalent mass of a carbon-based chemical using molar equivalency. The reference technology for calculation of the EE is first generation corn-based ethanol fermentation practiced in the United States in 2008. The measurable effectiveness of the reference technology is defined by its ethanol return of ethanol, ERoE,<sup>200</sup> which is 2.3, indicating that 1 unit is required to produce 2.3 units. The overall stoichiometry from carbon dioxide to ethanol via photosynthesis and fermentation is shown in Figure 16.

The authors defined a sustainability indicator ( $SUS_{ind}$ ) comprising a sustainability value of resource replacement ( $SV_{rep}$ ) and a sustainability value of the fate of waste ( $SV_{waste}$ ) according to the equation:

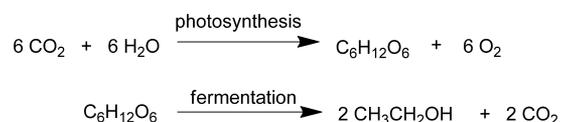


Figure 16. Stoichiometry of carbon dioxide to ethanol via glucose.

**Table 1. Amount of Bioethanol Required to Produce Six Basic Petrochemicals in the United States**

chemical	ethene	propene	toluene	<i>p</i> -xylene	styrene	ethene oxide	∑ chemicals
production <sup>a</sup> (mt)	24.7	13.3	5.0	4.8	4.4	2.5	54.7
EE <sub>necessary</sub> <sup>b</sup> (mt)	42.2	42.6	13.8	42.6	6.3	2.8	150.3

<sup>a</sup>Amount in million tonnes (mt) produced in 2014. <sup>b</sup>Amount of ethanol required (mt).

$$SUS_{ind} = \frac{SV_{rep} \times SV_{waste}}{SV_{rep} + SV_{waste}}$$

$SV_{rep}$  is determined by how much of the necessary resources,  $EE_{\text{necessary resource}}$  required in a given time can be replaced in the given time with the available biomass-based resources,  $EE_{\text{available resource}}$  using the best available technology. The  $EE_{\text{available resource}}$  is the total amount of bioethanol available on the market and has to be multiplied by  $2.3/(1 + 2.3) = 0.7$  to achieve sustainable production as 1 unit is required to produce 2.3 units of bioethanol.

$SV_{waste}$  is equal to one when the continuously generated waste,  $EE_{\text{generated waste}}$  is equal to the continuously treated waste in the same time frame and, hence, no waste is released to the environment. The authors included incineration, chemical and biological treatment, and disposal to official waste storage sites including landfill; although, in the general context of sustainability and the circular economy, waste disposal via incineration or landfill should be rigorously avoided. Indeed, the authors noted that “prevention of persistent waste formation by the development of efficient processes or integrated waste valorization are the preferred pathways to reach sustainability. Sustainability ensues when all resources are replaced ( $SV_{rep} = 1$ ) and all waste can be recycled or the remaining parts treated within a reasonable time frame.  $SUS_{ind} = 0.5$  is the minimum required for sustainability.

Previous calculations of EEs revealed<sup>199</sup> that replacement of the  $387 \times 10^6$  tons of gasoline used in the United States in 2008 by bioethanol is not a viable proposition. In contrast, the conversion of biomass to basic petrochemicals such as ethylene, propylene, and xylenes could be a sustainable future option, especially with second generation bioethanol from waste lignocellulose. Hence, the  $SUS_{ind}$  values of six basic petrochemicals, ethylene, propylene, toluene, *p*-xylene, styrene, and ethylene oxide, were determined assuming that they are produced from bioethanol by known reactions and processes and based its availability in 2008 and 2014 in the United States.

The production volumes of these 6 chemicals in the United States in 2008 and 2014 amounted to ca. 53 and 55 million tonnes, respectively. The sustainability analysis showed that to produce these amounts, ca. 150 million tonnes of bioethanol (Table 1) would be required which is substantially more than the total bioethanol production of 28 and 43 million tonnes in 2008 and 2014, respectively. The  $SUS_{ind}$  values of these chemicals were between 0.1 and 0.43 indicating that the global demand of none of these chemicals could be met with bioethanol-based production. This led the authors to suggest that biobased carbon products should be labeled “sustainable” only when the necessary land is available to produce the required bioethanol.

The calculations are all based on the state-of-the-art technology for producing bioethanol from corn starch, that requires 1 kg of additional bioethanol to produce 2.3 kgs of bioethanol, and the best available technology for converting ethanol to the required product. Production of the bioethanol from second generation lignocellulose in agricultural and

forestry residues and food supply chain wastes could significantly improve this scenario. It could be similarly improved by developing more effective technologies for converting ethanol to the various petrochemicals or by producing them via alternative pathways from lignocellulosic biomass, as discussed in the preceding sections.

## CONCLUDING REMARKS AND FUTURE PROSPECTS

A bioeconomy based on renewable biomass, primarily in the form of waste lignocellulose, is playing an important role in the transition from a linear take–make–dispose economy to a sustainable circular economy and will contribute significantly to climate change mitigation. However, this can be realized only if cost-effective, environmentally acceptable (sustainable) processes are developed for performing the conversion of lignocellulose to liquid fuels, commodity chemicals, and biomaterials.

Much progress has been made in the past decade in the pretreatment and subsequent hydrolysis of lignocellulose into its constituent sugars and lignin. Similarly, significant improvements have been achieved in the chemo- and biocatalytic conversion of the sugars to liquid transportation fuels and commodity chemicals. The latter is particularly important because biomass is the only source of renewable carbon chemicals. To be cost-effective, however, all components of the lignocellulose must be valorized: the cellulose, hemicellulose, and lignin. Although much progress has been made in lignin valorization, there is still a definite need for cost-effective conversion of the extremely large volumes of lignin to commodity chemicals and/or biomaterials. Progress has also been made in developing suitable sustainability metrics for comparing processes for commodity chemicals from renewable biomass versus fossil resources.

In short, we believe that the successful future development of cost-effective processes for the conversion of carbohydrates to commodity chemicals in integrated biorefineries will provide the basis for an alternative, more sustainable chemical industry.

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### Notes

The author declares no competing financial interest.

## Biography



Roger Sheldon ([www.sheldon.nl](http://www.sheldon.nl)) is a recognized authority on Green Chemistry and widely known for developing the E factor concept for assessing the environmental impact of chemical processes. He is currently Distinguished Professor of Biocatalysis Engineering at the University of the Witwatersrand (SA). He authored several books on catalysis, >460 papers, and 55 granted patents. He was Co-Chair of the 1999 Gordon Research Conference on Green Chemistry. Among other awards, he was a corecipient of a Presidential Green Chemistry Challenge Award in 2006 and received the RSC 2010 Green Chemistry Award and the Biocat 2010 lifetime achievement award for his important and lasting contributions to biocatalysis. He was elected a Fellow of the Royal Society in 2015. He has a Ph.D. (organic chemistry) from Leicester University (UK) and was Professor at Delft University (NL) (1991–2007), CEO of CLEA Technologies (2006–2015), and VP R&D at DSM-Andeno (1980–1990) and with Shell Research Amsterdam (1969–1980).

### ■ DEDICATION

The author dedicates this manuscript to Prof. Istvan Horvath, visionary, original thinker, and pioneer in green chemistry, sustainability, and the biobased economy, on the occasion of his 65th birthday.

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