Towards Lignin-Derived Chemicals Using Atom-Efficient Catalytic Routes

Putla Sudarsanam,[1,2,*] Dieter Ruijten,[1] Yuhe Liao,[1] Tom Renders,[1] Steven-Friso Koelewijn,[1]
and Bert F. Sels[1,*]

Lignin is a potential non-fossil resource of diverse functionalized phenolic units. The most important lignin-derived monomers are 4-alkylphenols, 4-hydroxybenzaldehydes, 4-hydroxybenzoic acids, and 4-hydroxycinnamic acids/esters. Efficient transformation of lignin and/or its monomers into valuable aromatics and their derivatives is crucial, not only for a sustainable lignocellulose biorefinery, but also to reduce our dependence on fossil feedstocks. This review provides a concise account of the recent advances in lignocellulose fractionation/lignin depolymerization processes towards lignin-derived monomers. Subsequently, numerous potential atom-efficient catalytic routes for upgrading lignin monomers into drop-in chemicals and new polymer building blocks are discussed.

Highlights

Efficient valorization of lignin into fuels and chemicals will boost the lignocellulose biorefinery industry and reduce our dependence on fossil fuel feedstocks.

Selective cleavage/conversion of lignin into specific monomers is the utmost goal in current biorefinery research; this can be achieved by controlling the catalyst properties and reaction conditions.

Atom-efficient catalytic routes can play a significant role in converting lignin monomers into desirable products.

Lignocellulose fractionation methodology, product separation technology, and process mass efficiency are also important for lignin biorefineries.

Lignin Valorization, Atom Efficiency, and Catalysis

Lignocellulosic biomass is considered as a versatile, non-fossil carbon feedstock for synthesizing a variety of renewable fuels and functionalized chemicals. Particularly, lignin, a key component of lignocellulosic biomass, is the largest source of renewable aromatics on Earth (Figure 1) that acts as an adhesive for cellulose and hemicellulose, solidifying the cell walls and making them more rigid and hydrophobic [1–3]. Lignocellulose processing usually provides carbohydrate- and lignin-derived fractions. Various thermochemical and (bio)catalytic methods have been developed for converting carbohydrates to high value chemicals, fuels, and materials [4,5]. By contrast, more than 95% of the lignin obtained from paper and biorefinery industries is burned directly as a low-value fuel [6]. However, efficient valorization of lignin into aromatics or their derivatives can boost the lignocellulose biorefinery, which is a primary topic in current biorefinery research.

Reducing waste generation by improving yields of desirable product(s) is crucial for the development of any chemical process. Both atom efficiency (also known as atom economy) and E-factor are often used to evaluate the extent of waste production (Box 1) [7,8]. Accurate E-factor determination is difficult due to the complex estimation of waste generated from solvents and reagents used during reaction and purification and, in most cases, these data are not available. Thus, this review uses the concept of atom efficiency to evaluate and compare strategies for upgrading lignin and its monomers into alternative bisphenols, phenol, alkenes, alkylated cyclohexanols, and styrene derivatives. Before this, an overview of both one-pot lignocellulose fractionation and lignin depolymerization processes for producing various lignin monomers is provided.

Common Lignin Monomers

Methoxylated phenols (e.g., *para*-substituted *n*-propanol-, *n*-propyl-, propylene-, and ethyl-guaiacols/syringols), phenolic aldehydes and acids (e.g., vanillin/vanillic acid and syringaldehyde/syringic acid), and hydroxycinnamic acid derivatives (*p*-coumaric/ferulic

[1] Center for Sustainable Catalysis and Engineering, Faculty of Bioscience Engineering, KU Leuven, Celestijnenlaan 200F, 3001 Heverlee, Belgium
[2] Catalysis and Inorganic Chemistry Division, CSIR-National Chemical Laboratory, Dr Homi Bhabha Road, Pashan, Pune 411008, India

*Correspondence:
s.putla@ncl.res.in (P. Sudarsanam) and
bert.sels@kuleuven.be (B.F. Sels).

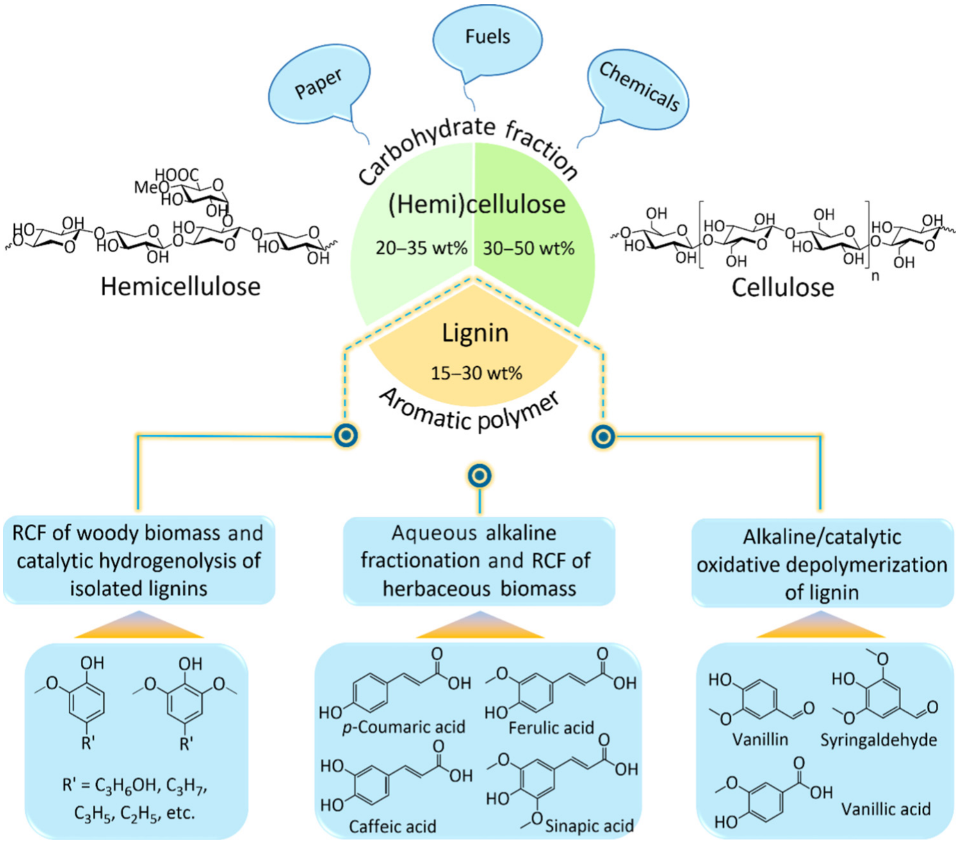

Figure 1. Lignocellulose Processing towards Lignin Platform Molecules. Cellulose is a linear polymer of glucose. Hemicellulose is a branched polymer of C5 (xylose and arabinose) and C6 carbohydrates (galactose, glucose, and mannose). The plant wall structure and a model chemical structure of lignin are provided in Figure 3. Abbreviation: RCF, reductive catalytic fractionation.

Glossary

Catalyst basket: used for holding a solid catalyst during the reaction in an autoclave reactor so that efficient catalyst's recovery/reusability can be achieved when one of the products is a solid (here: pulp).

Klason lignin: an insoluble residue obtained after the two-step acid hydrolysis of lignocellulose with 72 wt% H_2SO_4 at room temperature ca. 20°C as well as with 3–4 wt% H_2SO_4 for a few hours at high temperatures ca. 120°C.

Kraft lignin: obtained from kraft pulping process (also known as sulfate pulping process) that involves fractionation of lignocellulose into cellulose, hemicellulose, and lignin in the presence of a hot mixture of aqueous NaOH and Na_2S solution.

Organosolv processing: in the paper industry, organosolv is a pulping process that uses an organic solvent to solubilize lignin and hemicellulose, giving pure cellulose fibers from woody lignocellulose.

Soda pulping: a chemical process for producing pulp from woody lignocellulose using NaOH solution. In this process, anthraquinone is used as a pulping additive that will help to prevent carbohydrate degradation so that it can be efficiently converted into useful molecules and fuels like glucose and bioethanol.

Transalkylation: a chemical reaction involving the transfer of simple alkyl groups, such as methyl or ethyl from preferably one organic compound to another, especially between benzene rings, to produce valuable chemicals.

acid/sinapic acid and their esters) are commonly obtained lignin monomers (Figure 1) [2,9]. These accessible monomers exhibit potential in applications for aromatic chemicals and polymer building blocks, directing the development of economically viable processes for their synthesis from lignocellulose or isolated lignins.

Methoxylated 4-Alkylphenols

Reductive Catalytic Fractionation

Reductive catalytic fractionation (RCF) is a promising lignin-first valorization process that is able to convert lignocellulose to lignin oil and a valorizable solid (hemi)cellulose pulp [10,11]. RCF solvolytically extracts the lignin fraction from lignocellulose, followed by hydroprocessing using a metal-based redox catalyst. Stabilizing lignin-derived intermediates and reductive lignin depolymerization are the key steps occurring during hydroprocessing. These steps significantly improve the yield of lignin monomers, such as 4-*n*-propanolguaiacol (PohG) and 4-*n*-propylguaiacol (PG) and their corresponding syringols (PohS and PS). In addition, considerable amounts of phenolic dimers and oligomers are formed.

Numerous metal-based catalysts, including noble metals (Ru and Pd) [12], non-noble metals/metal oxides (Ni [13–16] and Mo [17,18]), bimetallic (NiFe [19] and PdZn [20]), and Raney Ni [21] are used for RCF of woody lignocellulose. The metal's nature can greatly influence the yield of lignin monomers. For instance, a Ru/carbon catalyst was found to show a high selectivity to PG/PS products with 50 wt% total yield of lignin monomers in RCF of birch wood in methanol [12]. At similar reaction conditions, a Pd/carbon catalyst is selective towards PohG/PohS products, which is likely due to lower activity of Pd/carbon for hydrogenolysis of C–OH in the propanol chain. However, Zn addition led to an improved selectivity of Pd/carbon towards PG/PS (54 wt% total yield of monomers) in RCF of poplar wood, which is the result of the synergetic Pd–Zn interactions [20]. Similarly, combining Ni and Fe with 1:1 atom ratio on a carbon support showed a high selectivity (88%) to PG/PS (39.5 wt% total yield of monomers) in RCF of birch wood [19]. This is ascribed to the optimal Lewis acidity of iron oxide, which promotes deoxygenation of lignin-derived compounds towards PG/PS monomers. Besides, suitable pore size and BET surface area (ZIF-8 support) are important to achieve a high selectivity to PG/PS monomers, as evidenced in the case of Ni@ZIF-8 catalysts [13], whereas an Al_2O_3-supported Ni catalyst is selective for PohG/PohS monomers [15]. Moreover, in the case of Ni@ZIF-8-catalyzed RCF of eucalyptus sawdust, relatively mild reaction conditions (220°C and 8 h) afforded 44 wt% total yield of monomers with 71% PohG selectivity, while harsh conditions (260°C and 12 h) gave PG as the major product (23 wt% yield with 63% selectivity). The solvent plays a crucial role in this RCF process: (i) detaching the lignin from the carbohydrates, (ii) cleaving the weak ether and ester bonds in lignin, and (iii) reducing the cellulose degradation [22,23]. It is also important to extract and solubilize the lignin fragments that are formed and to allow them to diffuse to the catalytic active site for further conversion via hydrogenation and hydrogenolysis.

Depending on lignocellulose feedstock and reaction conditions, 4-propenyl- and 4-ethylguaiacols/syringols could also be obtained in the RCF process. For instance, considerable yields of 4-propenylguaiacols/syringols were obtained in the case of Pd/carbon- [24] and core-shell [25] Ni-Al_2O_3/carbon-catalyzed transfer hydrogenolysis of woody lignocellulose using a mixture of formic acid, ethanol, and water. Herein, formic acid acts as a cocatalyst to enhance delignification by solvolysis as well as a hydrogen source to depolymerize lignin towards desirable monomers [25]. Note that PohG/PohS are the major monomers obtained in cases of molecular hydrogen with the similar types of supported Pd [12] and Ni catalysts [15]. It indicates that hydrogen source plays a key role in tuning the selectivity of lignin monomers during

Box 1. Atom Economy, E-Factor, and Catalysis

The atom efficiency of a chemical reaction is defined as the ratio of molar mass of desirable product(s) to the total molar mass of all reactants including stoichiometric reagents (Equation I). High atom efficiency means that (theoretically) all atoms of the reactants are incorporated in the targeted products, with no waste products being obtained. B.M. Trost coined the concept of atom efficiency in 1991, which was later (1998) included in the 'Green Chemistry Principles'. E-factor indicates the waste produced during the entire chemical process (Equation II). An important difference between these seemingly similar concepts is that atom efficiency does not consider waste generation from auxiliary reagents (e.g., solvents), which is included in the E-factor. Thus, atom efficiency determines the 'greenness' of an intrinsic chemical reaction, while E-factor represents the waste produced in the entire chemical process.

$$\text{Atom efficiency } (\%) = \frac{\text{Molar mass of desirable product(s)}}{\text{Molar mass of all reactants}} \times 100 \qquad [\mathrm{I}]$$

$$\text{E–factor} = \frac{\text{Mass of waste}}{\text{Mass of desirable product}} \qquad [\mathrm{II}]$$

Using stoichiometric reagents is the primary reason for low atom efficiency in organic synthesis. For instance, ketone reduction with stoichiometric $NaBH_4$ (reductant) generates two waste products, namely NaOH and BH_3 (Figure I). A promising solution to tackle these concerns is applying greener catalytic alternatives together with mild reagents, such as hydrogen. Using catalysts instead of stoichiometric reagents can control waste product formation because catalysts are used in relatively small concentrations and they are not consumed in the reaction. Therefore, catalysts are not considered in the equation for atom efficiency (Equation I). Thus, catalytic chemical reactions offer better atom efficiency than stoichiometric-based methods. Optimization of catalyst properties and reaction condition plays a crucial role in achieving higher product yields from atom-efficient reactions.

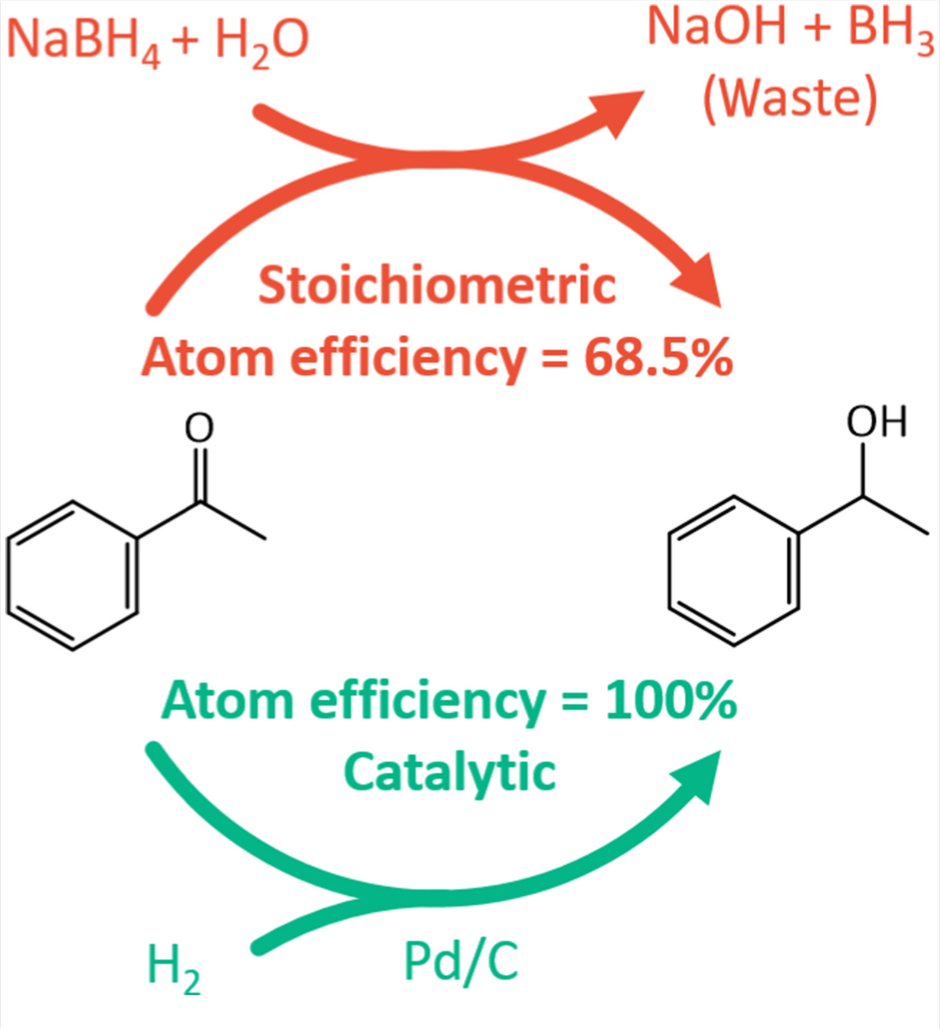

Figure I. Example of Stoichiometric- and Catalytic-Based Reactions with Low and High Atom Economy, Respectively.

the RCF process. Bark, a waste material (outer layer) of woody biomass, can be converted into fuel grade chemicals and lignin-derived monomers [26,27]. In the case of bark RCF processes, lignin was converted into 4-ethylguaiacol (12 wt% of lignin) with 90% selectivity over a Pd/carbon catalyst ($MeOH:H_2O$ = 2:1 v/v). Here, carbohydrates served as an inherent hydrogen donor under slightly alkaline conditions [27]. RCF of bark in MeOH not only depolymerizes lignin, but also enables depolymerization of suberin, giving and isolating decent amounts of multifunctional fatty acid methyl esters [28].

Catalyst recovery from solid carbohydrate pulp is a major concern in batch-scale RCF [29]. To circumvent this problem, Beckham and colleagues [30,31] and Samec and colleagues [32] developed promising flow-through strategies, which involve the solvolysis step and the catalytic hydroprocessing step either simultaneously in a single bed or separately in a dual-bed reactor. Based on metal catalysts and process conditions, good yields of 4-*n*-propanol-, 4-*n*-propyl-, and 4-propenyl-substituted guaiacols/syringols were obtained. Without using the hydroprocessing step, a considerable yield of lignin monomers (21 wt% yield) was achieved, but it is increased to 37 wt% yield when the solvolysis step is coupled with the hydroprocessing step in the presence of a Pd/carbon catalyst [32]. In addition to the above benefits, flow processing provides more insights into the mechanistic and kinetic aspects of the delignification step. Moreover, solid residue (rich in cellulose) contamination by the catalyst particles can be prevented during a flow RCF process. Hence, cellulose can be efficiently upgraded to value-added glucose or ethanol using an enzymatic hydrolysis or fermentation, respectively. A key concern from an industrial point of view is that flow-through RCF is not a fully continuous process as the solvolysis step and catalytic hydroprocessing step are carried out separately at different flow-bed reactors. Hence, developing a fully continuous process would be more desirable for viable RCF of lignocellulose. Besides, application of magnetically separable catalysts [21] and **catalyst basket** (see Glossary) [15] showed promising effects in RCF of woody biomass in terms of catalyst recovery/reusability and lignin monomer yields. More hydrothermally stable solid catalysts are still needed because biomass naturally has a high moisture content, causing leaching of the catalytically active species. Another catalyst deactivation route that requires more investigation is coke fouling. Lignin fragments and their ability to condense indeed may cover the active sites at the surface of the catalyst.

Acetal Formation-Assisted Delignification Followed by Catalytic Hydrogenolysis

In traditional delignification processes, lignin recondensation (i.e., formation of stable C–C bonds) is a major concern. It lowers the yields of lignin monomers from the subsequent catalytic hydrogenolysis step. Luterbacher and colleagues [33,34] and Barta and colleagues [35] circumvented this recondensation with formation of acetal adducts. They added a simple protective agent, such as ethylene glycol and aldehydes (e.g., formaldehyde, acetaldehyde, or propionaldehyde), during **organosolv processing** of lignocellulose under acidic conditions. The protective agent can react with α,γ-diol group of lignin to form relatively stable acetal, preventing lignin repolymerization (by inhibiting formation of reactive carbenium species). The stabilized intermediate can be hydrogenolyzed into methoxylated 4-alkylphenols with high yield (41.6–45.9% from birch wood) [35]. Utilizing acidic reagents and formaldehyde allowed considerable yields of xylose/furfural to be obtained from hemicellulose [33]. However, most of the cellulose was left as a solid residue, which can be converted into glucose using an enzymatic hydrolysis reaction. Inhibiting formation of a complex product mixture with six to ten types of lignin monomers, due to undesirable alkylation of aromatic rings, is challenging in catalytic hydrogenolysis of formaldehyde-protected lignin. For this, an alternative process using acetaldehyde and propionaldehyde as protective agents was developed [34]. Both protective agents efficiently inhibit the formation of alkylated aromatic monomers, thus a high selectivity to 4-*n*-propanolsyringol (80% selectivity at near-theoretical yields based on **Klason lignin**) was achieved over a Pd/carbon catalyst [34]. Similar results (78% selectivity to 4-*n*-propanolsyringol) were also obtained over a non-noble Ni/carbon catalyst. Deposition of aldehyde residue on cellulose was observed, demanding additional steps for carbohydrate purification. More studies must be done towards understanding the effect of protective agents on the characteristics of carbohydrates, providing useful information for efficient valorization of carbohydrates.

Methoxylated 4-Hydroxybenzaldehydes and 4-Hydroxybenzoic Acids

Vanillin and vanillic acid are very important chemicals for polymer, pharmaceutical, and agrochemical industries [36–38]. Hence, annual vanillin demand is growing at a rate of 2–4% in Europe/USA and it reached almost 10% in China, with the current global demand of around 20 kilotons per year [39,40]. However, only 15% of vanillin is produced by oxidation of **kraft lignin** and lignosulfonate, while the remaining 85% of vanillin is obtained from petroleum-based chemicals (i.e., guaiacol). Therefore, there is an urgent need to develop efficient methods for producing more vanillin from lignin.

Oxidative depolymerization of lignin with or without a transition metal-based catalyst in alkaline medium, or with a liquid acid catalyst, are used for vanillin/vanillic acid production [41]. These processes also give syringaldehyde, a key chemical for synthesizing trimethoprim, trimethoxybenzaldehyde, and anthraquinones [42]. Molecular oxygen, hydrogen peroxide, and nitrobenzene are commonly used oxidants for oxidative lignin depolymerization [43], with an obvious preference for oxygen (air). Since lignin degradation is a major concern in the presence of liquid acidic catalysts (diluted inorganic acids or concentrated/pure acetic acid), this section focused only on alkaline/catalytic oxidative depolymerization of lignin. Commercially, vanillin is produced via alkaline oxidation of lignosulfonate in air at pH = 14, 100–200°C, and 10 bar O_2/N_2 [44]. Alternatively, oxidant-free production of vanillin/vanillic acid (via lignosulfonate hydrolysis) is also possible above 100°C [44]. Adding air or oxygen-rich air led to a twofold increase of vanillin/vanillic acid yield. A linear correlation between lignin β-O-4 linkages and vanillin yield is observed in alkaline (2 M NaOH) oxidation of various lignins using nitrobenzene as the oxidant [45]. Interestingly, *p*-coumaric acid was the primary product from ammonia-extracted corn stover lignin in alkaline medium under oxygen-deficient conditions, while considerable yields of vanillin/vanillic acid were obtained with molecular oxygen [46]. Higher NaOH concentration and reaction temperatures are also vital for producing vanillin/syringaldehyde and their respective acids from poplar lignin [43]. Comparison studies revealed that nitrobenzene oxidation process gave higher yields of vanillin than the alkaline aerobic oxidation processes. Surprisingly, adding H_2O_2 to the reaction mixture led to decreased vanillin production over supported Nb catalysts, caused by further oxidation of vanillin [47].

Circumventing hazardous alkaline conditions is possible during catalytic lignin oxidation into aromatic aldehydes/acids (vanillin/vanillic acid and syringaldehyde), as proven for $ReO_x/\gamma\text{–}Al_2O_3$ [39] and Co–Fe mixed oxide catalysts [48]. The synergistic interactions of metal–metal or metal–metal oxide provide abundant redox species that can promote lignin oxidation even at neutral pH. Microwave heating can help to lower the activation energies of reactions more readily and convert polar solvents/reagents like H_2O and H_2O_2 into more free radicals. These radical species play a crucial role in lignin oxidation to vanillin/vanillic acid and syringaldehyde over $CuSO_4/H_2O_2$ [49] and La-modified SBA-15/H_2O_2 [50], as well as in oxidant-free cleavage of kraft lignin over Fe_2O_3, $LaFeO_3$, ZrO_2, and zeolite-Y hydrogen (ZYH) catalysts in DMSO/water medium [36]. For efficient catalyst recovery, a magnetically recyclable TEMPO-based nanocatalyst was developed for oxidative depolymerization of kraft lignin to vanillin with sodium hypochlorite as oxidant [51]. The amine groups anchored along with TEMPO on magnetic nanoparticles were hypothesized

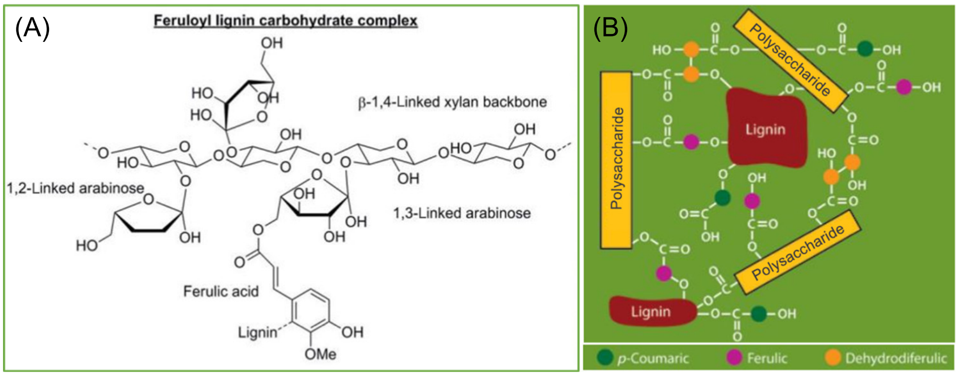

Figure 2. Ferulic Acid Linkage in a Grass Lignin–Carbohydrate Complex (A) [58] and Lignocellulose Network Mediated by Ferulic Acid (B) [57]. Here, polysaccharide (B) means hemicellulose.

to abstract protons from oxidized lignin, enabling the reaction to occur at neutral pH. To overcome batch-scale related concerns, a continuous-flow strategy was developed for the alkaline depolymerization of kraft lignin into aromatics, mainly vanillin and vanillic acid [52]. Most research used isolated lignin as the feedstock to produce vanillin and syringaldehyde, but quite lower yields were obtained due to the more recalcitrant structure of isolated lignin. To avoid the condensation of lignin during isolation, Wang and colleagues [53] and Beckham and colleagues [43] investigated oxidation of native lignin in biomass to vanillin and syringaldehyde under alkaline conditions. The yield of vanillin reached 21% from pine wood and 8.2% of vanillin and 20.4% of syringaldehyde were obtained from eucalyptus. However, hemicellulose and cellulose are also converted during this step. Research revealed that along with oxygen pressure and temperature, the stirring regime plays a crucial role during combined production of vanillin and remaining solid cellulose from wood [53]. Similar to RCF, this process was termed oxidative catalytic fractionation.

(Methoxylated) 4-Hydroxycinnamic Acid Derivatives

Herbaceous biomass (e.g., switchgrass, corn stover, wheat straw, and bagasse) contains functionalized lignin-based aromatic acids, such as ferulic acid and *p*-coumaric acid attached to the arabinose units of hemicellulose via ester linkages (Figure 2) [54–58]. Ferulic acid/*p*-coumaric acid and their derivatives exhibit potential applications for polymer and pharmaceutical industries [59]. Besides, they act as antioxidant, anti-inflammatory, and anticarcinogenic agents. Herbaceous biomass processing, particularly under aqueous alkaline conditions, gives considerable yields of ferulic acid/*p*-coumaric acid [60,61]. The aqueous alkaline pretreatment using NaOH or $Ca(OH)_2$ is similar to **soda pulping**, but uses quite mild conditions (e.g., 2–4 M base solution and 80–120°C). This pretreatment promotes hydrolysis of crosslinked ester bonds between lignin and hemicellulose, thus extracting about 55 wt% of the original lignin into the liquor [62,63]. This liquor mainly contains ferulic acid/*p*-coumaric acid, with vanillic acid constituting up to 27 wt% of the original lignin. The liquor also contains

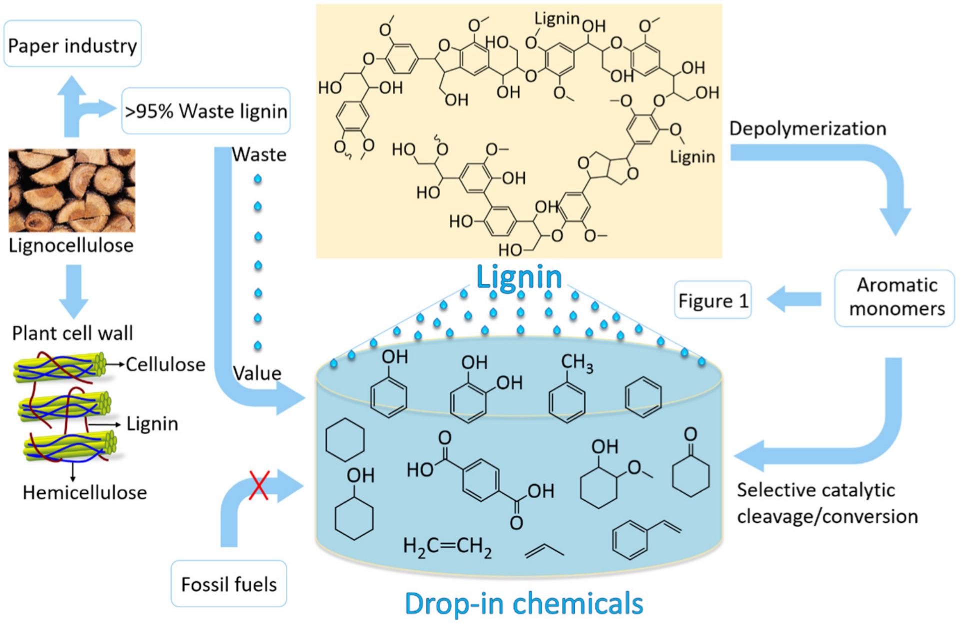

Figure 3. Schematic Representation of Lignin Conversion into Drop-in Chemicals. Drop-in chemicals are the biomass-derived chemicals identical to fossil-derived chemicals. Hence, they can be used directly in the petrochemical industry, while using the same technology and machinery.

lignin oligomers and carbohydrate-derived lactic acid/glycolic acid. By washing the residual mixture with water, the remaining lignin fraction (35 wt%) can be recovered.

Other strategies based on catalytic redox routes were also used for producing ferulic acid/*p*-coumaric acid from herbaceous biomass and isolated lignins. In the case of RCF of grass biomass with methanol under H_2 pressure, a Ni/carbon catalyst gave esters of *p*-coumaric acid and ferulic acid, along with 4-*n*-propenyl- and 4-*n*-propyl-substituted guaiacols/syringols (total yields of 30–69 wt%) [64]. Formation of methyl coumarate/ferulate via selective hydrogenolysis of isolated lignin under H_2 pressure was also found over $ZnMoO_4$/MCM-41 [65] and Ni/carbon catalysts [66]. Doherty and colleagues developed an effective oxidation-hydrogenation process for one-pot conversion of bagasse into esters of ferulic acid/*p*-coumaric acid (total yield of 32 wt%) using a Pd/carbon catalyst at atmospheric oxygen pressure with methanol [67]. In this process, molecular O_2 adsorbed on the catalyst surface promotes methanol oxidation to give atomic hydrogen species, which participate in the overall reductive depolymerization process. Besides, other lignin-derived aromatic acids, such as syringic, vanillic, and *p*-hydroxybenzoic acids, can be obtained from herbaceous biomass processing, based on the biomass feedstock and the process conditions [67–69].

One Pot of Lignin to Drop-in Chemicals

Besides depolymerization of lignin into monomers (Figure 1), integration of lignin depolymerization and monomer defunctionalization to obtain drop-in chemicals in one pot is also a challenging achievement. For instance, Wang and colleagues obtained 13 wt% of phenol yield from isolated pine lignin through an oxidation-hydrogenation route involving the conversion of lignin to 4-hydroxybenzoic acid, followed by decarboxylation of acid to phenol [70]. In another example, $La(OTf)_3$ is able to convert enzymatic mild acidolysis pine lignin towards guaiacol in methanol, showing a yield of 25.5 wt% [71].

Upgrading of Lignin Monomers: Atom Economy

This section provides an overview of promising catalytic routes for upgrading lignin monomers to marketable end-products, including both drop-in (phenol and alkenes) and new chemicals (alternative bisphenols, alkylated cyclohexanols, and styrene derivatives). An evaluation and comparison is made based on the concept of atom economy. This concept of atom economy is an important guide to select reactions to study, as they deliver only little waste. Nevertheless, not every reaction with high atom economy is, by definition, a sustainable reaction, since many other aspects that are studied in life cycle assessment (LCA) and techno-economic analysis (TEA) can and will influence the carbon footprint of the process and its products. Indeed, to ultimately build a commercial biofactory, many aspects, such as profitability and sustainability, but also safety, have to be considered as well. TEA and LCA are therefore highly recommended methods, but they are time consuming and many times difficult to execute due to lack of sufficient experimental data of mass flow and energy flow. When executed well, these analyses give a lot of insight into the sustainability of the overall biorefinery process with regard to both challenges and opportunities [1,72]. End-product value, potential market size, production cost, and availability of certain platform chemicals are only a few aspects that will shape the commercial landscape. Figure 3 shows the representative drop-in chemicals from lignin.

Selective Dimerization

Lignin monomers can be dimerized into bisphenols, which could serve as renewable alternatives for the polymer building block bisphenol A (BPA). BPA is indispensable for producing thermoplastic polycarbonates and thermosetting epoxy resins. However, BPA's ability to mimic the effect of natural estrogen links the long-term use of BPA-based products to possible adverse health issues, such as reproductive and developmental effects, as well as metabolic diseases. Consequently,

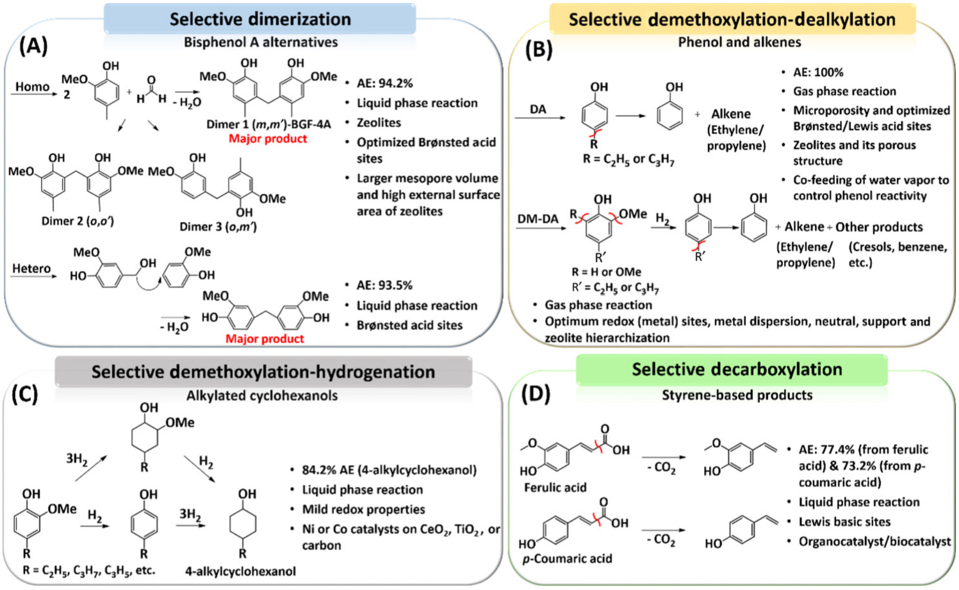

Figure 4. Promising Catalytic Atom-Efficient Routes for Upgrading of Lignin Monomers. Abbreviations: AE, atom economy; DA, dealkylation; DM, demethoxylation; hetero, heterocoupling; homo, homocoupling.

BPA has become highly controversial and currently a quest for safer BPA replacements exists [73], in which lignin-derived bisphenols are promising candidates.

An atom-efficient liquid-phase hydroxyalkylation/alkylation condensation of 4-alkylguaiacols and 4-alkylsyringols with formaldehyde gives novel 4-alkylated *meta*,*meta′*-coupled bisguaiacol F (*m,m′*-BGF-4A) and bissyringol F (*m,m′*-BSF-4A) structures, respectively, with water as the sole byproduct [74–79]. Product selectivity arises from (steric) hindrance on the aromatic ring and the *para*- and *ortho*-directing (electronic) effects of the substituents, yielding *m,m′*-regioisomers as the dominant product (>50% selectivity), with amounts of *m,o′*- and *o,o′*-regioisomers (Figure 4A). Traditional catalysts used for dimerization of lignin monomers are often toxic and corrosive (e.g., gaseous HCl) or thermo-labile and unrecyclable (e.g., sulfonated resins). Alternatively, zeolite based catalysts (e.g., BEA, MOR, FER, and FAU) were employed because they are nontoxic, thermostable, and recyclable [78]. Interestingly, the Lewis acidic zeolites (i.e., Al-β and Sn-β) were inactive, while high dimer yields were obtained over the Brønsted acidic zeolites (i.e., FAU), but the acid density should be in the range of 50–100 mmol H^+/g. This is because the Brønsted acidic zeolites with an acid density of above 100 mmol H^+/g promote undesirable reactions, giving waste oligomers and carbon deposits. Besides, suitable textural properties, such as larger mesoporous volume, higher external surface area, and hierarchical microporosity, are favorable for mass transport properties in dimerization of lignin monomers. As a result, the FAU (Si/Al = 40) zeolite showed the highest catalytic performance (TOF: 496 h^{-1}, dimer selectivity: >95%) and good recyclability. Besides 4-methylated and 4-ethylated substrates, further efforts by Koelewijn and colleagues investigated converting 4-*n*-propylguaiacol to 4-propylated *m,m′*-bisguaiacol F (*m,m′*-BGF-4P) [77] and 4-*n*-propylsyringol to 4-propylated *m,m′*-bissyringol F (*m,m′*-BSF-4P) [79]. All these lignin-derived bisphenols displayed a lower ability to mimic the effect of natural estrogen than BPA [77,79].

Alternatively, the atom-efficient liquid-phase alkylation condensation of vanillyl alcohol with guaiacol gives a (nonalkylated) *para,para′*-coupled bisguaiacol F (*p,p′*-BGF) without the need for a bridging chemical (e.g., formaldehyde or acetone) [80–83]. Under acidic conditions, the innate hydroxymethyl moiety of vanillyl alcohol facilitates and directs methylene bridge formation, favoring *p,p′*-regioisomers as the dominant product together with minor amounts of *m,p′*- and *o,p′*-regioisomers (Figure 4A) [83]. According to the same rationale, Nicastro and colleagues prepared ten bisguaiacols/bissyringols, differing in the number of methoxy groups and (*p,p′*-, *m,p′*-, *o,p′*,- and/or *o,o′*-) regioisomer content, by varying the number of methoxy groups in the starting reagents (i.e., *o*-methoxylated 4-hydroxybenzyl alcohols and *o*-methoxyphenol derivatives) [84]. The authors found that glass transition temperatures and high-temperature rubbery moduli of the corresponding diamine-cured epoxy resins were controllable by steering the relative number of methoxy moieties and the regioisomer content. The product ratio of (*p,p′*-, *m,p′*-, and *o,p′*-) BGF regioisomers can also be manipulated through judicious choice of starting reagent [85]. Based on the type of vanillyl alcohol isomer, acid-catalyzed alkylation condensation with guaiacol granted regioselective access to one of the three BGF regioisomers, which was ascribed to the absence of acid-catalyzed isomerization. Regarding their estrogenic activity, these BGF regioisomers also (either pure or as a mixture) displayed lower activity than BPA [85–87].

Selective Demethoxylation-Dealkylation

Selective hydroprocessing of lignin monomers, such as 4-propylguaiacol and 4-propylsyringol, can yield alkylphenols, which can be dealkylated into valuable drop-in chemicals, namely phenol and olefins (Figure 4B). Both phenol and olefins are useful products and atom loss is avoided if selective cleavage of alkylphenols is achieved with high carbon balance. The Sels group developed a catalytic atom-efficient route for gas-phase dealkylation of 4-ethyl- and 4-*n*-propyl-phenols to phenol and olefins [88]. Various zeolites (ferrierite, ZSM-22, H-ZSM-5, beta, USY, MFI, and BEA) and metal oxides (ZrO_2, MgO, ZnO, and Al_2O_3) were tested [89,90]. Results reveal that the microporosity of catalysts plays a key role to achieve high product selectivity. Besides, optimized amounts of Brønsted-Lewis acid sites are required for efficient dealkylation reaction [91]. For dealkylation of both 4-ethylphenol and 4-*n*-propylphenol, medium-pore zeolite H-ZSM-5 displayed the highest selectivity towards phenol and alkenes owing to its unique pore confinement, which inhibits undesired bimolecular reactions. Co-feeding of water inhibited phenol condensation to diphenyl ether, thus preventing pore blockage. Consequently, the catalytic durability of HZSM-5 was significantly improved. In the case of alkyl-substituted guaiacols and syringols, demethoxylation is also required, along with dealkylation to produce phenol. A highly dispersed Ni catalyst on silica showed selective catalysis for the demethoxylation step, providing yields above 75%. Interestingly, the monomer mixture from RCF of birch wood, containing a handful of methoxy phenolics, showed similar demethoxylation performance using the Ni catalyst. Further dealkylation over a hierarchical ZSM-5 gave phenol and propylene with close to quantitative selectivity. Overall, about 30 wt% of the birch lignin is converted into phenol and propylene through this catalytic funneling strategy (Figure 5) [1]. Besides, bifunctional catalysts with redox (hydro-demethoxylation) and acid (dealkylation) properties are needed. In this context, a physical mixture of Pt/carbon and H-ZSM-5 catalysts was applied, providing over 60% molar yield of phenol from 4-*n*-propylguaiacol in a single step [92]. Results revealed that Pt/carbon first catalyzed hydro-demethoxylation, followed by the zeolite-catalyzed dealkylation step. Besides, other products (cresols, benzene, etc.) were obtained, due to the partial cleavage of both methoxyl and alkyl chains, as well as recondensation of phenol with alkene. Hence, tuning the redox and acid properties of the catalyst, with optimizing reaction conditions, helps to inhibit undesired reactions, thereby obtaining higher yield of phenol.

Interestingly, a **transalkylation** strategy (instead of dealkylation), coupled with demethoxylation, was developed to produce phenol from 4-*n*-propylguaiacol in benzene [93]. The reaction

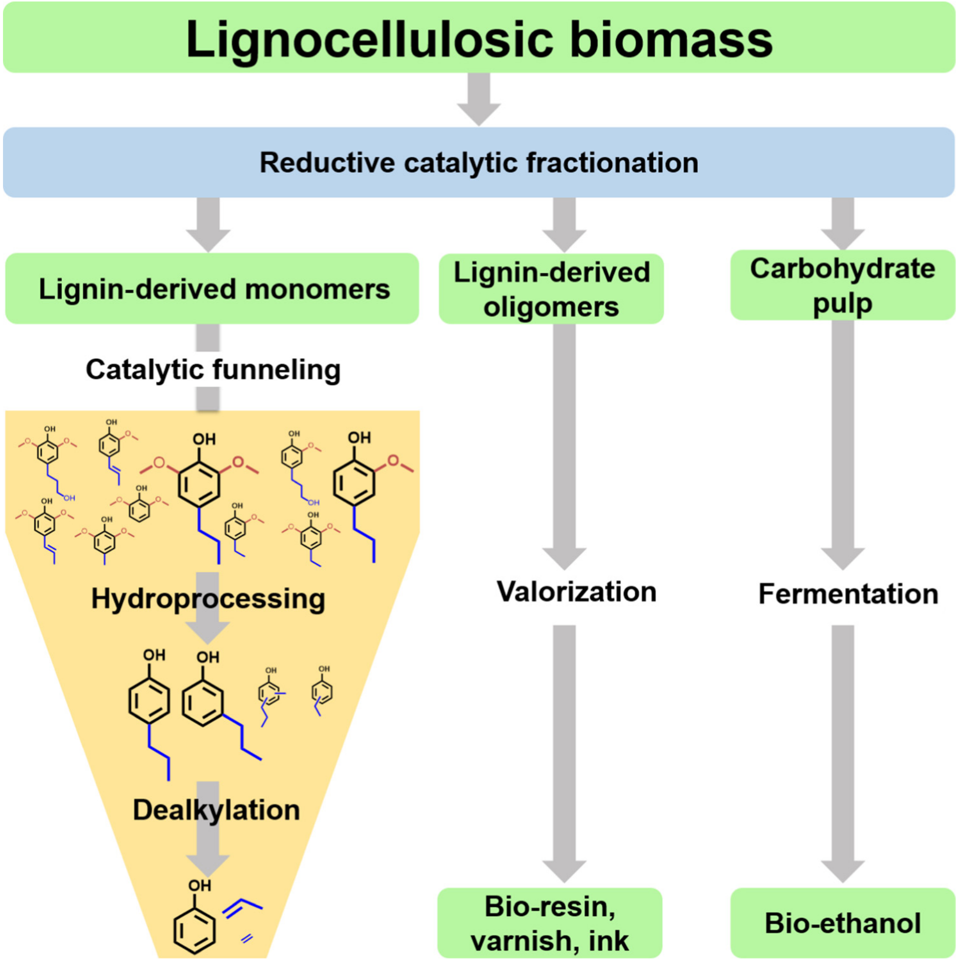

Figure 5. Catalytic Funneling (via Hydroprocessing and Dealkylation) of Lignin Monomers Obtained from RCF of Lignocellulose towards Phenol and Alkenes in an Integrated Biorefinery [1]. Abbreviation: RCF, reductive catalytic fractionation.

pathway involves Au/TiO_2-catalyzed hydro-demethoxylation of 4-*n*-propylguaiacol to propylphenol, followed by its transalkylation with benzene over HZSM-5 catalyst, giving phenol yields of 50% and 60% in stacked- and mixed-bed reactors, respectively. Despite the lower phenol yield, this transalkylation strategy showed two benefits: (i) minimizing coke formation from intermediates (methoxy and propyl side chains), which could be effectively stabilized by benzene; and (ii) the transalkylation agent (i.e., benzene) can be upgraded to more valuable propylbenzene, cumene, and toluene.

Selective Demethoxylation-Hydrogenation

Cyclohexanols are important chemicals for polymer, spice, and medicine production. Demethoxylation of 4-alkylguaiacols/syringols, followed by aromatic ring hydrogenation or hydrogenation of aromatic ring, followed by demethoxylation, gives alkylated cyclohexanols. This process is considered as atom-efficient as it involves the addition of hydrogen atoms to the aromatic ring (Figure 4C) [94]. Some atom loss via cleavage of methoxy and hydroxyl species is inevitable, but it is essential to obtain high-value chemicals. Using an efficient metal-based redox catalyst and suitable reaction conditions (especially H_2 pressure) are crucial to achieve improved yields of cyclohexanols. Particularly, the properties of a metal catalyst can be improved using a suitable supporting material. The Ni catalyst supported on CeO_2 provides the highest yield of 4-*n*-propylcyclohexanol (~80%) from 4-*n*-propylguaiacol compared with the Ni catalyst supported on MgO, Al_2O_3, SiO_2, and ZrO_2 [94]. The removal of the methoxy group from 4-alkylated 2-methoxycyclohexanol formed by hydrogenation of the aromatic ring of 4-alkylguaiacol was found to be the rate-limiting step (Figure 4C). In another work, TiO_2 was found to be a suitable support for 10 wt% Co catalyst compared with HZSM-5, ZrO_2, CeO_2, SiO_2, and Al_2O_3 supports, giving an equivalent of 4-*n*-propylcyclohexanol (>99.9%) from eugenol, due to the strong Co–TiO_2 interaction [95]. Mechanistic studies revealed that all Co catalysts show a high selectivity towards C_{aryl}–OCH_3 bond cleavage prior to aromatic ring hydrogenation when the –OCH_3 group presented at the *ortho*-position. Interestingly, compared with noble metal-based catalysts (5 wt% Ru/carbon and 5 wt% Pd/carbon), 65 wt% Ni/SiO_2–Al_2O_3 catalyst showed the highest 4-*n*-propylcyclohexanol (PCol) yield (85%) PG [96]. This is because the Ni/SiO_2–Al_2O_3 catalyst favors: (i) a suitable mechanism (PG hydrodemethoxylation to 4-n-propylphenol, followed by its hydrogenation into PCol); (ii) high reactivity of 4-*n*-propyl-2-methoxycyclohexanol (obtained from PG hydrogenation) over PCol (because PCol can further react to give hydrocarbons); and (iii) a high carbon balance. Owing to strong redox properties, the Ru/carbon catalyst gave good yields of cyclohexane (via phenolic C–O bond cleavage), along with cyclohexanols, which was also demonstrated by Vriamont and colleagues [97]. Compared with the acidic support (ZSM-5), high guaiacol conversion (96%) with cyclohexanol as the main product was obtained over a mild acidic γ-Al_2O_3-supported NiCo catalyst [98]. Therefore, appropriate amounts of both redox and acid properties are needed for achieving improved yields of cyclohexanols.

To ease recovery of the catalyst, a magnetically separable AgPd/Fe@carbon nitride catalyst was developed for cyclohexanol production from lignin-derived guaiacol using formic acid as hydrogen source under visible light irradiation [99]. The synergetic effect of Ag and Pd on carbon nitride enhanced formic acid decomposition to give hydrogen species, needed to convert guaiacol into cyclohexanol at ambient temperature (Figure 6). Additional research needs to evaluate the catalytic efficiency of magnetic AgPd/Fe@carbon nitride catalyst for demethoxylation-hydrogenation of lignin monomers to cyclohexanols.

Selective Decarboxylation

Decarboxylation is another promising strategy to defunctionalize biomass into more practicable chemicals, but it does not need the flammable or toxic hydrogen reagents [100,101]. Selective decarboxylation of ferulic acid, *p*-coumaric acid, caffeic acid, and sinapic acid provides high-value styrene-based products, having widespread applications in polymer and pharmaceutical industries (Figure 4D). Decarboxylation of lignin monomers is generally a base-catalyzed reaction with CO_2 as the main byproduct. For instance, in the presence of methylimidazole and aqueous $NaHCO_3$ mixture, about 38% and 34% yields of styrene-based products were obtained from decarboxylation of ferulic acid and *p*-coumaric acid, respectively, under microwave irradiation for 20 min in polyethylene glycol [102]. Water was found to enhance the equilibrium constant in the base-catalyzed decarboxylation. Concurrently, water stabilized the transition state/intermediate (s) via hydrogen bonding and intermolecular charge-dipole interactions, thus improving yields of styrene-based products. Trimethylamine base was also found to be catalytically active for ferulic acid decarboxylation to styrene-based monomers for poly(vinylcatechol) and poly(vinylguaiacol) [103]. Liquid base catalysts are toxic and unrecoverable; thus their use is environmentally unfriendly. To develop a sustainable catalytic route, a recyclable base catalyst (i.e., N-heterocyclic carbene-based organocatalyst) was developed for decarboxylation of aromatic acids, giving

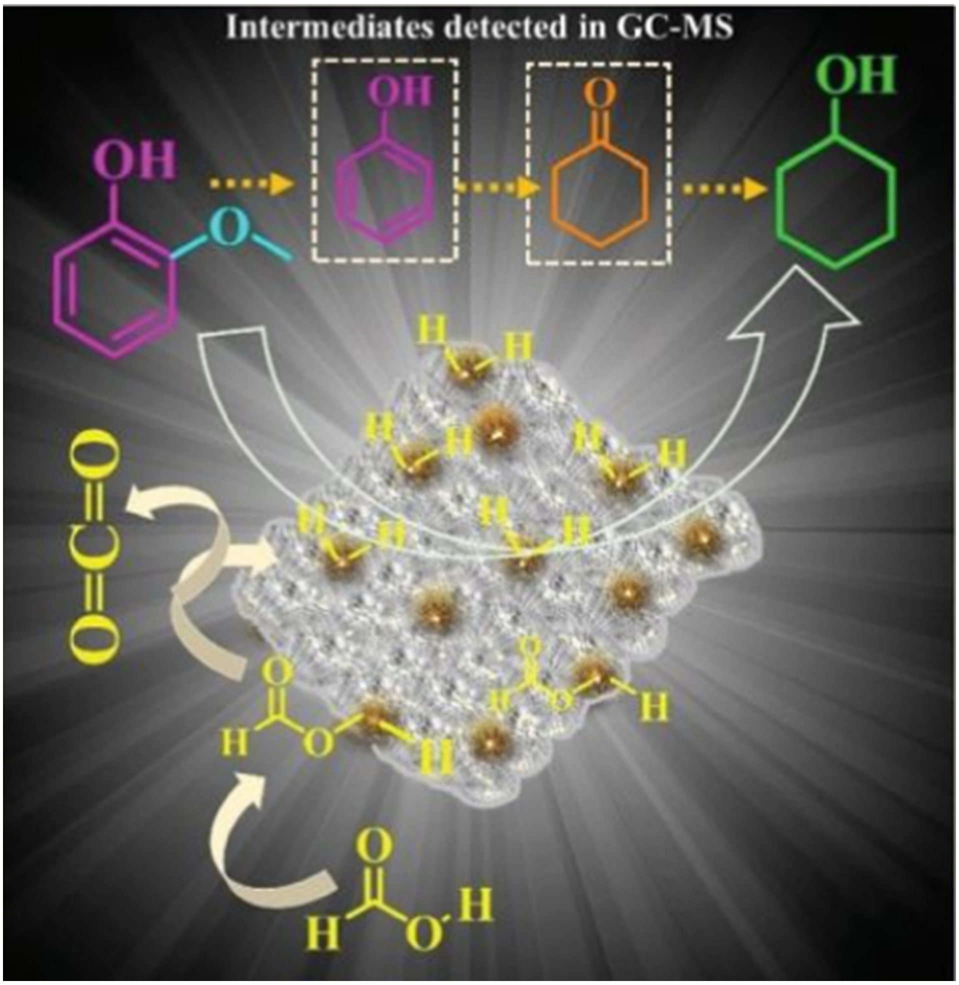

Figure 6. The Reaction Pathway for Hydrodeoxygenation of Guaiacol [99]. The formation of two intermediates, namely phenol and cyclohexanone, was identified using gas chromatography–mass spectrometry (GC-MS) analysis of the reaction mixture taken during the 6 hours of reaction time. Cyclohexanol is the major product from this reaction.

excellent yields of styrene-based products (94–100%) [100]. Improved product yields were obtained in the case of sinapinic acid decarboxylation, due to the presence of two electron-donating methoxy groups in sinapinic acid. Mechanistic studies revealed that N-heterocyclic carbene species, generated *in situ* via self-protonation of organocatalyst, are the catalytically active (Lewis base) sites for decarboxylation. Using both polyethylene glycol as green solvent, as well as a facile product separation by distillation, allowed efficient solvent and $Cu(OH)_2$ catalyst reuse for at least four cycles in ferulic acid decarboxylation to 4-vinylguaiacol [101].

In addition, biocatalytic ferulic acid/*p*-coumaric acid decarboxylation towards styrene-based products is being studied [69]. For example, a temperature and pH directed, coenzyme-free biocatalytic route was developed towards 4-vinylphenol [104]. The favorable role of the biphasic organic/aqueous system was realized to partly extract the hydrophobic styrene products from the aqueous phase containing more hydrophilic lignin monomers, resulting in an improved productivity of the coenzyme-free decarboxylation. The versatile nature of coenzyme-free biocatalyst could efficiently convert a variety of lignin-derived aromatics to valuable chemicals.

Concluding Remarks

In summary, lignin is a promising non-fossil resource for diverse functionalized aromatic platform chemicals, such as *para*-substituted guaiacols/syringols, vanillin/vanillic acid, syringaldehyde, and ferulic acid/*p*-coumaric acid/sinapic acid. These accessible platform chemicals can be obtained by alkaline oxidative and hydrogenolytic cleavage of isolated lignins. Besides, one-pot lignocellulose fractionation processes, such as RCF and aqueous alkaline fractionation, can give considerable yields of lignin monomers, while giving a valorizable carbohydrate solid pulp (rich in cellulose). Catalysts play a key role in efficient upgrading of lignin and its platform molecules into desirable chemicals with high atom efficiency and lower amounts of waste generation. This review summarized the most significant catalytic atom-efficient routes for upgrading of lignin platform chemicals into new polymer building blocks and drop-in chemicals. These routes include: (i) dimerization; (ii) demethoxylation-dealkylation; (iii) demethoxylation-hydrogenation; and (iv) decarboxylation. Although most synthesis and upgrading routes summarized in this review are laboratory scale, they provide indispensable information concerning methodologies, atom efficiency, and reaction characteristics essential for future development of large-scale lignin upgrading processes. Fractionation methodology, full characterization of lignin fraction, separation technology for lignin-derived chemicals, catalyst stability/reusability, advanced atom-efficient routes, and E-factor estimation are the very important parameters that should be taken into consideration to develop an economically viable lignin valorization process (see Outstanding Questions). Finally, always keep in mind that reactions with high atom efficiency are the best candidates to select with regard to sustainability, but they do not necessarily always lead to a sustainable process; other aspects studied in LCA and TEA can also determine the overall carbon footprint of the final process and its products.

Outstanding Questions

Are we successful in fully understanding heterogeneities in lignin structure?

Can the molecular structure of the lignin oligomers be fully unraveled?

Do such lignin oligomers serve as potential feedstock for the production of value-added chemicals and new polymer building blocks?

Can an atom efficient one-pot catalytic process be developed for lignin conversion towards drop-in chemicals?

Can the formation of lignin depolymerization products be traced and quantified by analytical techniques in real time?

Is the definition of atom efficiency sufficient to ultimately achieve a sustainable process?

Acknowledgments

Y.L. acknowledges KU Leuven internal research funds for a postdoc mandate (PDM). S-F.K. acknowledges Catalisti cSBO ARBOREF and BIO-HArT (Interreg VA Vlaanderen-Nederland) funding from the Flemish government. B.F.S. would like to thank the following for funding: FWO Flanders via the SBO project Biowood (S003518N), BIOFACT (FNRS – FWO EOS project G0H0918N), and the Catalisti cluster SBO project SPICY ('Sugar-based chemicals and polymers through innovative chemocatalysis and engineered yeast'), with the financial support of VLAIO (Flemisch Agency for Innovation and Entrepreneurship).

References

1. Liao, Y. *et al.* (2020) A sustainable wood biorefinery for low–carbon footprint chemicals production. *Science* 367, 1385–1390
2. Schutyser, W. *et al.* (2018) Chemicals from lignin: an interplay of lignocellulose fractionation, depolymerisation, and upgrading. *Chem. Soc. Rev.* 47, 852–908
3. Bidlack, J.E. and Dashek, W.V. (2017) Plant cell walls. In *Plant Cells and Their Organelles* (Dashek, W.V. and Miglani, G.S., eds), pp. 209–238, Wiley-Blackwell
4. Liao, Y. *et al.* (2020) The role of pretreatment in the catalytic valorization of cellulose. *Mol. Catal.* 487, 1108863
5. Sudarsanam, P. *et al.* (2018) Functionalised heterogeneous catalysts for sustainable biomass valorisation. *Chem. Soc. Rev.* 47, 8349–8402
6. Rinaldi, R. *et al.* (2016) Paving the way for lignin valorisation: recent advances in bioengineering, biorefining and catalysis. *Angew. Chem. Int. Ed.* 55, 8164–8215
7. Erythropel, H.C. *et al.* (2018) The Green ChemisTREE: 20 years after taking root with the 12 principles. *Green Chem.* 20, 1929–1961
8. Trost, B.M. (1991) The atom economy - a search for synthetic efficiency. *Science* 254, 1471–1477
9. Sun, Z. *et al.* (2018) Bright side of lignin depolymerization: toward new platform chemicals. *Chem. Rev.* 118, 614––678
10. Renders, T. *et al.* (2017) Lignin-first biomass fractionation: the advent of active stabilisation strategies. *Energy Environ. Sci.* 10, 1551–1557
11. Van den Bosch, S. *et al.* (2015) Reductive lignocellulose fractionation into soluble lignin-derived phenolic monomers and dimers and processable carbohydrate pulps. *Energy Environ. Sci.* 8, 1748–1763
12. Van den Bosch, S. *et al.* (2015) Tuning the lignin oil OH-content with Ru and Pd catalysts during lignin hydrogenolysis on birch wood. *Chem. Commun.* 51, 13158–13161
13. Liu, X. *et al.* (2019) Chemodivergent hydrogenolysis of eucalyptus lignin with Ni@ZIF-8 catalyst. *Green Chem.* 21, 1498–1504
14. Song, Q. *et al.* (2013) Lignin depolymerization (LDP) in alcohol over nickel-based catalysts via a fragmentation–hydrogenolysis process. *Energy Environ. Sci.* 6, 994–1007
15. Van den Bosch, S. *et al.* (2017) Integrating lignin valorization and bio-ethanol production: on the role of Ni-Al_2O_3 catalyst pellets during lignin-first fractionation. *Green Chem.* 19, 3313–3326
16. Chen, J. *et al.* (2016) High yield production of natural phenolic alcohols from woody biomass using a nickel-based catalyst. *ChemSusChem* 9, 3353–3360

17. Xiao, L.P. *et al.* (2017) Catalytic hydrogenolysis of lignins into phenolic compounds over carbon nanotube supported molybdenum oxide. *ACS Catal.* 7, 7535–7542
18. Sun, J. *et al.* (2019) Fragmentation of woody lignocellulose into primary monolignols and their derivatives. *ACS Sustain. Chem. Eng.* 7, 4666–4674
19. Zhai, Y. *et al.* (2017) Depolymerization of lignin via a non-precious Ni–Fe alloy catalyst supported on activated carbon. *Green Chem.* 19, 1895–1903
20. Parsell, T. *et al.* (2015) A synergistic biorefinery based on catalytic conversion of lignin prior to cellulose starting from lignocellulosic biomass. *Green Chem.* 17, 1492–1499
21. Ferrini, P. and Rinaldi, R. (2014) Catalytic biorefining of plant biomass to non-pyrolytic lignin bio-oil and carbohydrates through hydrogen transfer reactions. *Angew. Chem. Int. Ed.* 53, 8634–8639
22. Renders, T. *et al.* (2016) Synergetic effects of alcohol/water mixing on the catalytic reductive fractionation of poplar wood. *ACS Sustainable Chem. Eng.* 4, 6894–6904
23. Schutyser, W. *et al.* (2015) Influence of bio-based solvents on the catalytic reductive fractionation of birch wood. *Green Chem.* 17, 5035–5045
24. Galkin, M.V. and Samec, J.S. (2014) Selective route to 2-propenyl aryls directly from wood by a tandem organosolv and palladium-catalysed transfer hydrogenolysis. *ChemSusChem* 7, 2154–2158
25. Park, J. *et al.* (2019) Fractionation of lignocellulosic biomass over core–shell Ni@Al_2O_3 catalysts with formic acid as a cocatalyst and hydrogen source. *ChemSusChem* 12, 1743–1762
26. Kumaniaev, I. *et al.* (2020) Conversion of birch bark to biofuels. *Green Chem.* 22, 2255–2263
27. Kumaniaev, I. and Samec, J.S.M. (2018) Valorization of *Quercus suber* bark toward hydrocarbon bio-oil and 4-ethylguaiacol. *ACS Sustain. Chem. Eng.* 6, 5737–5742
28. Vangeel, T. *et al.* (2019) Reductive catalytic fractionation of black locust bark. *Green Chem.* 21, 5841–5851
29. Cooreman, E. *et al.* (2020) A perspective on overcoming scale-up hurdles for the reductive catalytic fractionation of lignocellulose biomass. *Ind. Eng. Chem. Res.* Published online July 16, 2020. http://doi.org/10.1021/acs.iecr.0c02294
30. Anderson, E.M. *et al.* (2018) Kinetic studies of lignin solvolysis and reduction by reductive catalytic fractionation decoupled in flow-through reactors. *ACS Sustain. Chem. Eng.* 6, 7951–7959
31. Anderson, E.M. *et al.* (2017) Flow through reductive catalytic fractionation of biomass. *Joule* 1, 613–622
32. Kumaniaev, I. *et al.* (2017) Lignin depolymerization to monophenolic compounds in a flow-through system. *Green Chem.* 19, 5767–5771
33. Shuai, L. *et al.* (2016) Formaldehyde stabilization facilitates lignin monomer production during biomass depolymerization. *Science* 354, 329–333
34. Lan, W. *et al.* (2018) Protection group effects during alpha, gamma-diol lignin stabilization promote high-selectivity monomer production. *Angew. Chem. Int. Ed.* 130, 1370–1374
35. Deuss, P.J. *et al.* (2017) Phenolic acetals from lignins of varying compositions via iron(III) triflate catalysed depolymerisation. *Green Chem.* 19, 2774–2782
36. Dhar, P. and Vinu, R. (2018) Microwave-assisted catalytic solvolysis of lignin to phenols: kinetics and product characterization. *ACS Omega* 3, 15076–15085
37. Fache, M. *et al.* (2016) Vanillin production from lignin and its use as a renewable chemical. *ACS Sustain. Chem. Eng.* 4, 35–46
38. Rautiainen, S. *et al.* (2016) Oxidation of vanillin with supported gold nanoparticles. *Top. Catal.* 59, 1138–1142
39. Luo, J. *et al.* (2016) Selective lignin oxidation towards vanillin in phenol media. *ChemistrySelect* 1, 4596–4601
40. Wongtanyawat, N. *et al.* (2018) Comparison of different kraft lignin-based vanillin production processes. *Comput. Chem. Eng.* 117, 159–170
41. Vangeel, T. *et al.* (2018) Perspective on lignin oxidation: advances, challenges, and future directions. *Top. Curr. Chem.* 376, 1–16
42. Tarabanko, V.E. and Tarabanko, N. (2017) Catalytic oxidation of lignins into the aromatic aldehydes: general process trends and development prospects. *Int. J. Mol. Sci.* 18, 2421–2450
43. Schutyser, W. *et al.* (2018) Revisiting alkaline aerobic lignin oxidation. *Green Chem.* 20, 3828–3844
44. Pacek, A.W. *et al.* (2013) Catalytic conversion of sodium lignosulfonate to vanillin: engineering aspects. Part 1. Effects of processing conditions on vanillin yield and selectivity. *Ind. Eng. Chem. Res.* 52, 8361–8372
45. Wang, Y. *et al.* (2018) Production of vanillin from lignin: The relationship between β-O-4 linkages and vanillin yield. *Ind. Crop. Prod.* 116, 116–121
46. Lyu, G. *et al.* (2018) Alkaline oxidative cracking for effective depolymerization of biorefining lignin to mono-aromatic compounds and organic acids with molecular oxygen. *Biomass Bioenergy* 108, 7–14
47. Das, L. *et al.* (2017) Oxidative depolymerization of lignin using supported niobium catalysts. *ChemEngineering* 1, 17–30
48. Hdidou, L. *et al.* (2018) Synthesis of CoFeO mixed oxides via an alginate gelation process as efficient heterogeneous catalysts for lignin depolymerization in water. *Catal. Sci. Technol.* 8, 5445–5453
49. Dai, J. *et al.* (2018) $CuSO_4/H_2O_2$-catalyzed lignin depolymerization under the irradiation of microwaves. *ACS Omega* 3, 10433–10441
50. Gu, X. *et al.* (2012) La-modified SBA-15/H_2O_2 systems for the microwave assisted oxidation of organosolv beech wood lignin. *Maderas. Cienc. Tecnol.* 14, 31–42
51. Pantankar, S.C. *et al.* (2019) Isolation of phenolic monomers from kraft lignin using a magnetically recyclable TEMPO nanocatalyst. *Green Chem.* 21, 785–791
52. Abdelaziz, O.Y. *et al.* (2018) Continuous catalytic depolymerisation and conversion of industrial kraft lignin into low-molecular-weight aromatics. *Biomass Convers Biorefinery* 8, 455–470
53. Zhu, Y. *et al.* (2020) Complementing vanillin and cellulose production by oxidation of lignocellulose with stirring control. *ACS Sustain. Chem. Eng.* 8, 2361–2374
54. Jiang, J.-G. *et al.* (2018) Upgrading traditional pulp mill into biorefinery platform: wheat straw as a feedstock. *ACS Sustain. Chem. Eng.* 6, 15284–15291
55. Oliveira, D.M. *et al.* (2015) Ferulic acid: a key component in grass lignocellulose recalcitrance to hydrolysis. *Plant Biotechnol. J.* 13, 1224–1232
56. Upton, B.M. and Kasko, A.M. (2019) Biomass-derived poly(ether-amide)s incorporating hydroxycinnamates. *Biomacromolecules* 20, 758–766
57. U.S. Department of Energy (2006) Breaking the Biological Barriers to Cellulosic Ethanol, A Joint Research Agenda. In *Report from the December 2005 Workshop, DOE/SC-0095*, U.S. Department of Energy Office of Science
58. Brandt, A. *et al.* (2013) Deconstruction of lignocellulosic biomass with ionic liquids. *Green Chem.* 15, 550–583
59. Karlen, S.D. *et al.* (2020) Assessing the viability of recovery of hydroxycinnamic acids from lignocellulosic biorefinery alkaline pretreatment waste streams. *ChemSusChem* 13, 2012–2024
60. Salvachua, D. *et al.* (2015) Towards lignin consolidated bioprocessing: simultaneous lignin depolymerization and product generation by bacteria. *Green Chem.* 17, 4951–4967
61. Kim, S. and Holltzapple, M.T. (2005) Lime pretreatment and enzymatic hydrolysis of corn stover. *Bioresour. Technol.* 96, 1994–2006
62. Linger, J.G. *et al.* (2014) Lignin valorization through integrated biological funneling and chemical catalysis. *Proc. Natl. Acad. Sci. U. S. A.* 111, 12013–12018
63. Karp, E.M. *et al.* (2016) Quantification of acidic compounds in complex biomass-derived streams. *Green Chem.* 18, 4750–4760
64. Luo, H. *et al.* (2016) Total utilization of miscanthus biomass, lignin and carbohydrates, using earth abundant nickel catalyst. *ACS Sustain. Chem. Eng.* 4, 2316–2322
65. Wang, S. *et al.* (2018) Selective fragmentation of biorefinery corncob lignin into p-hydroxycinnamic esters with a supported zinc molybdate catalyst. *ChemSusChem* 11, 2114–2123
66. Wang, S. *et al.* (2019) Hydrogenolysis of biorefinery corncob lignin into aromatic phenols over activated carbon-supported nickel. *Sustain. Energy Fuels* 3, 401–408

67. Tana, T. *et al.* (2019) Valorization of native sugarcane bagasse lignin to bio-aromatic esters/monomers via a one pot oxidation–hydrogenation process. *Green Chem.* 21, 861–873
68. Lochab, B. *et al.* (2014) Naturally occurring phenolic sources: monomers and polymers. *RSC Adv.* 4, 21712–21752
69. Tinikul, R. *et al.* (2018) Biotransformation of plant-derived phenolic acids. *Biotechnol. J.* 13, 1700632
70. Wang, M. *et al.* (2018) Dealkylation of lignin to phenol via oxidation–hydrogenation strategy. *ACS Catal.* 8, 6837–6843
71. Shen, X. *et al.* (2020) Selective catalytic transformation of lignin with guaiacol as the only liquid product. *Chem. Sci.* 11, 1347–1352
72. Tschulkow, M. *et al.* (2020) Integrated techno-economic assessment of a biorefinery process: the high-end valorization of the lignocellulosic fraction in wood streams. *GJ. Clean. Prod.* 266, 122022
73. Schug, T.T. *et al.* (2013) Designing endocrine disruption out of the next generation of chemicals. *Green Chem.* 15, 181–198
74. Van der Klashorst, G.H. and Strauss, H.F. (1986) Polymerization of lignin model compounds with formaldehyde in acidic aqueous medium. *J. Polym. Sci. Pol. Chem.* 24, 2143–2169
75. Meylemans, H.A. *et al.* (2012) Synthesis of renewable bisphenols from creosol. *ChemSusChem* 5, 206–210
76. Chen, Q. *et al.* (2015) Synthesis of lignin-derived bisphenols catalyzed by lignosulfonic acid in water for polycarbonate synthesis. *ChemCatChem* 7, 1083–1089
77. Koelewijn, S.-F. *et al.* (2017) Sustainable bisphenols from renewable softwood lignin feedstock for polycarbonates and cyanate ester resins. *Green Chem.* 19, 2561–2570
78. Ferrini, P. *et al.* (2017) Zeolites as sustainable catalysts for the selective synthesis of renewable bisphenols from lignin-derived monomers. *ChemSusChem* 10, 2249–2257
79. Koelewijn, S.-F. *et al.* (2018) Promising bulk production of a potentially benign bisphenol A replacement from a hardwood lignin platform. *Green Chem.* 20, 1050–1058
80. Dimmel, D.R. *et al.* (1981) The influence of anthrahydroquinone and other additives on the condensation reactions of vanillyl alcohol. *J. Wood Chem. Tech.* 1, 123–146
81. Xu, H. and Lai, Y.Z. (1999) Reactivity of lignin diphenylmethane model dimers under alkaline pulping conditions. *J. Wood Chem. Tech.* 19, 1–12
82. Cavani, F. *et al.* (2002) A note on the role of methanol in the homogeneous and heterogeneous acid-catalyzed hydroxymethylation of guaiacol with aqueous solutions of formaldehyde. *J. Mol. Catal. A Chem.* 182–183, 447–453
83. Hernandez, E.D. *et al.* (2016) Synthesis and characterization of bio-based epoxy resins derived from vanillyl alcohol. *ACS Sustain. Chem. Eng.* 4, 4328–4339
84. Nicastro, K.H. *et al.* (2018) Potential lignin-derived alternatives to bisphenol A in diamine hardened epoxy resins. *ACS Sustain. Chem. Eng.* 6, 14812–14819
85. Koelewijn, S. *et al.* (2019) Regioselective synthesis, isomerisation, *in vitro* oestrogenic activity, and copolymerisation of bisguaiacol F (BGF) isomers. *Green Chem.* 21, 6622–6633
86. Szafran, A.T. *et al.* (2017) Characterizing properties of non-estrogenic substituted bisphenol analogs using high throughput microscopy and image analysis. *PLoS One* 12, 1–19
87. Peng, Y. *et al.* (2018) Evaluation of estrogenic activity of novel bisphenol A alternatives, four bioinspired bisguaiacol F specimens, by in vitro assays. *J. Agric. Food Chem.* 66, 11775–11783
88. Verboekend, D. *et al.* (2016) Alkylphenols to phenol and olefins by zeolite catalysis: a pathway to valorize raw and fossilized lignocellulose. *Green Chem.* 18, 297–306
89. Liao, Y. *et al.* (2018) Shape selectivity vapor-phase conversion of lignin-derived 4-ethylphenol to phenol and ethylene over acidic aluminosilicates: Impact of acid properties and pore constraint. *Appl. Catal. B Environ.* 234, 117–129
90. Liao, Y. *et al.* (2018) Propylphenol to phenol and propylene over acidic zeolites: role of shape selectivity and presence of steam. *ACS Catal.* 8, 7861–7878
91. Liao, Y. *et al.* (2020) Aromatics production from lignocellulosic biomass: shape selective dealkylation of lignin-derived phenolics over hierarchical ZSM-5. *ACS Sustain. Chem. Eng.* 8, 8713–8722
92. Zhang, J. *et al.* (2018) Single-step conversion of lignin monomers to phenol: bridging the gap between lignin and high-value chemicals. *Chin. J. Catal.* 39, 1445–1452
93. Huang, X. *et al.* (2018) Selective production of biobased phenol from lignocellulose derived alkylmethoxyphenols. *ACS Catal.* 8, 11184–11190
94. Schutyser, W. *et al.* (2015) Selective nickel-catalyzed conversion of model and lignin-derived phenolic compounds to cyclohexanone-based polymer building blocks. *ChemSusChem* 8, 1805–1818
95. Liu, X. *et al.* (2017) Selective hydrodeoxygenation of lignin-derived phenols to cyclohexanols over Co-based catalysts. *ACS Sustain. Chem. Eng.* 5, 8594–8601
96. Schutyser, W. *et al.* (2016) Selective conversion of lignin-derivable 4-alkylguaiacols to 4-alkylcyclohexanols over noble and non-noble-metal catalysts. *ACS Sustain. Chem. Eng.* 4, 5336–5346
97. Vriamont, C.E.J.J. *et al.* (2019) From lignin to chemicals: hydrogenation of lignin models and mechanistic insights into hydrodeoxygenation via low-temperature C–O bond cleavage. *ACS Catal.* 9, 2345–2354
98. Zhou, M. *et al.* (2017) Water-assisted selective hydrodeoxygenation of guaiacol to cyclohexanol over supported Ni and Co bimetallic catalysts. *ACS Sustain. Chem. Eng.* 5, 8824–8835
99. Verma, S. *et al.* (2019) Visible light-mediated and water-assisted selective hydrodeoxygenation of lignin-derived guaiacol to cyclohexanol. *Green Chem.* 21, 1253–1257
100. Liu, D. *et al.* (2018) N-heterocyclic carbene promoted decarboxylation of lignin-derived aromatic acids. *ACS Sustain. Chem. Eng.* 6, 7232–7238
101. Cadot, S. *et al.* (2014) Preparation of functional styrenes from biosourced carboxylic acids by copper catalyzed decarboxylation in PEG. *Green Chem.* 16, 3089–3097
102. Kumar, V. *et al.* (2007) Remarkable synergism in methylimidazole-promoted decarboxylation of substituted cinnamic acid derivatives in basic water medium under microwave irradiation: a clean synthesis of hydroxylated (E)-stilbenes. *Tetrahedron* 63, 7640–7646
103. Takeshima, H. *et al.* (2017) Bio-based functional styrene monomers derived from naturally occurring ferulic acid for poly(vinylcatechol) and poly(vinylguaiacol) via controlled radical polymerization. *Macromolecules* 50, 4206–4216
104. Ni, J. *et al.* (2018) A coenzyme-free biocatalyst for the value-added utilization of lignin-derived aromatics. *J. Am. Chem. Soc.* 140, 16001–16005