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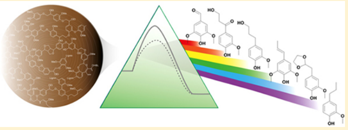
Bright Side of Lignin Depolymerization: Toward New Platform Chemicals

Zhuohua Sun,[†] Bálint Fridrich,[†,‡] Alessandra de Santi,[†,‡] Saravanakumar Elangovan,[†] and Katalin Barta*,[†]

[†]Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

Supporting Information



ABSTRACT: Lignin, a major component of lignocellulose, is the largest source of aromatic building blocks on the planet and harbors great potential to serve as starting material for the production of biobased products. Despite the initial challenges associated with the robust and irregular structure of lignin, the valorization of this intriguing aromatic biopolymer has come a long way: recently, many creative strategies emerged that deliver defined products via catalytic or biocatalytic depolymerization in good yields. The purpose of this review is to provide insight into these novel approaches and the potential application of such emerging new structures for the synthesis of biobased polymers or pharmacologically active molecules. Existing strategies for functionalization or defunctionalization of lignin-based compounds are also summarized. Following the whole value chain from raw lignocellulose through depolymerization to application whenever possible, specific lignin-based compounds emerge that could be in the future considered as potential lignin-derived platform chemicals.

CONTENTS

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1. INTRODUCTION

Living with limited resources on the planet represents a tremendous challenge due to our increasing global population.[1] The growing demand for fuels and chemicals and the society's dependence on nonrenewable petroleum should be addressed simultaneously through the development of sustainable technologies that would enable the efficient utilization of renewable resources.[2−5] Such an attractive, carbon-neutral and nonedible starting material is lignocellulose, generated in considerable quantities from forestry and agricultural activity worldwide.[5,6] Moreover, food waste has been put forward as an economically significant, lignocellulose-rich resource.[7] In the past decade, significant advances have been achieved regarding the development of biorefineries suitable for the fractionation of lignocellulose to its main constituents: cellulose, hemicellulose, and lignin.[8−10] However, in order to create economically feasible biorefineries and overcome the initial energy cost associated with processing and pretreatment, all three major constituents should be fully valorized.[7−10] Novel chemo- or biocatalytic routes should enable the conversion of these biobased starting materials to chemicals and fuels. In this regard, the catalytic conversion of lignin was found extremely challenging,[11] mainly due to the robustness and complexity of its structure.[12−14]

Despite these encountered challenges, the catalytic conversion of lignin has remained a scientifically intriguing research problem that can bring clear rewards.[15] Lignin is the largest renewable source of aromatic building blocks in nature and has significant potential to serve as starting material for the production of bulk or functionalized aromatic compounds to offer suitable alternatives to the universally used, petroleum-derived BTX (benzene, toluene, and xylene).[11,16]

The quest for novel catalytic methods and lignin-derived platform chemicals[17,18] initiated tremendous activity in fundamental research, especially in the past decade. Creative approaches in many fields such as homogeneous catalysis,[19−22] heterogeneous catalysis,[11,23,24] or alternative solvents[25] have emerged and were extensively reviewed. Furthermore, recent reviews have summarized recent progress regarding thermochemical,[26−30] oxidative,[31,32] photocatalytic,[33] or biochemical[34,35] depolymerization methods that focused on conversion of lignin to various product classes.

In order to solve one of the greatest challenges, which is to deliver high product yields in an energy- and material efficient manner, integrated biorefinery approaches that bridge multiple disciplines are desired.[36,37] It has been shown that the native structure of lignin should be as regular as possible, which opens possibilities for modification of lignin biosynthesis pathways.[37,38] The selection of suitable processing conditions during lignocellulose fractionation has proven crucial, since fractionation methods may significantly alter the native lignin structure, frequently producing extremely refractory lignin streams.[39,40] It became clear, that the development of efficient catalytic methods for lignin depolymerization will play a central role in lignin valorization. Several promising catalytic methods have been developed, especially in recent years, and in many cases, the new methods delivered surprising new product structures in significant amounts.[37,40,41] Recent research has been devoted to the valorization of these structures, as well as other potential lignin-derived monomers, especially for the production of new lignin-based polymers.

The core of this review (section 2) summarizes the recent advances in chemical catalysis regarding the conversion of lignin to product mixtures that consist of a limited number of low molecular weight products in high yield, under 250 °C, and the lignin isolation methodologies used by the various research groups are compared. Where discussion requires, processes in the range of 250−300 °C are also included. In section 3, the possibilities for functionalization and defunctionalization of frequently encountered lignin-derived scaffolds are summarized. Section 4 provides an overview of the recently described applications of lignin-derived compounds for the production of biobased polymers and the properties of such polymers. In section 5, structures of known pharmaceutically active compounds that can be obtained from some of the monomers provided by the novel lignin depolymerization strategies are summarized along with existing synthetic routes.

Thus, this review gives an overview of existing value chains starting from the raw lignocellulose through catalytic lignin depolymerization to potential final application of lignin-based monomers and bridges heterogeneous and homogeneous catalytic or synthetic routes. Several structures may be, in the future, evaluated with respect to serving as "lignin-derived platform chemicals".

1.1. General Considerations

Lignin depolymerization is an intriguing task that is challenged by the structural complexity and recalcitrance of this aromatic biopolymer, which is randomly held together by strong C−C and

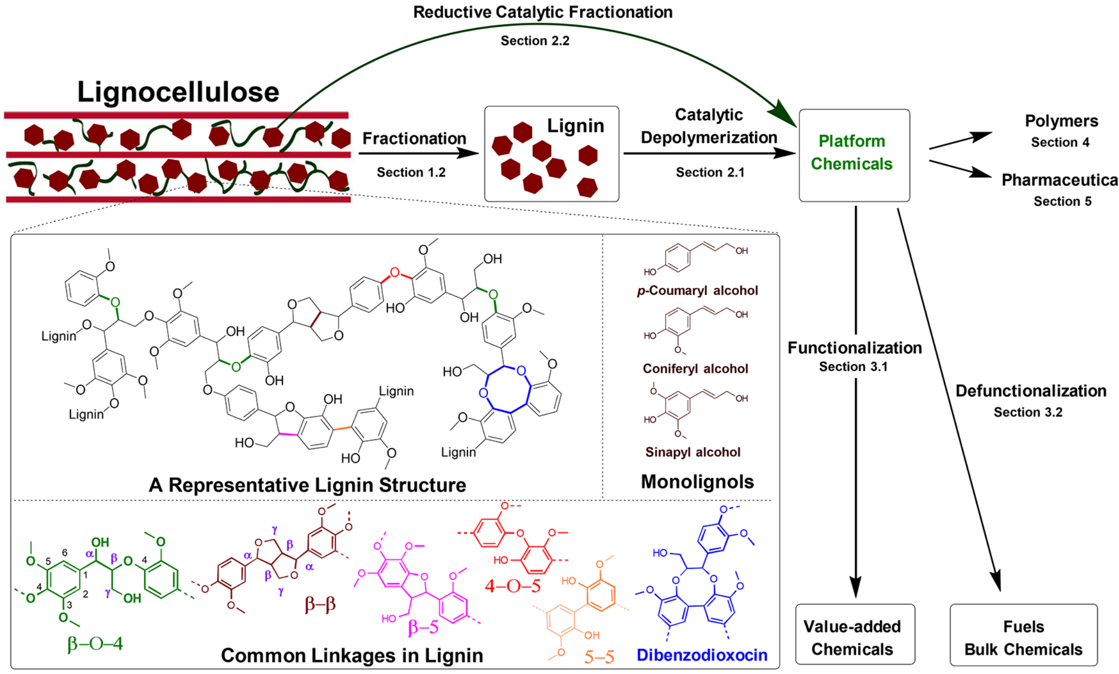

Figure 1. (Left) A representative lignin structure displaying typical lignin subunits and linkages encountered. (Right) General strategies for depolymerization of lignin and application of lignin-derived platform chemicals.

C−O bonds.[21] Several types of linkages exist in lignin, and their type and ratio is dependent on the plant source.[15] The most common linkages are shown in Figure 1. Systematic theoretical studies by Beckham determined the bond dissociation energies of the most representative lignin linkages.[42] The most recurring type is the β-O-4 linkage that typically makes up about 50% of all linkages and therefore has been the focus of most depolymerization strategies. The cleavage of this linkage takes between 68.2 and 71.8 kcal/mol, depending on substitution pattern. Any sustainable methodology aiming for lignin depolymerization should deliver specific (preferably) aromatic compounds in high enough yield and selectivity to allow separation and subsequent valorization to well-defined products. Since the β-O-4 linkage is most abundant, the vast majority of catalytic methods focus on the scission of the C−O linkage in this moiety in order to affect depolymerization.

1.2. Fractionation

1.2.1. Considerations Regarding Lignocellulose Pretreatment. Several methods are available for the isolation of lignin from lignocellulosic biomass. The existing strategies can be divided into two main categories related to the extent of structural modification induced in lignin by the fractionation conditions, an important aspect when considering catalytic valorization of any lignin feed.

One major source of lignin is provided by the pulp and paper industry that produces roughly 50 million tons of lignin annually, of which less than 2% is actually recovered for utilization as a chemical product.[43] However, the money equivalent of lignin used as fuel is estimated to be 0.18 US $/kg while 1.08 US $/kg in case it is converted to useful chemicals.[44] Thus, the importance of concentrating on the latter approach appears clear.

The second main lignin source is related to the production of cellulosic ethanol, which was estimated to make up 125 million liters for the year 2013 in the USA alone, and its volume is expected to grow. With every liter of produced ethanol 0.5−1.5 kg of lignin is cogenerated; however, it is still generally considered as waste and burned to produce energy.[45]

Techno-economic analysis of lignocellulose-based biorefineries was recently described.[46−54] In several cases, lignin was treated as waste or burnt for energy recovery;[49,52] however, more favorable carbon yields were found when lignin was valorized by hydrotreating, (hydro)pyrolysis, or gasification.[46−48]

Foust and Aden carried out a detailed techno-economic analysis of an ethanol biorefinery that operates based on cornstover (18% lignin content) with a 2000 dry tones/day capacity.[50] From one ton of cornstover, 340 L of ethanol was produced while the lignin byproduct was converted to 1.64 tons of steam and 326 kWh electricity of which 40% was used on the spot and 60% was sold for the grid. Besides sustaining the energy demand of the plant, 26.7$ worth of steam[55] and 13$ worth of electricity was generated next to the primary product bioethanol. However, it was concluded that if the energy demand of the process would be covered from other renewable resources such as wind or tidal energy, the lignin content could be utilized to produce chemicals, which hold more added value.

The summary report for biochemical ethanol production in 2013 and biochemical hydrocarbon production report in 2015 completed by the National Renewable Energy Laboratory with the Harris Group Inc., proposed improvements to already existing procedures in order to achieve the 2022 DOE target of 3$/gallon gasoline equivalent (GGE).[56,57] An important recommendation was to maximize the overall carbon efficiency by converting currently underutilized lignocellulose fractions, such as lignin. Four specific chemicals: 1,3-butadiene, 1,4-butanediol, cyclohexane, and adipic acid were suggested as potential valuable lignin-derived products with sufficient market volumes (greater than 1 MM tons/year world market). On the basis of a minimum fuel selling price (MFSP) of $5.10/GGE, the targeted $3/GGE can be achieved if 60−80% of available lignin is converted to coproducts adipic acid and 1,4-butanediol.

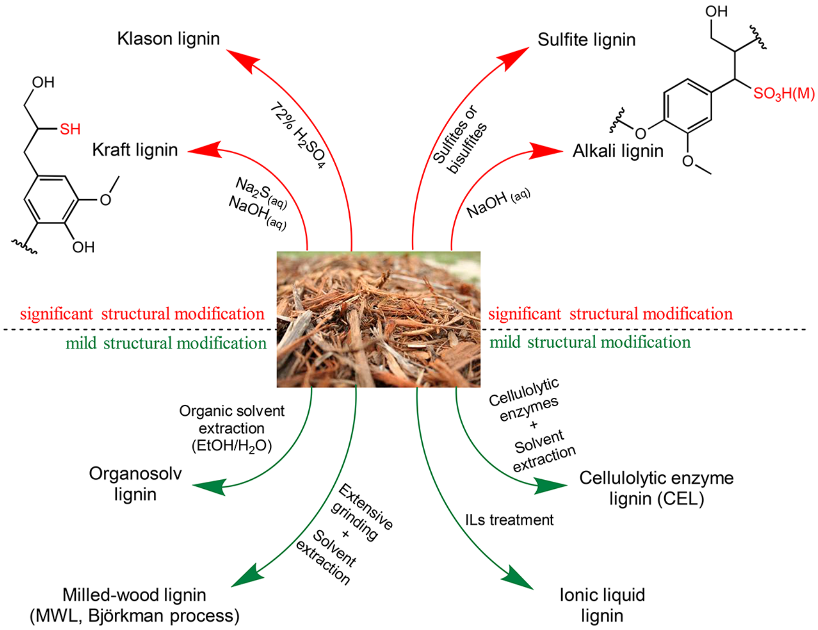

Figure 2. A summary of procedures for isolation of lignin from lignocellulose.

From the statements above, it is clear that in order to guarantee the economic feasibility of biorefinery processes, every lignocellulose component should be fully valorized,[58,59] and therefore it is of paramount importance to find novel ways of lignin valorization.[5,10,37,43] Before providing a detailed description of such new catalytic methods (section 2), we will give a short summary of the most important lignin isolation procedures used on the industrial and laboratory scale. This reviews the various lignin sources that can be used as starting materials in subsequent catalytic conversions.

1.2.2. Methods Resulting in Significant Structural Modification.

Pulping methods such as the Kraft,[60,61] the Sulfite,[39,62] the Alkaline,[63] and the Klason[64,65] process (Figure 2) generally focus on obtaining high quality cellulose from lignocellulose and result in structurally heavily modified lignins under relatively harsh processing conditions such as the extensive use of inorganic salts, base, or acid.[66,67] For instance, Kraft lignin is modified by cleavage of most α-aryl ether and β-aryl ether bonds[61] and in addition to recondensation reactions, the system is attacked by strongly nucleophilic hydrogen sulfide ions, leading to a sulfur-enriched structure (1.5−3% sulfur). The presence of sulfur poses an additional difficulty to catalyst development since it frequently leads to decreased activity of, especially, noble metal catalysts. Due to its abundance, there is increasing interest to develop novel catalytic methods for the efficient valorization methods of Kraft lignin to valuable chemicals[12,68,69] and fuels.[70] In this review, we do not focus on Kraft lignin depolymerization, since these novel approaches usually result in more complex product mixtures.[29]

Similarly to Kraft, sulfite lignin is also characterized by the incorporation of about 4−8% of sulfur, albeit in the form of sulfonate groups, providing water-soluble lignin. As a result, catalytic depolymerization of lignosulfonate to aromatics without it being negatively affected by sulfur is a challenging task. A promising solution is the catalytic removal of sulfur from the reaction system in the form of H_2S gas, as proposed by Song and co-workers with heterogeneous Ni catalysts.[71] The Klason process that employs 72% sulfuric acid causes a significant damage to the native lignin structure, while the soda pulping process presents structural modification to a lesser extent compared to the other technical lignins allowing for catalytic conversion, as reviewed recently.[24]

1.2.3. Methods Resulting in Mild Structural Modification.

Björkman Process. The Björkman process involves extensive grinding followed by extraction of lignin with an organic/aqueous solvent (usually dioxane/water 96/4 v/v for 24 h) to produce the so-called milled-wood lignin (MWL). This lignin has a more similar structure to native lignin due to the pH neutral and mild conditions used during extraction. However, the milling process can cause structural modification such as the presence of additional carbonyl and hydroxyl groups, especially in hardwood.[72] The obtained lignin yields, typically 20−40%, depend on the raw material used.[62]

Cellulolytic Enzyme Lignin and Enzymatic Mild Acidolysis Lignin (EMAL). The procedure to obtain cellulolytic enzyme lignin (CEL) involves the treatment of the finely ground wood with cellulolytic enzymes, which cause the partial hydrolysis of cellulose and hemicellulose. Afterward, the residue is extracted with a solvent (typically dioxane/water), the solution is concentrated, and lignin precipitated in water. This procedure typically requires a few days and leads to protein and carbohydrates impurities. An improvement is represented by enzymatic mild acidolysis lignin (EMAL), where the enzymatic treatment is combined with mild acidolysis of biomass.[73] This procedure is reported to offer gravimetric lignin yields 2−5 times greater than those of the corresponding MWL and CEL.[74] Interestingly, Guerra et al.[74] then investigated the differences in the lignins obtained by MWL, CEL, and EMAL treatment,[75] employing several raw materials and showed that EMAL is characterized by a highest molecular weight (M_n ~ 30000−63000 g/mol) followed by CEL (M_n ~ 17000−30000 g/mol) and MWL being the lowest value (M_n ~ 6000−16000 g/mol).

Ionic Liquid Treatment. It has to be mentioned that ionic liquids (IL) have also been proposed as solvents for lignocellulose fractionation due to their special and highly tunable solvent properties.[25,76−82] Limitations exist related to the cost of IL as well as ease of product separation and solvent recyclability. Interestingly, George et al.[80] reported the synthesis

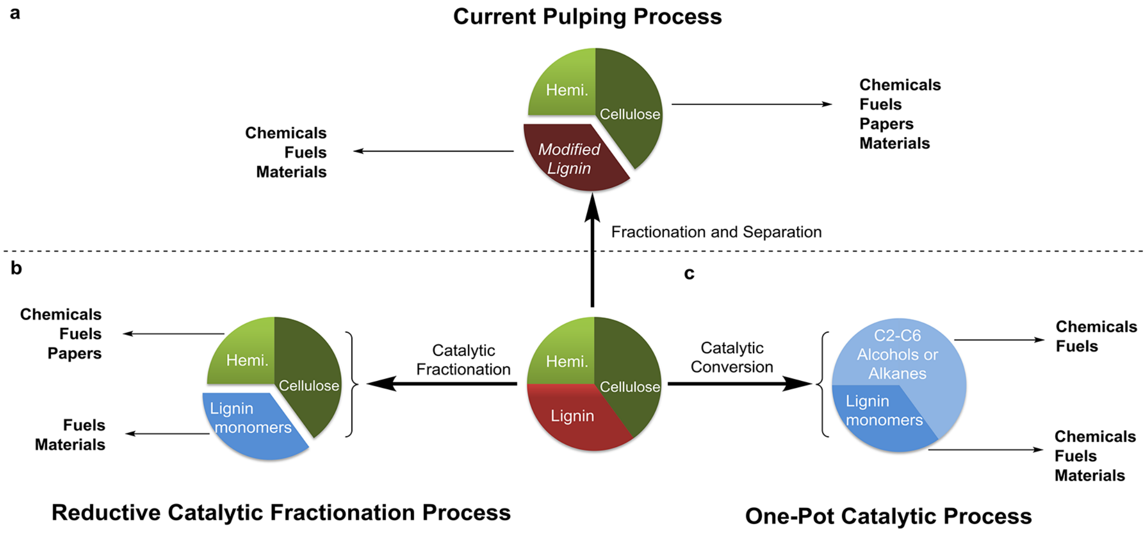

Figure 3. Types of starting materials used for the development of novel catalytic methods targeting high yield production of aromatics from lignin. (a) Isolation of lignin by lignocellulose fractionation prior to catalytic processing. (b) Reductive catalytic fractionation (RCF) using lignocellulose in the presence of a catalyst. (c) Complete conversion of all lignocellulose components by one-pot catalytic processing.

of several ethylammonium sulfate ILs resulting in efficient delignification without significant reduction of cellulose crystallinity. In addition, a production cost close to conventional organic solvents was shown. Furthermore, ILs can act as reaction media for lignin dissolution and depolymerization due to the incorporation of acidic or other catalytic properties.[83−87]

Organosolv Process. Organosolv lignin originates from treatment of lignocellulose with organic solvents such as ethanol, acetic acid, methanol alone, or mixed with water at 140−220 °C.[88] This delignification method is known to be more environmentally friendly compared to Kraft or sulphite lignin, especially when performed without added acid. The most well-known example is the Alcell process where a mixture of EtOH/water (1:1) is employed as the cooking medium at 175−195 °C for 1 h, enabling the dissolution of lignin and producing furfural as a byproduct.[89] Several variations have been reported, mainly in order to improve the yield of lignin, involving different solvent mixtures (including glycerol,[90] THF,[91−93] MeTHF,[94] and GVL[95]) and several catalysts (oxalic acid,[94] HCl,[96] Lewis acids,[97] metal chlorides,[98] and ammonia[99]), indicating varying efficiencies.[39,100] Typically, cleavage of the β-O-4 linkages occurs to a lesser extent compared to technical lignins, leading to a more nativelike structure, and the recovered materials are characterized by molecular weights (M_n) typically between 500 and 5000 g/mol[101−103] and good solubility in polar organic solvents.[18] However, organosolv processing does lead to partial degradation of the native structure and some decrease in the fraction of β-O-4 linkages, the extent of which depends on the plant source and specific reaction parameters used.[104]

However, the presence of repolymerization reactions and the formation of stable C−C linkages during organosolv processing is still inevitable, especially when a small amount of acid[105] is introduced to the system. The recent review of Rinaldi et al.[37] discusses several aspects of the influence of pulping conditions on the structure of resulting lignins in great detail. For instance, the gradual structural changes observable by HSQC NMR spectroscopy in acetolysis lignin upon low-, mild- and high-severity conditions are described. It was concluded that mild processing conditions (110 °C, no H_2SO_4, 15 min) produce nativelike lignin structure, while more severe conditions (160 °C, 0.6% H_2SO_4, 45 min) result in completely modified lignin structure, in which, besides the $-OCH_3$ and general aromatic signals, no beta-ethers are left. Another excellent way to provide a more quantitative description of the extent of structural modifications is to compare lignins originating from the same lignocellulose source but via a different treatment method by subjecting them to the same catalytic treatment conditions.[37] The yield of aromatic monomers thus obtained would correlate with the content of cleavable β-O-4 linkages (assuming that the catalytic methodology targets these linkages). The influence of processing conditions on the aromatic monomer yields obtained via acidolysis in conjunction with stabilization of reactive intermediates with ethylene glycol to produce C2 acetals (see also section 2) was also studied by Deuss, Barta, and co-workers.[101] It was confirmed that the highest monomer yields were obtained from lignins that were obtained by mild organosolv methods.

The addition of formaldehyde during organosolv processing as was reported recently by Luterbacher and co-workers (see section 2)[105] is an excellent approach to avoid repolymerization.

Thus far, specific methods of general applicability have not been developed, and the groups working on the development of novel catalytic methods typically reported on specific organosolv procedures prior to catalytic treatment (Figure 2). Indeed, structural modification during pretreatment is one of the greatest challenges in catalytic lignin valorization since the β-O-4 linkages are required for efficient depolymerization with the catalytic methods currently available. Therefore, the formation of more robust C−C bonds causes low efficiency of depolymerization and decreases monomer yields.

1.3. Types of Starting Materials

Generally, the catalytic methods targeting lignin depolymerization can be divided into three categories as illustrated in Figure 3 according to the nature of the starting material used for catalytic processing. Most research has focused on the conversion of lignin streams that were first isolated from the lignocellulose matrix usually by “organosolv processing”. A large quantity of similar lignin wastes can also be generated by the wood pulping process[106] or cellulosic ethanol production, however, as described in section 1.2, where both will result in lignins with

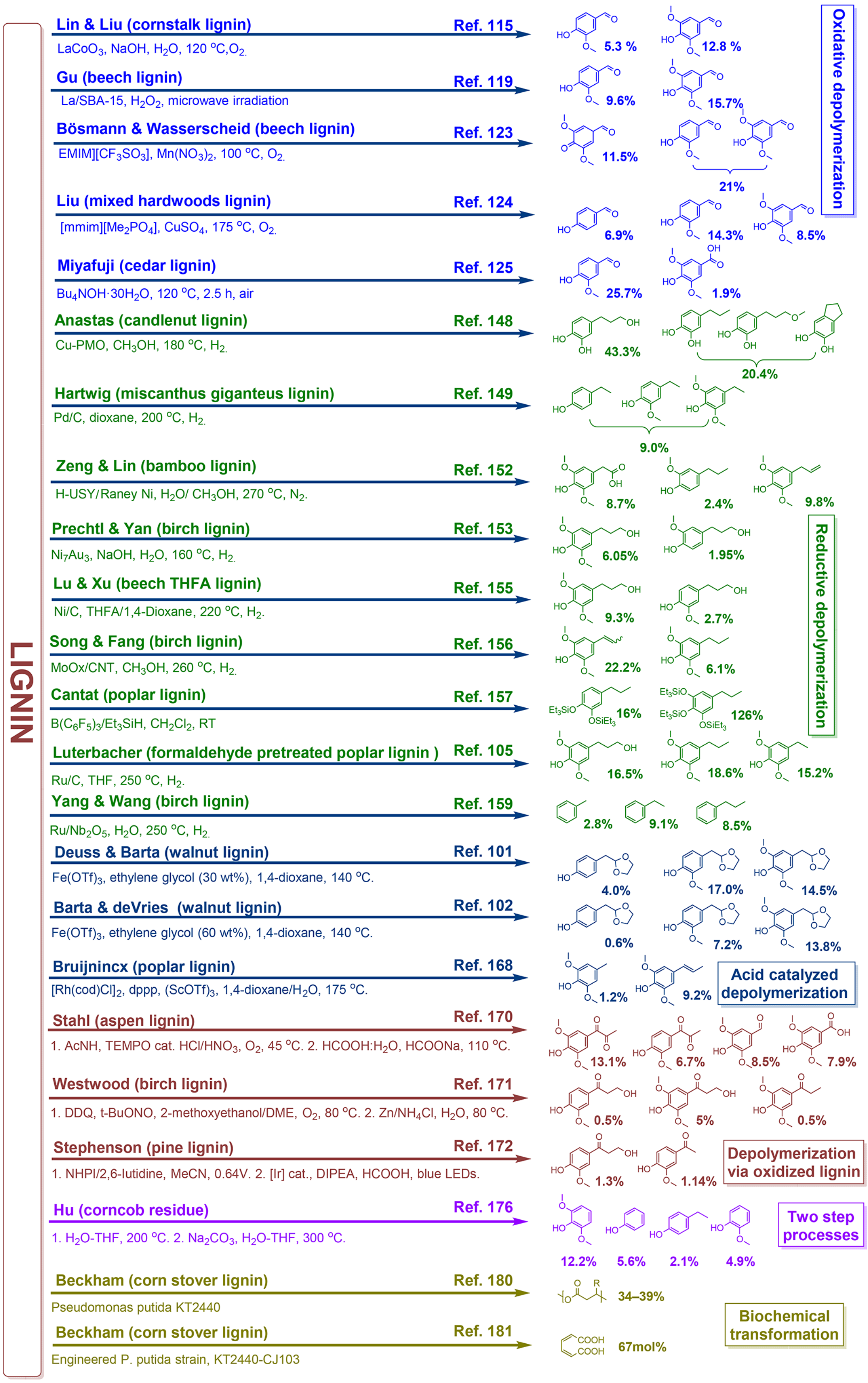

Figure 4. Strategies and yields of main products established for the depolymerization of lignins isolated from lignocellulose prior to catalytic treatment.

different degree of structural modification depending on the lignocellulose fractionation conditions.[37,101,107] Since the structure of lignin directly effects the monomer yield obtained,[101,105] novel methods enabling reductive catalytic fractionation (RCF) have recently emerged as promising alternative technologies (see section 2.2). These methods involve the extraction and immediate catalytic conversion of lignin to monomers in a one-pot process applying lignocellulose

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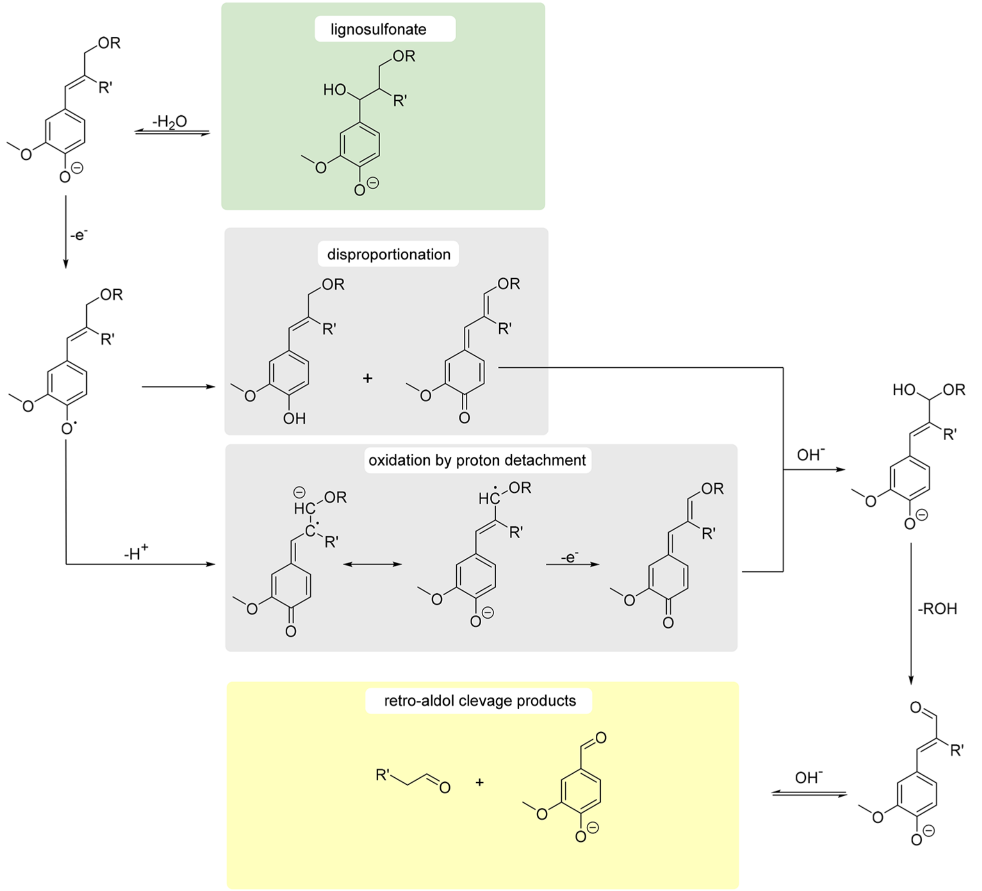


Figure 5. Proposed reaction mechanism for vanillin formation during alkaline oxidation of lignin. Reproduced with permission from ref 111. Copyright 2000, Springer Nature. Reproduced with permission from ref 112. Copyright 2004, Springer Nature.

directly in the presence of a catalyst usually under reductive conditions. The immediate catalytic processing of lignin, largely in its unmodified, native form, will result in higher yield of aromatic monomers due to the higher presence of cleavable C—O linkages and less C—C linkages. The products resulting upon reductive catalytic fractionation are a solid carbohydrate pulp plus the catalyst as solids, and a mixture of aromatic monomers, dimers and oligomers derived from catalytic lignin depolymerization in solution, as two easily separable fractions. Finally, it is also possible that lignocellulose itself is directly converted to (typically) mixtures of products both from the lignin as well as the cellulose fraction.

2. CATALYTIC STRATEGIES AIMING AT HIGH YIELD AND SELECTIVE PRODUCTION OF DEFINED AROMATIC MONOMERS FROM LIGNIN AND LIGNOCELLULOSE

2.1. Methods Using Lignins Isolated from Lignocellulose Prior to Catalytic Processing

In this section, we provide a detailed discussion of the novel catalytic methodologies that were developed using lignin isolated from lignocellulose using the organosolv, enzymatic processing or were obtained from biorefineries or as byproduct of paper production (Kraft lignin). An overview of these methods, which can be related to six main strategies, is shown in Figure 4.

2.1.1. Oxidative Depolymerization. In the past few years, novel strategies for oxidative depolymerization of lignin model compounds[19,31] or lignin have been developed,[32] including electrochemistry,[108] photocatalysis,[33] and use of heterogeneous catalysts[32] or ionic liquids.[25] Among these, several systems lead to high yield or selectivity of lignin-derived monomers. Oxidative strategies for lignin depolymerization, especially employing oxygen, hydrogen peroxide, or peroxyacids may become important and economically feasible delignification technologies, since oxidative methods are already widely employed in the papermaking industry for pulp bleaching.[31] Oxidative methods have the potential to use generally mild conditions; however, it requires sufficient selectivity to avoid overoxidation of the substrate to gaseous products. In addition, especially contrary to reductive depolymerization methods, oxidation reactions may lead to addition of functionalities to the already complex lignin-derived aromatic compounds, thereby increasing the possibility of formation of isomers that leads to increase of complexity of the obtained product mixtures. Also, processes involving radicals during oxidation may lead to decreased product yields due to lignin repolymerization. Ideally, oxidation methods should enable efficient depolymerization under mild conditions, directly converting lignin to specific fine chemicals bearing alcohol, aldehyde, or carboxylic acid moieties.[25,31,32]

The oxidative cleavage of lignin to produce vanillin is one of the oldest processes known in this field,[14,29] yet the reaction mechanism, which has been studied extensively[31,109] is still the subject of much debate. In 1977, Imsgard and co-workers[110] proposed several reaction pathways regarding selected lignin model compounds in alkaline media, involving oxygen or hydrogen peroxide. Later, Tarabanko and co-workers[111] performed mechanistic studies involving lignosulfonate as well as a range of model compounds such as lignosulfonates, eugenol, isoeugenol, guaiacylethanol, and guaiacylpropanol and postulated a reaction mechanism (Figure 5),[112,113] which suggests that vanillin is formed through a retro-aldol condensation as last step and the process involves several unsaturated intermediates. It can be generally concluded that the vanillin yield crucially depends on pH as well as oxygen concentration.

Considering the high activity and stability of perovskite-type oxides in the catalytic oxidation of hydrocarbons, Liu, Lin, and co-workers found that $LaMnO_3$ and $LaCoO_3$ are highly active and robust non-noble metal catalysts for the catalytic wet aerobic oxidation (CWAO) of lignin to aromatic aldehydes.[114,115] In these studies, $LaMnO_3$ and $LaCoO_3$, prepared by sol−gel method, enhanced the selectivity toward vanillin (**M1G**) (~5%) and syringaldehyde (**M1S**) (~10%) compared to most other oxidative methods and noncatalytic oxidation (see supplementary Table S1 for structures, codes and names of identified lignin monomers). Changes in lignin conversion or in aromatic aldehyde yield were not observed even after five successive catalytic runs. Although the precise role of this catalyst system in lignin oxidation has yet to be elucidated, XPS and TPR measurements confirmed the existence of surface bound Mn^{4+}/Mn^{3+} (for $LaMnO_3$) and Co^{3+}/Co^{2+} (for $LaCoO_3$) redox couples as well as chemisorbed oxygen, which were proposed to play a crucial role in achieving high activity and selectivity. Lignin conversions were in the range of 40−60%, while the yield of identified aromatic products were lower likely due to competing oxidation pathways that lead to gaseous products. The authors have also found that addition of 10−20% Cu dopant to the $LaCoO_3$ catalyst increased the surface chemisorbed oxygen species in this perovskite type catalyst.[116] As a result the maximum yield of *p*-hydroxybenzaldehyde (**M1P**), vanillin (**M1G**), and syringaldehyde (**M1S**) increased to 2.8%, 5.3%, and 12.8%, respectively. The use of Cu as dopant in steam reforming, oxidative steam reforming, CO oxidation, and NO reduction was also reported.[117,118]

Gu and co-workers[119] have developed a new method using La/SBA-15 as heterogeneous catalyst and hydrogen peroxide as an environmentally friendly and low-cost oxidant, for the efficient oxidation of organosolv beech lignin yielding vanillin (**M1G**, 9.6%) and syringaldehyde (**M1S**, 15.7%) under microwave irradiation.

Pinto and co-workers[120] have studied the oxidative degradation of Eucalyptus globulus pulping liquors obtained upon different stages of industrial Kraft liqueur processing compared to isolated lignins in the presence of oxygen in an alkaline medium. Syringaldehyde (**M1S**) and vanillin (**M1G**) were found as main products, alongside with smaller amounts of the corresponding acids. The best **M1S** yield (10.3%) was obtained starting from Kraft lignin.

Wang and co-workers[121] described the use of cerium oxide-supported palladium nanoparticles (Pd/CeO_2) in the oxidative conversion of 2-phenoxy-1-phenylethanol in the presence of O_2 to produce phenol, acetophenone, and methyl benzoate as major products. The Pd nanoparticles played a crucial role in the selective oxidation of the secondary alcohol moiety to the corresponding ketone. Subsequent C−O bond cleavage afforded phenol and acetophenone. Oxidative cleavage of the $C_\alpha-C_\beta$ bond also took place producing benzoic acid, which was, in the presence of methanol as solvent, further converted to methyl benzoate. The Pd/CeO_2 catalyst could also catalyze the oxidative conversion of organosolv lignin, albeit obtaining products different from model studies: under mild conditions (185 °C, O_2 1 bar), vanillin (**M1G**, 5.2%), guaiacol (**M24G**, 0.87%), and 4-hydroxybenzaldehyde (**M1P**, 2.4%) were obtained.

Ionic liquids (IL) have shown promise in oxidation of lignin model compounds, promoting the cleavage of strong aromatic ether bonds.[122] Bosmann, Wasserscheid, and co-workers[123] have found that $Mn(NO_3)_2$ in 1-ethyl-3-methylimidazolium trifluoromethanesulfonate $[EMIM][CF_3SO_3]$ results in the formation of a unique and relatively simple product mixture consisting of aromatic aldehydes, phenols, and unsaturated propyl-aromatics under mild conditions (100 °C). Interestingly, 2,6-dimethoxy-1,4-benzoquinone (**M2S**) was isolated as a pure compound in 11.5 wt % yield by a simple extraction/crystallization procedure.

An interesting catalyst system relying on the use of several dimethylphosphonium-based ionic liquids and $CuSO_4$ as metal catalyst was developed by Liu et al.[124] Key for obtaining a high total yield (30%) of aromatic aldehydes was the use of an IL/methyl isoutyl ketone (MIBK) biphasic system, whereby the continuous separation of the aromatic products to the extraction phase (MIBK) from the oxidation phase (IL) avoided their over oxidation. The experiments were performed in a batch reactor and the best results, e.g. 100% conversion, and nearly 30% total yield of aromatic aldehydes (**M1S, M1G, M1P**) were achieved with $[MMim][Me_2PO_4]$ and $[mPy][Me_2PO_4]$. In addition, after easy product separation the IL phase demonstrated good reusability.

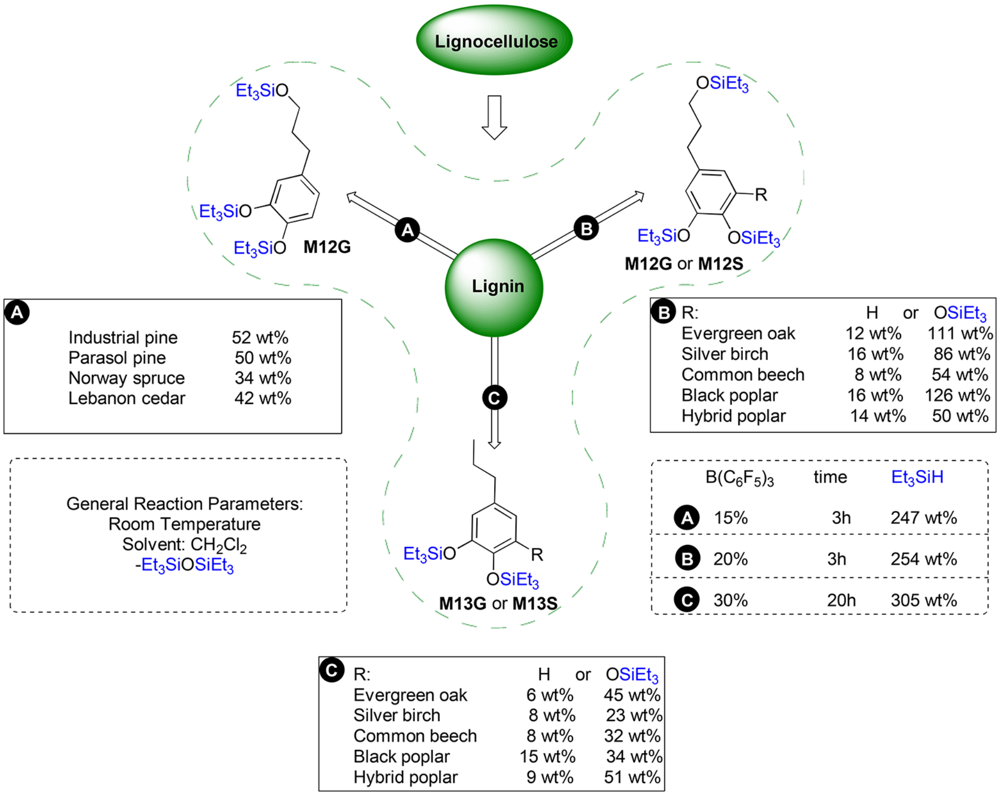
Recently, Miyafuji et al.[125] found that using $Bu_4NOH{\cdot}30H_2O$ (tetrabutylammonium hydroxide 30-hydrate) instead of the commonly used aqueous NaOH solution during aerobic oxidative degradation of lignin improved the yield of aromatic monomers. At 120 °C, total monomer yield of 6.5−22.5% was obtained with vanillin (**M1G**) and vanillic acid (**M20G**) as the main products.

2.1.2. Reductive Depolymerization.

Reductive treatment of lignin dates back to early works on structural elucidation, when lignin was treated in the presence of CuCr catalysts[126−128] under relatively harsh reaction conditions (250−260 °C, 220−240 bar), to obtain aliphatic compounds (mainly 4-propylcyclohexanol **M3**) which were isolated and characterized mainly based on boiling or melting points and elemental analyses.

Reductive approaches[552] require catalysts capable of selective scission of C−O bonds leading to depolymerization.[129] This approach is attractive since the stepwise reductive deoxygenation of the aromatic monomers obtained after depolymerization generally leads to a decrease of complexity in the product mixtures, increasing the selectivity to defined aromatic compounds.[130] A factor decreasing selectivity, on the other hand, is the presence of competing ring hydrogenation reactions, which is one of the major challenges related to this method. To this end, novel catalysts that do not lead to over-reduction of the obtained aromatic monomers have also been developed, for example a PdFe/C catalyst, which exhibits a high selectivity to benzene without ring saturation or ring opening.[131−133] At this point it should be mentioned that total and selective hydrogenation/deoxygenation would provide clean mixtures of alkanes (mainly C9 cycloalkanes) as demonstrated by the two step method developed by Kou and co-workers,[134] as well as recent elegant work of Yang[135] and Lercher and Zhao.[136−142]

Excellent recent reviews provide a comprehensive overview of reductive depolymerization of lignin and model compounds by both homogeneous and heterogeneous catalysts.[11,21,24] Reductive approaches generally use hydrogen gas or hydrogen-donor solvents and mainly focus on the production of bio-oils and fuels.[143−147] In this section, we focus on systems that use lignin



A

Industrial pine	52 wt%
Parasol pine	50 wt%
Norway spruce	34 wt%
Lebanon cedar	42 wt%

B

R:	H	or	OSiEt$_3$
Evergreen oak	12 wt%		111 wt%
Silver birch	16 wt%		86 wt%
Common beech	8 wt%		54 wt%
Black poplar	16 wt%		126 wt%
Hybrid poplar	14 wt%		50 wt%

General Reaction Parameters:
Room Temperature
Solvent: CH_2Cl_2
-Et$_3$SiOSiEt$_3$

	$B(C_6F_5)_3$	time	Et$_3$SiH
A	15%	3h	247 wt%
B	20%	3h	254 wt%
C	30%	20h	305 wt%

C

R:	H	or	OSiEt$_3$
Evergreen oak	6 wt%		45 wt%
Silver birch	8 wt%		23 wt%
Common beech	8 wt%		32 wt%
Black poplar	15 wt%		34 wt%
Hybrid poplar	9 wt%		51 wt%

Figure 6. First example of transition metal free, room temperature reductive depolymerization of formacell lignin using $B(C_6F_5)_3$/Et$_3$SiH.

directly for the production of monomeric phenols in high yield and selectivity, typically below 250 °C.

One of the first reductive systems displaying high isolated yield for specific aromatic compounds was described by Anastas and co-workers[148] under mild reaction conditions at 140−180 °C. In this work, organosolv lignin extracted from candlenut shells was depolymerized to well-defined aromatic monomers over copper-doped porous metal oxide (CuPMO) in the presence of hydrogen gas (50 bar). The main product at 140 °C was 4-propanolcatechol (**M4**) that was isolated by column chromatography in 43.3% yield and the total monomer yield reached 63.7%.

Hartwig and co-workers[149] reported that complex β-O-4 model compounds can be selectively cleaved by commercially available Pd/C catalyst resulting in acetophenone or ethyl-substituted arenes and phenols. The process occurred through dehydrogenation of the secondary alcohol in the β-O-4 moieties, followed by hydrogenolysis of the alkyl C−O bond through the hydrogen generated in the first step. When applied to organosolv lignin, the addition of a small amount of hydrogen was necessary as the presence of olefins in natural lignin samples consumed the generated hydrogen. Under optimized conditions, acetonesolv lignins from *miscanthus giganteus* produced 12−15% combined yields of seven major products and 9% yield of alkyl-substituted phenols (4-ethylphenol **M6P**, 4-ethylguaiacol **M6G**, and 4-ethylsyringol **M6S**) was obtained from pine lignin.

Samec and co-workers developed a robust catalyst system for cleavage of C−O bond in lignin β-O-4 linkages in model compounds that used Pd/C and formic acid as a reducing agent under very mild reaction conditions (80 °C in air).[150] Further degradation experiments with organosolv lignin revealed partial lignin depolymerization to lower molecular weight species based on GPC analysis. Interestingly, the group has found that the addition of catalytic amounts of a hydrogen source (e.g., HCOOH, NH_4HCO_2, 2-propanol, and $NaBH_4$) was sufficient to promote the redox neutral cleavage of the β-O-4 linkage.[151]

Similarly to the reactivity of Pd/C, a dehydrogenation/hydrogenation sequence can be also implemented using Raney Ni, as was demonstrated by Lin and co-workers[152] in the depolymerization of cellulolytic enzyme lignin from bamboo without addition of any external hydrogen source. Compared to the use of Raney Ni alone, the combination of Raney Ni and zeolites lead to an increased yield of phenolic monomers, which mainly included 4-propylguaiacol **M7G**, 4-hydroxy-3,5-dimethoxy-benzeneacetic acid **M8S**, and 4-allyl-2,6-dimethoxyphenol **M9S** (12.9% to 27.9%), and more than 60 wt % bio-oil yield was achieved under optimized conditions (270 °C, 1 atm N_2). The authors concluded that a synergistic effect exists as this catalyst combination lead to highly efficient depolymerization while minimizing the formation of undesired high molecular weight polymers.

Yan and co-workers[153] studied the influence of pH in the range of 1 to 14 on the reductive depolymerization of lignin using Ni_7Au_3 catalyst in water and found a positive correlation between the rate of hydrogenolysis and increasing pH values. In an experiment using organosolv lignin from birch sawdust and Ni_7Au_3 catalyst under 10 bar hydrogen at 160 °C, the total monomer yield increased from 7.6% to 10.9% after addition of NaOH. The main products included 4-propylguaiacol (**M7G**), 4-propanolguaiacol (**M10G**), and 4-propanolsyringol (**M10S**) and the addition of base accounted for more selective depolymerization. After characterization by TEM, UV−vis, and XPS, the catalyst itself was found structurally and chemically unchanged after the addition of NaOH. The authors concluded that the basic reaction medium leads to an increase of selectivity as the base hinders the coordination of the bulky aromatic ring to the catalyst, thereby inhibiting arene hydrogenation. More impor-

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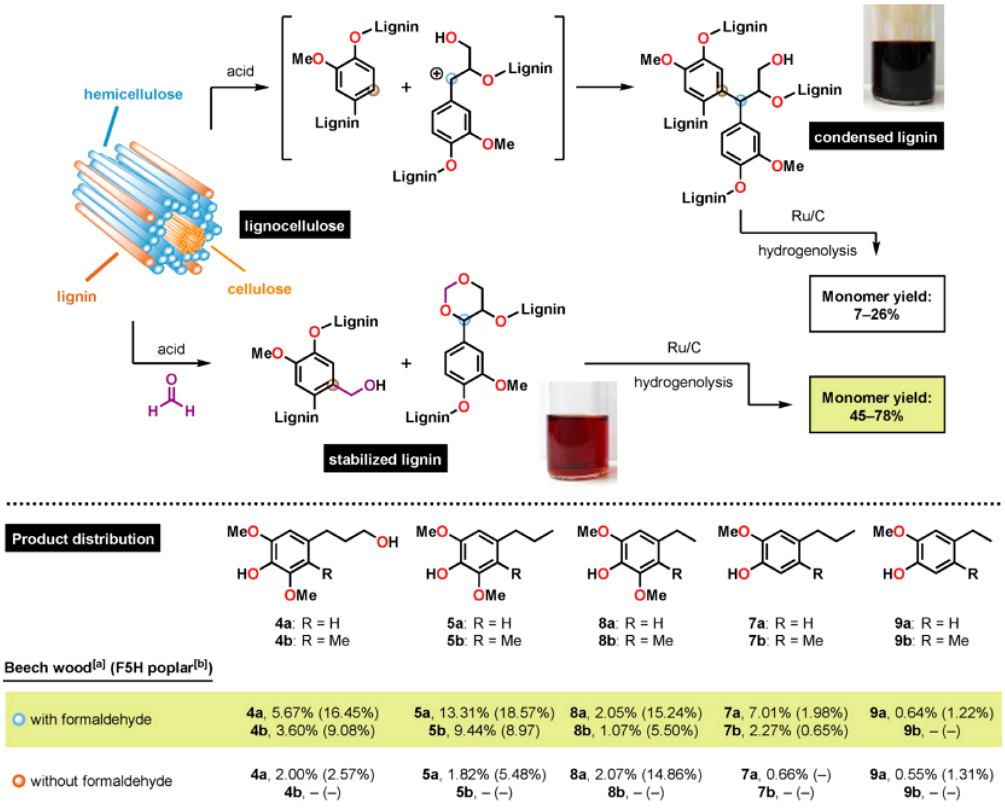


Beech wood[a] (F5H poplar[b])					
○ with formaldehyde	**4a**, 5.67% (16.45%) **4b**, 3.60% (9.08%)	**5a**, 13.31% (18.57%) **5b**, 9.44% (8.97)	**8a**, 2.05% (15.24%) **8b**, 1.07% (5.50%)	**7a**, 7.01% (1.98%) **7b**, 2.27% (0.65%)	**9a**, 0.64% (1.22%) **9b**, – (–)
○ without formaldehyde	**4a**, 2.00% (2.57%) **4b**, – (–)	**5a**, 1.82% (5.48%) **5b**, – (–)	**8a**, 2.07% (14.86%) **8b**, – (–)	**7a**, 0.66% (–) **7b**, – (–)	**9a**, 0.55% (1.31%) **9b**, – (–)

Figure 7. Highly efficient catalytic conversion of lignin through formaldehyde stabilization (top) and product distribution for beech wood and F5H poplar lignin with or without formaldehyde stabilization (bottom). Reprinted with permission from ref 158. Copyright 2017 Wiley-VCH.

tantly, the depolymerization of organosolv lignin into aromatic monomers is enhanced considerably using NaOH as an additive.

On the other hand, Singh and Ekhe[154] have investigated the effect of solid acids on depolymerization. The research group developed a one-pot process using Cu/Mo loaded ZSM-5 catalyst for the production of alkyl phenols using methanol as a hydrogen donor, and water was used as cosolvent. At 220 °C, Kraft lignin was almost fully converted (>95%) after 7 h, and only a little amount of char (<0.5%) was formed. The products were then analyzed on a GC-MS/FID, which showed 3-methoxy-2,5,6-trimethyl phenol (**M11**) as the predominant product with a high selectivity (70.3%) in the reaction catalyzed by Cu/Mo-ZSM-5 with a solvent ratio of 1:1 (methanol/H_2O).

Xu and co-workers[155] found that treating woody biomass (170–200 °C) in the combination of tetrahydrofurfuryl alcohol (THFA) and water in the absence of acid, leads to 92.8% yield of good-quality cellulose and high yield of lignin (77.4%), simultaneously. Because no acid was used, high-quality lignin was obtained with high retention of β-O-4 linkages that was well-suited for obtaining a high yield of aromatic monomers upon catalytic treatment. Hydrogenolyis using Ni/C at 220 °C resulted in a total monomer yield of 14.7% (mainly **M10G** and **M10S**).

Song and co-workers[156] reported a low-cost nanostructured MoOx/CNT catalyst that is comparable to precious-metal-based catalysts in terms of activity, reusability, and biomass feedstock compatibility. High aromatic product yield (up to 47%) was obtained from enzymatic mild acidolysis lignins (EMALs). Interestingly, unsaturated monomeric phenols (**M18G** and **M18S**) were obtained in high yields.

Cantat and co-workers[157] presented the first example of reductive depolymerization of lignin under metal-free conditions at room temperature to obtain well-defined aromatic products in high yield (Figure 6). In place of hydrogen gas, hydrosilanes were used as reductants and $B(C_6F_5)_3$ as a Lewis acid catalyst. This versatile approach could be successfully applied to different lignin species extracted by a formacell process, which included 15 gymnosperms and angiosperms woods. Several aromatic products (**M12G**, **M12S**, **M13G**, and **M13S**) were obtained in excellent selectivity, depending on wood type, and the isolated yield ranged from 7–24 wt % based on lignin or 0.5–2.4 wt % based on lignocellulose. In order to evaluate the efficiency of the depolymerization step, it is important to estimate the maximum yield of monoaromatics from lignins. Thus, the authors also included a more quantitative assessment of the theoretical yield based on equation 1 in order to determine the efficiency of depolymerization:

$$Y = \frac{(N-2)P^2 + 2P}{N} \times 100 \tag{1}$$

where Y represents the theoretical yield of total monomers, N is the number of monomers occurring in the polymer chain, and P corresponds to the cleavable linkages (e.g., α-O-4 and β-O-4 linkages). On the basis of this calculation, depolymerization with the hydrosilane–$B(C_6F_5)_3$ systems showed an efficiency of 28 to 85% depending on the wood source and the targeted product.

As mentioned in section 1.2, lignocellulose pretreatment inevitably modifies the native structure of lignin, by formation of robust C–C linkages.[158] To minimize this structural modification Luterbacher and co-workers[105] devised an elegant strategy that involved addition of formaldehyde during biomass pretreatment, leading to a soluble lignin fraction that could be subsequently converted by reductive treatment to a mixture of guaiacyl and syringyl monomers at near theoretical yield. As

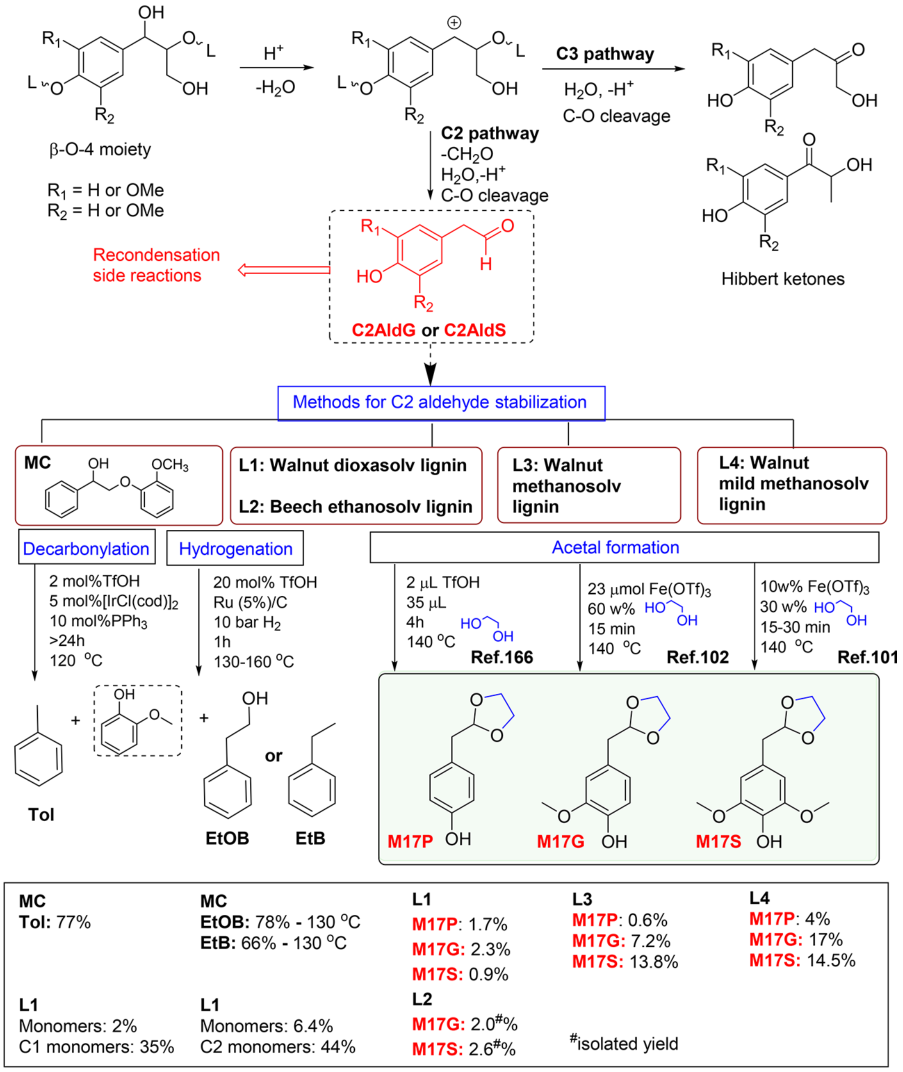


Figure 8. Acid catalyzed depolymerization of lignin in conjunction with stabilization of reactive C2-aldehydes. Comparison of the yields of aromatic C2-acetals obtained by the addition of ethylene glycol obtained from various lignin sources.

shown in Figure 7, the role of the formaldehyde was to stabilize the native lignin structure via the formation of a 1,3-dioxane moiety. The lignin obtained this way was substantially lighter in color compared to the lignin obtained in the absence of formaldehyde, qualitatively confirming the lack of recondensation processes. After hydrogenolysis with Ru/C at 200 °C for 6 h, a combined yield of 45% of monomeric species (mainly **M7S**, **M7G**, **M10S**, and methylated analogues) was achieved from the isolated beech lignin extracted with formaldehyde, whereas in the absence of formaldehyde, a much lower 7% monomer yield was obtained. With "formaldehyde stabilized" poplar lignin a monomer yield (mainly **M6S**, **M7S**, **M10S**, and methylated products) as high as 78% was achieved upon hydrogenolysis with Ru/C at 250 °C.

Very recently, Wang and co-workers[159] developed a catalytic method that enabled the complete removal of oxygen content and resulted in liquid aromatic hydrocarbons with a yield of 35.5 wt % from lignin. Remarkably, a near-quantitative carbon yield was observed when using birch lignin, and the selectivity to arenes (methylbenzene **M14**, ethylbenzene **M15**, and propylbenzene **M16**) was as high as 71 wt %. The arenes were obtained by direct hydrodeoxygenation of organosolv lignin over a porous Ru/Nb_2O_5 catalyst in water at 250 °C. A combined inelastic neutron scattering (INS) and density functional theory (DFT) calculation analysis confirmed the existence of an active Nb_2O_5 species, and the catalytic activity was attributed to the combination of strong adsorption and selective activation of the phenols and a synergistic effect between the Ru and NbO_x species.

Besides using hydrogen gas or other reducing reagents, Wang and co-workers found that the aliphatic alcohol moieties (C_αH—OH) in lignin itself can act as the hydrogen donor.[160] Lignin β-O-4 linkages were initially dehydrogenated on $ZnIn_2S_4$ to form a "hydrogen pool", and the adjacent C_β—O bond subsequently underwent hydrogenolysis by hydrogen derived from the "hydrogen pool". With this strategy, 71—91% yield of phenols in the conversion of lignin β-O-4 models and a 10% yield of *p*-hydroxy acetophenone derivatives were obtained from organosolv lignin.

2.1.3. Acid-Catalyzed Depolymerization in Conjunction with Stabilization of Reactive Intermediates.

The first acid-catalyzed lignin hydrolysis reaction was reported in 1924 by Hägglund and Björkman[161] when they distilled lignin with 12% hydrochloric acid and attempted to obtain thiobarbituric acid, phloroglucinol, and barbituric acid. More recently, different types of acids including mineral and Lewis acids, zeolites, ionic liquids

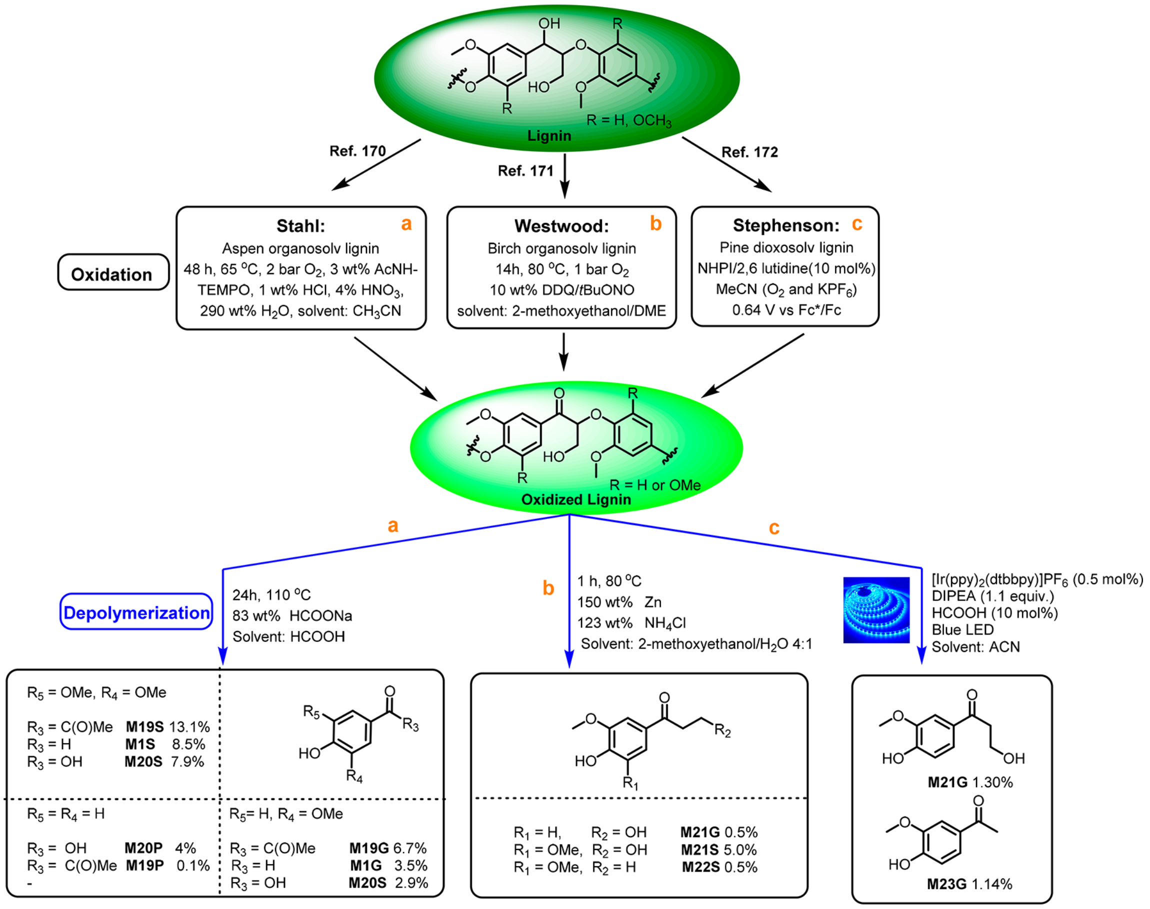


Figure 9. Selective oxidation and cleavage of isolated lignin into monomeric aromatic products.

with Bronsted acidic functionalities, as well as organic acids have been tested for depolymerization of lignin and these were summarized in recent reviews of Zhang,[24] Barta,[21] Yokoyama,[162] and Weckhuysen.[11]

Pulping under acidic conditions is one of the most classical methods used for the fractionation of lignocellulose into its main components.[21] In early days, acidolysis was relevant regarding the structural determination of lignin.[163−165] During these studies it became apparent that treatment of lignin with acid resulted in low yield of aromatic chemicals, and recondensation of the formed fragments were observed under these reaction conditions. However, the precise reasons for these phenomena were not fully elucidated. Barta, de Vries, and co-workers have established that triflic acid, even in catalytic amounts, is very efficient in cleaving the *β*-O-4 linkage in lignin model compounds.[166] Labeling studies revealed that the formed C2-aldehyde products undergo recondensation reactions under depolymerization conditions and are one of the reasons for the formation of high molecular weight side products. To prevent this, a stabilization strategy was developed that entailed the in situ conversion of the reactive C2 aldehydes to more stable products, leading to well-defined classes of aromatic chemicals. By "trapping" the aldehyde by addition of ethylene glycol, the corresponding (more stable) C2-acetals were obtained. Alternatively, catalytic hydrogenation of the C2 aldehyde lead to the corresponding ethanol-aromatics (**EtOB**) or ethyl-aromatics (**EtB**), and decarbonylation resulted in methyl-aromatics, such as toluene. Applying these methods on actual dioxasolv lignin resulted in a decrease of undesired side products and the same classes of aromatics as found in model compound studies. Especially the acetal formation method gave a 3-fold increase in monomer yields relative to the control experiments and acetals (**M17P**, **M17G**, **M17S**) as main products. Next, Barta and Westwood developed scalable synthetic routes to next generation model compounds combining the *β*-O-4 as well as the *β*-5 linkages and have all functionalities to serve as realistic models of the lignin structure. An in-depth research using such advanced lignin models confirmed that ethylene glycol also plays a role in "trapping" the formaldehyde released both from the *β*-O-4 as well as the *β*-5 linkage.[167] Importantly, it was possible to quantify the amount of released formaldehyde in model and lignin reactions via the corresponding 1,3-dioxolane formed. Later the reactivity of a broad range of metal triflates was evaluated,[102] and it was found that $Bi(OTf)_3$, $Fe(OTf)_3$, and $Hf(OTf)_4$ performed the best for the depolymerization of methanosolv walnut lignin to three major aromatic products (**M17P**, **M17G**, and **M17S**). The best aromatic monomer yield of 19.3 wt % was obtained with $Fe(OTf)_3$. Aiming to further increase the yield of phenolic monomers, lignins obtained from a range of different biomass sources and pretreatment methods were investigated.[101] After screening a library of 27 lignins obtained from 13 different pretreatment methods, it was found that a *β*-aryl ether rich organosolv lignin gave the best combined yield of up to 35.5 wt % of acetal products and the best yield of a single component (**M17G**, 16.5 wt %) was achieved starting from walnut lignin obtained by a specially developed, mild organosolv procedure (Figure 8).

In line with the previous strategy, Bruijnincx and co-workers[168] described the tandem acidolysis/decarbonylation using water-tolerant Lewis acids to promote depolymerization and a homogeneous Rh complex to enable decarbonylation of the C2-aldehyde formed in the first step. The method was established using model compounds and subsequently applied to dioxasolv lignin, isolated from brewer's spent grain. Poplar dioxasolv lignin was successfully depolymerized using $Yb(OTf)_3$ to obtain an overall monomer yield of 12.4% at 175 °C in dioxane/H_2O and the major products were 4-(1-propenyl)-phenols (**M18G** and **M18S**).

2.1.4. Highly Efficient Depolymerization via Oxidized Lignin.

Innovative two-step methodologies lead to efficient lignin depolymerization relying on cleavage of the most abundant β-O-4 unit by selective preoxidation of the secondary alcohol followed by a reductive C−O ether bond rupture. The rationale behind preoxidation is that it decreases the bond dissociation energy of the C−O bond and therefore makes the β-O-4 linkage more labile. An analogous Ru-catalyzed hydrogen neutral method on simplified lignin β-O-4 model compound resulted in efficient cleavage of the phenyl ether bond, resulting in the formation of acetone and guaiacol.[169]

Following this strategy, Stahl and co-workers[170,173] have achieved very efficient lignin depolymerization. The secondary alcohol in the β-O-4 linkage was first selectively oxidized to the corresponding ketone using catalytic amount of 4-acetamido-TEMPO/HNO_3/HCl under aerobic conditions (Figure 9, left). This oxidization step activated the linkage for the desired C−C or C−O bond scission in the second step that was accomplished by an excess of sodium formate in aqueous formic acid (85−90 wt %) at 110 °C. With this method, cellulolytic enzyme lignin from aspen wood was successfully converted to low-molecular-mass aromatics (mainly **M1S**, **M19S**, **M19G**, and **M20S**) in more than 60 wt % yield.

Westwood and co-workers[171] presented a new approach using selective oxidation of the secondary alcohol in a β-O-4 moiety (Figure 9, middle). This methodology used molecular oxygen as the oxidant and catalytic amounts of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and *tert*-butyl nitrite (tBuONO). Upon preoxidation, Zn/NH_4Cl was applied in the second step at 80 °C. In this case, birch lignin was converted to phenolic monomer (**M21S**) and the major product was also isolated in a 5 wt % yield. This two-step method for lignin depolymerization could also be conducted in one-pot.

The concept of utilizing solar energy via photocatalysis under mild conditions is one of the most intriguing strategies for lignin depolymerization.[33] In addition, electrochemical oxidation is an environmentally benign alternative to chemical oxidations due to the absence of chemical oxidants in the reaction media.[174] Combining these two emerging technologies, Stephenson and co-workers presented the first electrocatalysis/photoredox catalysis sequence for the depolymerization of lignin in a two-step, one-pot process at ambient temperature, which is conceptually related to the works of Stahl and Westwood (Figure 9, right).[172] The work first explored different hydrogen transfer mediators for the selective oxidation of the benzylic position in β-O-4 lignin dimers under electrocatalytic conditions. Then, a NHPI/2,6-lutidine-catalytic system was found to be more efficient for the oxidation of 1-(3,4-dimethoxyphenyl)-ethanol. The scope of this methodology was examined on a variety of different lignin models and isolated pinewood lignin. The two-step protocol could also be conducted on a large scale. For example, when using 0.5 g lignin β-O-4 model compound, a 67% yield of ketone and a 67% yield of guaiacol was obtained. When lignin isolated from pine wood with dioxane was subjected to optimized (one-pot) reaction conditions, two monomers with the yield of 1.30% (**M21G**) and 1.14 wt % (**M23G**) were obtained, respectively.

This two-step methodology is suitable for dissociating interlinking lignin units; however, researchers following this strategy mainly focused on the scission of β-O-4 linkages. In order to improve the efficiency of lignin conversion, the transformation of other ether linkages should also be taken into consideration. With this in mind, Wang and co-workers[175] recently reported a two-step oxidation−hydrogenation strategy which was also able to cleave the α-O-4 linkages. In the first step, an organocatalytic system O_2/$NaNO_2$/DDQ/NHPI was used to oxidize the (C_αH−OH) moieties in lignin. In the second step, the obtained preoxidized β-O-4 as well as the α-O-4 moiety was further hydrogenated over a NiMo sulfide catalyst, leading to the cleavage of C_β−OPh and C_α−OPh bonds to aromatics. This system worked well for β-O-4 lignin models; however, an organosolv lignin isolated from birch powder gave lower monomer yield (<5%). This sharp contrast was attributed to new connections among isolated lignin molecules caused by hydrogen bonds. Finally the authors found that a 32% monomer yield, including mainly **M7G**/**M7S** and **M18G**/**M18S**, could be obtained from birch powder.

2.1.5. Depolymerization of Lignin via an Alternative Two-Step Processes.

Corncob residue is a high volume process waste typically left behind after the conversion of the hemicellulose component in corncob to xylose. With this raw material Hu and co-workers developed the selective conversion of the lignin component in corncob residue to phenolic monomers via a two-step process without addition of hydrogen.[92,176] In the first step, a H_2O-THF (3:7, v/v) solvent mixture was used for the selective degradation of lignin to oligomers at 200 °C for 1 h, the extent of delignification being as high as 89.8%. In the second step, the THF soluble, oligomeric fraction was depolymerized to phenolic monomers, with the total monomer yield of 24.3 wt % at 300 °C after 8 h. It was postulated that in this two-step process H_2O was responsible for the cleavage of numerous intermolecular and intramolecular hydrogen bonds of cellulose in corncob residue under the hydrothermal reaction conditions used, while THF dissolved the fragments derived from lignin. Next, it was found that the addition of Na_2CO_3 to this already established solvent system further improved product yields. Selective dissolution of lignin was achieved with 94.6% conversion in the first step, and further treatment at 300 °C lead to a 26.9 wt % yield of phenolic monomers with 4-ethylphenol (**M6P**, 10.5 wt %), guaiacol (**M24G,** 6.6 wt %), and 4-ethylguaiacol (**M6G,** 4.0 wt %) as the predominant product.

2.1.6. Biochemical Transformation of Lignin.

In nature, lignin is depolymerized by means of fungi and bacteria that generally use powerful oxidative enzymes.[177−179] The research toward finding or engineering an organism that is able to depolymerize lignin to specific chemicals is a very exciting prospect. By using the natural aromatic-catabolizing organism *Pseudomonas putida* KT2440, Beckham and co-workers[180] demonstrated that certain aromatic metabolic pathways (Figure 10) can be used to convert both lignin model compounds and lignin-enriched streams derived from pilot-scale biomass pretreatment into medium chain-length polyhydroxyalkanoates (**M25**) with high yield (34−39%). They further demonstrated that mcl-PHAs can be depolymerized to alkenoic acids, which are

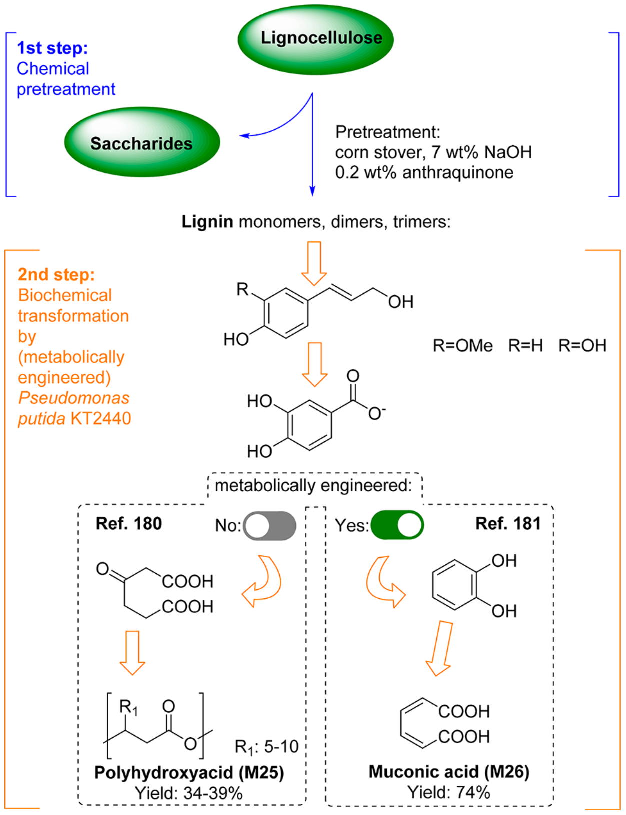


Figure 10. Biochemical transformation of lignin to polyhydroxyalkanoates and muconic acid.

precursors for diverse chemical applications. Subsequently, alkenoic acids were converted to alkanes by a bimetallic catalyst.

Beckham and his group have then introduced modification of the mentioned aromatic-catabolizing organism to demonstrate an integrated scheme for the conversion of lignin via biologically derived muconic acid (**M26**) to adipic acid that is one of the most widely produced dicarboxylic acid.[181] First, *Pseudomonas putida* KT2440 was metabolically engineered to funnel lignin-derived aromatics through an atom-efficient biochemical transformation to cis,cis-muconate (Figure 10). Subsequently, cis,cis-muconic acid was recovered in high purity (>97%) and yield (74%) by activated carbon treatment and crystallization and hydrogenated over Pd/C to adipic acid with exceptional conversion (>97%) and selectivity (>97%).

2.1.7. Summary of Processes Related to Lignin Extraction and Depolymerization. It is important to mention that the presented novel methods and corresponding yield values are difficult to compare since the organosolv or enzymatic lignins that were used as starting materials have been isolated from different plant sources through different isolation methods. The isolation methods in some cases compare well to the organosolv processing that would take place in a biorefinery for the production of high purity cellulose; in other cases the fractionation has been already adjusted to gain high quality lignin with preferably large fraction of β-O-4 bonds. These isolation methods have been frequently developed in the corresponding laboratories, together with the catalytic processing. Therefore, here we also give an overview of the methods as well as isolation processes and lignin yields (Figure 11).

2.2. Catalytic Fractionation of Lignocellulose: Aromatic Monomers from Native Lignin

Reductive catalytic fractionation (RCF) of lignocellulose or "lignin first" processes employ heterogeneous catalysis directly during lignocellulose fractionation, converting native lignin to low molecular weight products.[37,40,41] The advantage of converting the lignin released from lignocellulose in situ, is that generally higher yields and selectivity for aromatic monomers can be obtained due to the higher fraction of cleavable β-O-4 linkages in the yet unmodified substrate. The lignin-derived aromatic monomers are dissolved in the reaction solvent, allowing for easy separation from the solids that contain cellulose and the heterogeneous catalyst. In Figure 12 and Table 1, selected systems are summarized that use this methodology and result in high product yield and selectivity. Variations exist related to lignocellulose sources, the type of solvent as well as catalyst used, and occasionally additives are used to improve the release of lignin from the lignocellulose matrix.

2.2.1. Structure of Monomers Related to the Starting Materials. Woody biomass as well as herbaceous plants has been used for the production of aromatic compounds using the reductive catalytic fractionation process. The type and structure of these aromatic monomers is highly dependent on the original structure of native lignins contained in these resources. As shown in Figure 13, depolymerization of hardwood lignins generally results in high aromatic monomer yields because these feedstocks typically display high syringyl-to-guaiacyl (S/G) monolignol ratios. The higher portion of syringyl units in which both the 3 and 5 position of the aromatic ring are "blocked" from C−C bond formation result in less robust C−C linkages and higher proportions of easily cleavable β-O-4 linkages.[37] In contrast, softwoods or herbaceous plants that have much lower S/G ratios contain higher proportion of more robust C−C linkages, leading to more challenging depolymerization. However, while hardwoods result in higher monomer yields, they typically deliver mixtures of guaiacyl/syringyl related products. On the other hand, softwoods containing exclusively G-type units may result in fewer, all G-type components.

Sels and co-workers[188] (Table 1, entry 8) have compared the product yield obtained during the reductive catalytic fractionation of birch (hardwood), miscanthus (grass), and pine/spruce (softwood) lignocelluloses under identical reaction conditions (5% Ru/C, 3 h, 30 bar H_2, 250 °C) and obtained monomer yields (mainly **M7G** and **M7S**) of 50%, 27%, and 21%, respectively. In contrast to woody biomass, herbaceous plants contain ferulate linkages which result in methyl coumarate (**M27P**) and methyl ferulate (**M27G**) monomers when methanol is used as solvent;[195,199] saturated products methyl 3-(4-hydroxyphenyl)-propionate (**M28P**) and methyl 3-(4-hydroxy-3-methoxyphenyl)propionate (**M28G**) will be generated by following hydrogenation reaction at higher hydrogenation pressure[195] or longer reaction time.[199]

Among several different hardwoods, birch has been identified as suitable starting material as it normally affords higher monomer yields (32%−55%).[134,186−191,198,200−203,205] This could be attributed to its high β-O-4 linkages content as demonstrated by Samec and co-workers (Table 1, entry 13).[193] In their study, the effect of the lignin structure on the yield and distribution of products was investigated by treating wood chips of different origin under the same condition (Pd/C, 210 °C, Ar, ethanol/H_2O as solvent). A direct correlation between the β-O-4 content of the native lignin and monomer yield was observed (Figure 14). This also means that hardwood species that are rich

Figure 11. Summary of processes including the isolation and depolymerization of lignin.

in β-O-4 bonds could result in higher monomer yield and more efficient delignification in comparison with softwood species.

Song and co-workers[186] (Table 1, entry 6) reported the use of a Ni/C catalyst in the presence of alcohol as the hydrogen donor. The established method depolymerized birch woodmeal and resulted in a mixture of 4-propylphenols (mainly **M7G** and **M7S**) in very high selectivity (89%) and total monomer yield of 54% at 200 °C. Abu-Omar[191] (Table 1, entry 11) attempted to explore this catalyst in the treatment of different lignocellulose sources. Compared to poplar and eucalyptus, birch resulted in the highest monomer yields (mainly **M7G** and **M7S**, 32%) at 200 °C. However, when birch woodmeal was tested with the same catalyst by using the reaction conditions reported by Song and co-workers, only 20% monomer yield (versus 54%) was obtained. The authors pointed out that the difference may be attributed to the variation of biomass composition since it is known that the structure of lignin could be different across regions, growing periods, and even age of the lignocellulose.[206]

The advantage of using softwoods is that they normally deliver higher selectivity of guaiacol type monomers [e.g., 4-

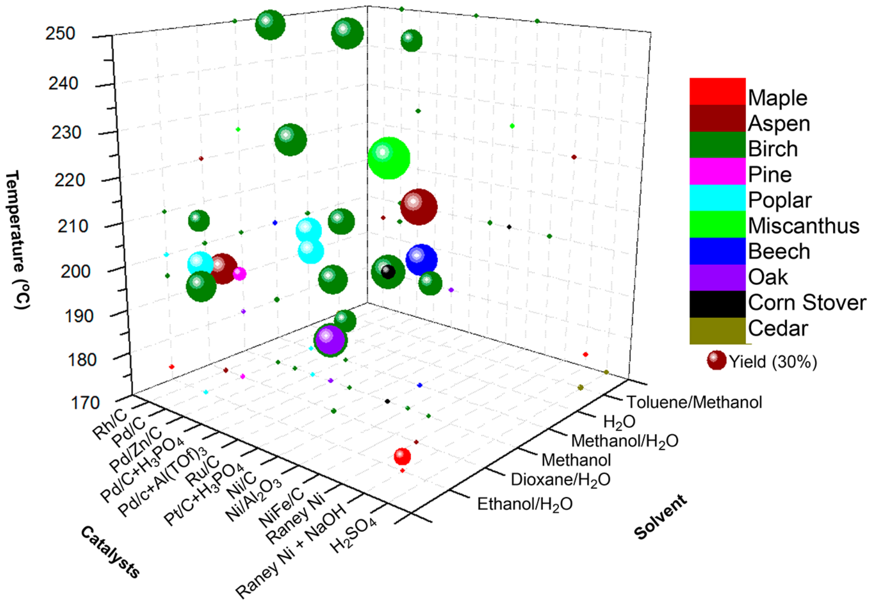


Figure 12. Summary of reductive catalytic fractionation processes developed to obtain aromatic monomers at high yield and selectivity. (The ball size represents the total monomer yield).

propylguaiacol (**M7G**) and 4-propanolguaiacol (**M10G**)], although in a lower yield compared to hardwood, due to the lower β-O-4 content as evidenced by Torr and co-workers[185] (Table 1, entry 5) who have found that the treatment of *Pinus radiata* (a species of pine native to the Central Coast of California and Mexico) with Pd/C at 195 °C for 24 h in dioxane/water (1:1) under hydrogen, results in high yield (~20%) of 4-propanolguaiacol (**M10G**). Due to the high product selectivity in these systems, the further isolation of pure products is much easier compared to using hardwoods. For example, Abu-Omar and co-workers could obtain 4-propylguaiacol (**M7G**) in 100% selectivity from softwood (WT-lodgepole pine) in the presence of their Pd/Zn/C catalytic system.[189]

2.2.2. Role of the Catalyst Used. Catalysts play a central role in the reductive catalytic fractionation process since the hydrogenolysis of C−O bonds is metal dependent.[11,21,24,32] Thus, a high degree of delignification and product yield can be accomplished by appropriate choice of the metal catalysts. In Figure 15, the most typical supported metal catalysts used for reductive catalytic fractionation processes are shown and these typically contain Ru, Pd, Rh, and Ni on activated C or occasionally Al_2O_3 supports. On the basis of these results it can be concluded that Ni,[196,203] Pd,[197,198] and Rh[184] based catalyst normally lead to 4-propanolguaiacol (**M10G**) and 4-propanolsyringol as main products. On the other hand, when using Ru, mainly 4-propylguaiacol (**M7G**) and 4-propylsyringol (**M7S**) can be obtained.[188] Interestingly, when Fe[202] or W[207] was added to the Ni catalysts, the − OH content in the monomer mixtures decreased dramatically and shifted the main products to 4-propylguaiacol (**M7G**) and 4-propylsyringol (**M7S**).

In order to further address the role of catalyst composition, Sels and co-workers compared Ru/C and Pd/C catalysts under identical reaction conditions (250 °C, 30 bar, 3 h in methanol)[190] (Table 1, entry 10). With the use of identical starting material, the liquid product yields were very similar for both catalysts, as expected; however, with Ru/C preferentially 4-propylphenolics (**M7G** and **M7S**) were obtained among which 75% accounted for 4-propylguaiacol (**M7G**) and 4-propylsyringol (**M7S**), while the use of Pd/C favored the formation of 4-propanol-derivatives with a combined 91% selectivity toward 4-propanolguaiacol (**M10G**) and 4-propanolsyringol (**M7S**).

Abu-Omar and co-workers[208] designed an easy method to prepare and fully recyclable Zn/Pd/C catalyst, which was far more effective than Pd/C alone for the hydrogenolysis of the β-O-4 lignin model compounds and the subsequent reductive deoxygenation of the obtained aromatic fragments. Dimer as well as polymer (all β-O-4 synthetic lignin polymer that has a Mn of 3390 and DPn of 12.1) model compounds[209] were used to confirm the rapid hydrogenolysis of the aromatic ether bonds as well as selective removal of the hydroxyl groups on the alkyl chains. The same catalyst was successfully applied in the conversion of lignocellulose as well[189] (Table 1, entry 9). Three different types of poplar lignocelluloses were depolymerized using the Zn/Pd/C catalyst in methanol, which resulted in 40−54% conversion of the native lignin and 4-propylguaiacol (**M7G**) and 4-propylsyringol (**M7S**) as main products. Surprisingly, when pine lignocellulose was used as feedstock, 100% selectivity of 4-propylguaiacol (**M7G**) was achieved. A detailed mechanistic study to explain the synergistic effect between Pd/C and Zn^{II} system was conducted, using both lignin model compounds and lignocellulosic biomass.[210] As shown in Figure 16, reaction of lignin model compound with Pd/C in the absence of Zn^{II} removes the benzylic OH group at C_α, leaving the OH group at C_γ intact to selectively produce 4-propylguaiacol (**M7G**) and guaiacol (**M24G**). While using the Zn/Pd/C catalyst, a six-membered intermediate involving Zn^{II} was formed (confirmed by NMR spectroscopy), which resulted in the removal of the primary OH at $C\gamma$ of the β-O-4 ether linkage. After further hydrogenation reaction, 4-propylguaiacol (**M7G**) was obtained as the main product.

2.2.3. Influence of Additives. Regarding the use of reductive catalytic fractionation (RCF) in a biorefinery, the extent and rate of delignification as well as the activity of the catalyst toward depolymerization are key factors determining the yield and chemical structure of the obtained products. Both these processes can be strongly affected by the choice of an appropriate catalyst. Without any additives, delignification is relatively inefficient, generally requiring long reaction times or relatively

Table 1. Reductive Catalytic Fractionation of Lignocellulose[a,b,c,d]

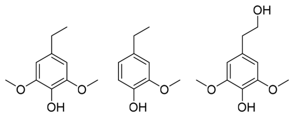
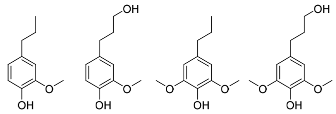
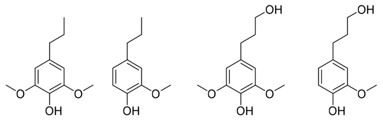
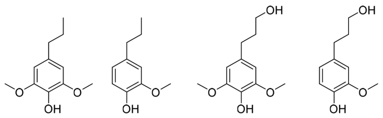
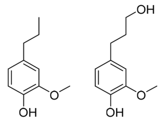
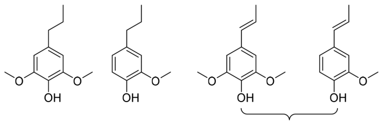
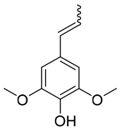
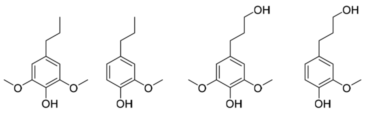
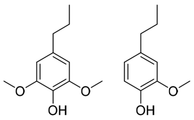
Entry	Feedstock	Catalyst	Reaction conditions				Sugar retention	Yield of main products	Monomer Yield[a]	Year[ref.]
			Solvent	T (°C)	P (bar)	T (h)				
1	Maple	Raney Ni + NaOH	Dioxane/ H_2O (1:1)	173	H_2 (210)	6	N. R.[b]	 Others 15.4 wt% 2.2 wt% 6.2 wt% 3.6 wt%	27.3 wt%	1948[182]
2	Aspen	Raney Ni	Dioxane/ H_2O (1:1)	220	H_2 (35)	5	N. R.	 Others 5.6wt% 6.6wt% 28.5wt% 12.7wt% 5.7wt%	59.1 wt%	1963[183]
3	Aspen	Rh/C	Dioxane/ H_2O (1:1)	195	H_2 (34)	5	N. R.	 12.9 wt% 7.4 wt% 25.6 wt% 4.2 wt%	50.1 wt%	1978[184]
4	Birch	H_3PO_4 + Pt/C	Dioxane/ H_2O (1:1)	200	H_2 (40)	4	N. R.	 21.1 wt% 6.1 wt% 14.5 wt% 4.8 wt%	46.5 wt%	2008[134]
5	Pine	Pd/C	Dioxane/ H_2O (1:1)	195	H_2 (34.5)	24	N. R.	 1.6 wt% 20.8 wt%	22.4 wt%	2011[185]
6	Birch	Ni/C	Methanol	200	Ar (1)	6	N. R.	 Others 36.2 wt% 11.9 wt% 0.5 wt% 5.4 wt%	54 wt%	2013[186]
7	Birch	Pd/C	Ethanol/ H_2O (1:1)	195	Ar (4)	1	N. R.	 49 %	49 % (C- Yield)	2014[187]
8	Birch	Ru/C	Methanol	250	H_2 (30)	6	81 % (C-Yield)	 Others 30.5 % 10.4 t% 2.3 % 2.3 % 6.0 %	51.5% (C- Yield)	2015[188]
9	Poplar	Zn/Pd/C	Methanol	225	H_2 (34.5)	12	79 wt%	 29.7 wt% 24.3 wt%	54 wt%	2015[189]

Table 1. continued

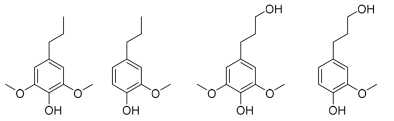
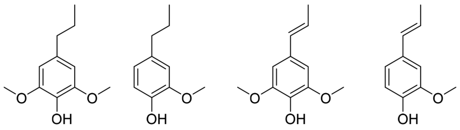
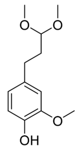
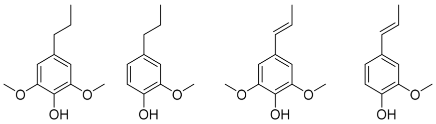
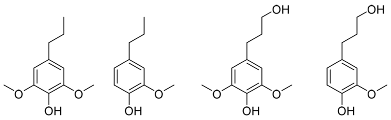
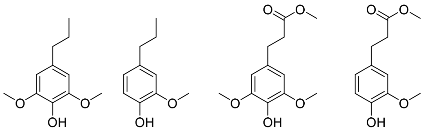
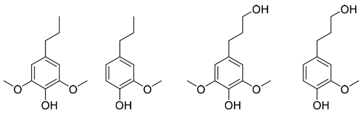
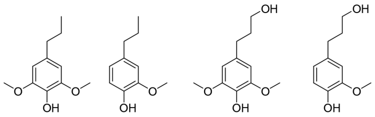
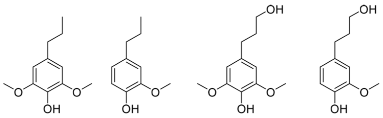
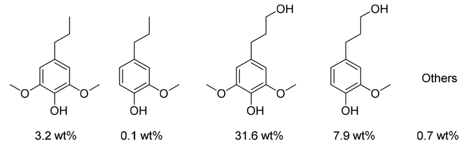
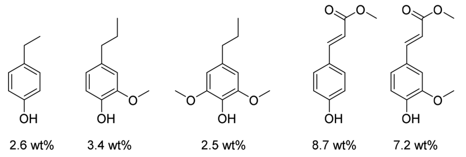
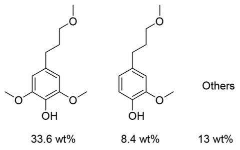
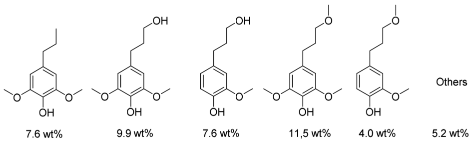
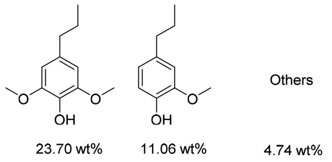
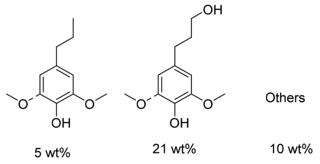
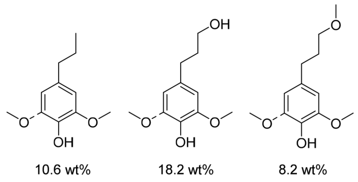
Entry	Feedstock	Catalyst	Reaction conditions				Sugar retention	Yield of main products	Monomer Yield[a]	Year[ref.]
			Solvent	T (°C)	P (bar)	T (h)				
10	Birch	Pd/C	Methanol	250	H_2 (30)	3	89 % (C-Yield)	 Others 1.4 % 0.4 % 35.2 % 9.7 % 2.6 %	49.3 % (C-Yield)	2015[190]
11	Birch	Ni/C	Methanol	200	N_2 (2)	6	N. P.	 18 wt% 10 wt% 3 wt% 1 wt%	32 wt%	2015[191]
12	Cedar	H_2SO_4	Toluene/ Methanol	170	Air	0.1	N. P.	 Others ~5.4 % ~4.6 %	10 wt%	2015[192]
13	Birch	Pd/C	Ethanol/ H_2O (1:1)	210	Ar	15	84.4 wt%	 20 wt% 4 wt% 11 wt% 1 wt%	36 % (C-Yield)	2016[193]
14	Poplar	H_3PO_4 + Pd/C	Methanol	200	H_2 (20)	3	72 wt%	 Others 4 % 1 % 21 % 14 % 2 %	42 % (C-Yield)	2016[194]
15	Miscanthus	Ni/C	Methanol	225	H_2 (60)	12	86 wt%	 19 wt% 21 wt% 16 wt% 12 wt%	68 wt%	2016[195]
16	Beech	Ni/C	Methanol/ H_2O (3:2)	200	H_2 (60)	5	N. P.	 Others 7.9 wt% 0.7 wt% 28.9 wt% 9.8 wt% 4.1 wt%	51.4 wt%	2016[196]
17	Poplar	Pd/C	Methanol/ H_2O (7:3)	200	H_2 (20)	3	~66.7 wt%	 Others 4.4 wt% 0.6 wt% 21.5 wt% 14.0 wt% 2.9 wt%	43.5 wt%	2016[197]
18	Poplar	Pd/C	Ethanol/ H_2O (1:1)	200	H_2 (20)	3	~73.2 wt%	 Others 5.0 wt% 0.5 wt% 21.5 wt% 14.2 wt% 2.2 wt%	43.3 wt%	2016[197]

Table 1. continued

Entry	Feedstock	Catalyst	Reaction conditions				Sugar retention	Yield of main products	Monomer Yield[a]	Year[ref.]
			Solvent	T (°C)	P (bar)	T (h)				
19	Birch	Pd/C	H_2O	200	H_2 (30)	3	55 wt%	 3.2 wt% 0.1 wt% 31.6 wt% 7.9 wt% Others 0.7 wt%	43.8 wt%	2016[198]
20	Corn Stover	Ni/C	Methanol	200	H_2 (30)	3	76 wt%	 2.6 wt% 3.4 wt% 2.5 wt% 8.7 wt% 7.2 wt%	24.5 wt%	2016[199]
21	Birch	Pd/C + $Al(OTf)_3$	Methanol	180	H_2 (30)	2	76.5 wt%	 33.6 wt% 8.4 wt% Others 13 wt%	55 wt%	2017[200]
22	Oak	Pd/C + $Al(OTf)_3$	Methanol	180	H_2 (30)	2	76.6 wt%	 7.6 wt% 9.9 wt% 7.6 wt% 11,5 wt% 4.0 wt% Others 5.2 wt%	46 wt%	2017[201]
23	Birch	NiFe/C	Methanol	200	H_2 (20)	6	N. R.	 23.70 wt% 11.06 wt% Others 4.74 wt%	39.5 wt%	2017[202]
24[c]	Birch	Ni/Al_2O_3	Methanol	250	H_2 (30)	3	84.9 wt%	 5 wt% 21 wt% Others 10 wt%	36 wt%	2017[203]
25[d]	Birch	Pd/C + H_3PO_4	Methanol/ H_2O (7:3)	180	H_2 (30)	3	~56 wt%	 10.6 wt% 18.2 wt% 8.2 wt%	37 wt%	2017[204]

[a] Yield calculated based on lignin content in each wood. [b] N. R. means not reported. [c] Ni/Al_2O_3 pellets in basket. [d] Reaction operated in a flow-through system.

high temperatures and operating pressures (large energy input); however, a near-complete delignification is desired for achieving high monomer yields. Lignocellulose fractionation processes usually require the addition of acid or alkaline additives in order to enhance lignin and/or hemicellulose removal at lower temperature and pressure.[11] Therefore, such additives were also applied in the catalytic lignocellulose fractionation (Figure 17). The effect of these additives on the catalyst and the depolymerization step was studied.

Sels and co-workers studied the influence of H_3PO_4 and NaOH additives on the Pd/C catalyzed reductive processing of poplar lignocellulose in methanol[194] (Table 1, entry 14). The addition of small quantities of H_3PO_4 resulted in the modification of the carbohydrate fraction: instead of a carbohydrate-rich pulp and stable lignin oil, three product streams were obtained consisting of lignin oil, cellulose pulp, and hemicellulose alcoholysis products. The addition of H_3PO_4 strongly promoted delignification and resulted in lignin product oil with narrow molecular weight distribution and a monomer yield close to the theoretical maximum. These results are similar to those reported by Yan and co-workers[134] (Table 1, entry 4). The yield of lignin-derived monomers and dimers both increased when 1 wt % H_3PO_4 was added to the Pt/C catalyst. The addition of NaOH under similar catalytic conditions also enhanced

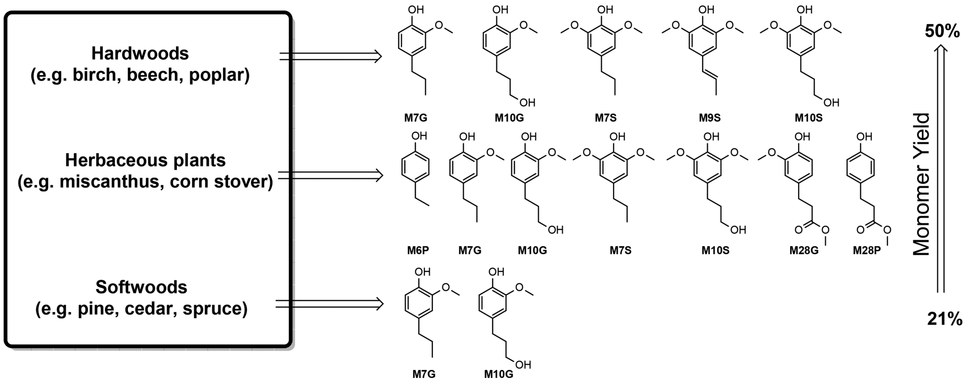


Figure 13. Structures of phenolic monomers derived from native lignin of different resources. On the basis of results of ref 188. Reaction conditions: 2 g of substrate, 0.3 g of 5% Ru/C, 40 mL of methanol, 250 °C, 3 h, 30 bar H_2.

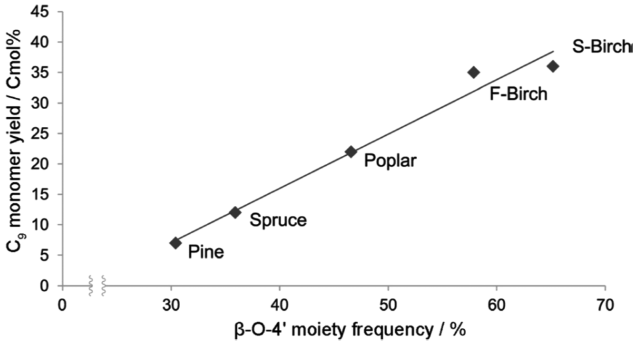


Figure 14. Correlation between the yield of phenolic monomers and the frequency of the β-O-4 moiety in native lignin for different lignocellulose substrates. Reprinted with permission from ref 193. Copyright 2016 Wiley-VCH.

delignification but led to lower monomer yield. This has been attributed to base-catalyzed repolymerization under these reactions, especially when softwood comprising mainly guaiacol units was used, whereby the free 3 position in the G-type monomers can participate easier in condensation reactions. Another disadvantage of using NaOH was the loss of cellulose, through partial cellulose amorphization and/or swelling, making the cellulose structure more accessible for catalytic processing. Pepper and Hibbert also reported the addition of NaOH when using Raney Ni as catalysts[182] (Table 1, entry 1), and a high yield of phenolic monomers (mainly **M6G**, **M6S** and 4-(2-hydroxyethyl)-2-methoxyphenol **M29G**, 27.3%) at 175 °C were obtained; however, the influence of base on delignification and carbohydrate retention was not discussed.

Hensen and co-workers found that water-tolerant metal triflates are very active Lewis acid catalysts for the cleavage of the chemical bonds between lignin and carbohydrates, leading to very efficient delignification and removal of a significant fraction of hemicellulose sugars from lignocellulose, leaving behind a cellulose-rich solid residue. The combination of Lewis and Brønsted acids with metal-catalyzed lignin depolymerization resulted in high aromatic monomer yields.[200,201,205] In the presence of Pd/C as the hydrogenation and Al(III) triflate as acid catalyst, an excellent 46 wt % aromatic monomer yield was obtained (30 bar H_2, 180 °C). In order to understand possible synergistic effects between the metal triflates and Pd/C, the reactivity of several dimer model compounds was studied and it was concluded that both the metal triflate as well as the Pd/C played a role in the depolymerization step. Compared to Pd/C alone, the addition of metal triflates facilitated the cleavage of C—O bonds in (β-O-4) ether linkages. Further it was found that Pd/C is able to cleave a wide range of ether linkages such as α-O-4, 4-O-5, and β—β. Lower Pd/Al ratios resulted in 4-*n*-methoxypropylsyringol (**M30S**)/4-*n*-methoxypropylguaiacol (**M30G**) as dominant reaction products, while higher ratios led to formation of 4-propanolguaiacol (**M10G**)/4-propanolsyringol (**M10S**) and 4-propylguaiacol (**M7G**)/4-propylsyringol (**M7S**) products (Figure 18). The system was successfully upscaled to 100 g lignocellulose without any change in monomer yield. However, the authors considered the relatively high price of metal triflates for future industrial application. Therefore, strong Brønsted acids (H_2SO_4 and HCl) were successfully used in search for a cheaper acid cocatalysts[201] (Table 1, entry 22), both resulting in high yields of lignin monomers (40% and 44%) from oak sawdust. Weaker acid (H_3PO_4) was also able to cleave phenyl glycoside bonds and β-O-4 ether bonds but not the ester type lignin-carbohydrate linkages so the products contained lower amount of lignin monomers (26%).

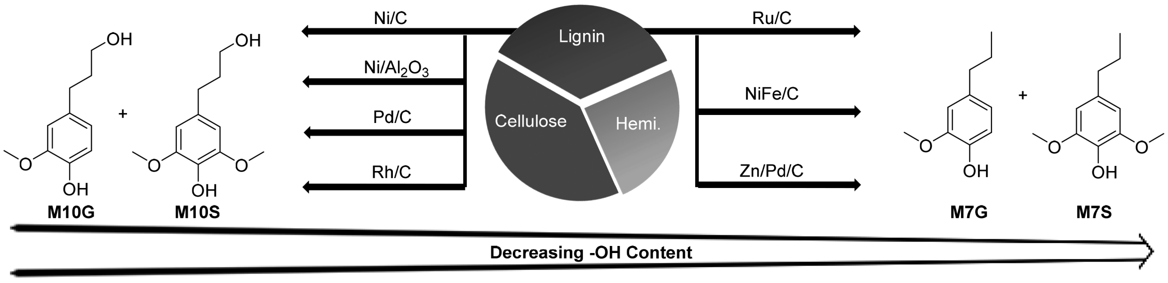


Figure 15. Structures of main products depending on type of catalyst after reductive catalytic fractionation under H_2 pressure.

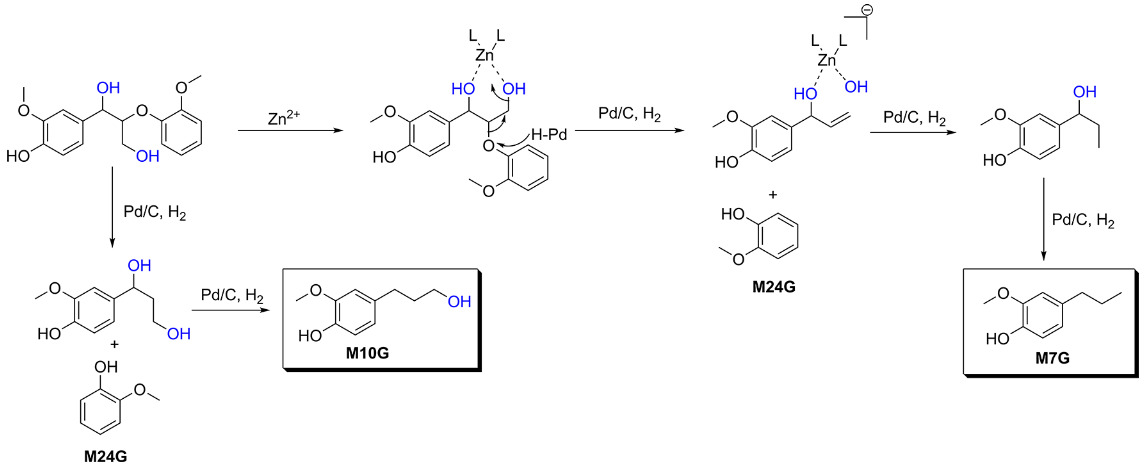


Figure 16. Proposed mechanism of cleavage and hydrodeoxygenation of β-O-4 ether linkage by Pd/C catalyst and Pd/C and Zn^{II} catalysts. Adapted with permission from ref 210. Copyright 2016 Royal Society of Chemistry.

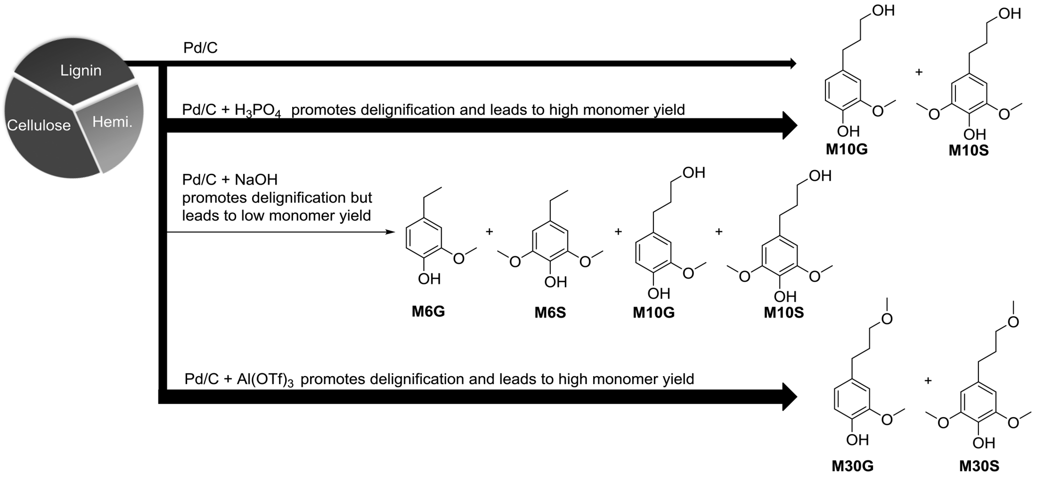


Figure 17. Reductive catalytic fractionation using Pd/C only or Pd/C in combination with different additives.

Román-Leshkov[199] (Table 1, entry 20) confirmed the promoting effect of homogeneous and heterogeneous acid cocatalysts in the reductive catalytic fractionation of corn stover using carbon-supported Ru and Ni catalysts at 200 and 250 °C in methanol. In one experiment, the application of acidified carbon support increased monomer yields to 32%, that is comparable to other systems in which phosphoric acid (38%) was used in combination with a Ni/C catalyst at 200 °C.

Watanabe and co-workers[192] (Table 1, entry 12) treated two types of wood species, namely eucalyptus globulus and cedar, with a catalytic amount (<1%) of sulfuric acid in a mixture of hydrophobic solvent (e.g., toluene) and alcohol (e.g., methanol) to result in homovanillyl aldehyde dimethyl acetal (**M31G**) and homosyringaldehyde dimethyl acetal (**M31S**) at 140 °C. Owing to the presence of methanol, the aromatic C2 enol ether intermediate obtained upon acid catalysis underwent acetal formation in situ. This method also generated oligolignols besides the corresponding dimethyl acetal derivatives.

2.2.4. Influence of Solvents.

Solvents also play a crucial role in delignification as well as depolymerization, influencing the yield of phenolic monomers and dimers, and the amount of carbohydrates retained.[39,211] In this part, the impact of the solvent on both cellulose and hemicellulose retention and delignification efficiency will be addressed.

Sels and co-workers[198] (Table 1, entry 19) studied the solvent effects using bio-derived solvents with varying properties in the Pd/C catalyzed reductive processing of birch wood. The extent of delignification was found most favorable in water and decreased with increasing apolar character of the solvents (Figure 19). With ethylene glycol as well as methanol, high delignification was seen. This effect was lower in cyclic ethers, tetrahydrofuran, and 1,4-dioxane and totally disfavored in nonpolar solvents such as *n*-hexane. The phenolic mono-, di-, and oligomer yields roughly followed a similar trend. The phenolic monomer distribution was very similar in all solvents, mainly containing 4-propanolsyringol (**M10S**) and 4-propanolguaiacol (**M10G**). In contrast, the composition of the dimer fraction obtained in the various solvents was substantially different: in water and methanol mainly β-1- and β-5-linked dimers with a $-CH_2OH$-substituted ethylene bridge were obtained, while in ethylene glycol unsubstituted analogues were found in much greater extent.

Several earlier studies for the valorization of *proto*lignin described the application of ethanol/water,[187] isopropanol/water,[212,213] and dioxane/water[134,183−185] solvent mixtures. Similarly, Sels and co-workers[197] then studied the effect of different MeOH/water and EtOH/water mixtures on the reductive catalytic fractionation of poplar wood (Table 1, entries 17 and 18). It was demonstrated that the addition of water to an

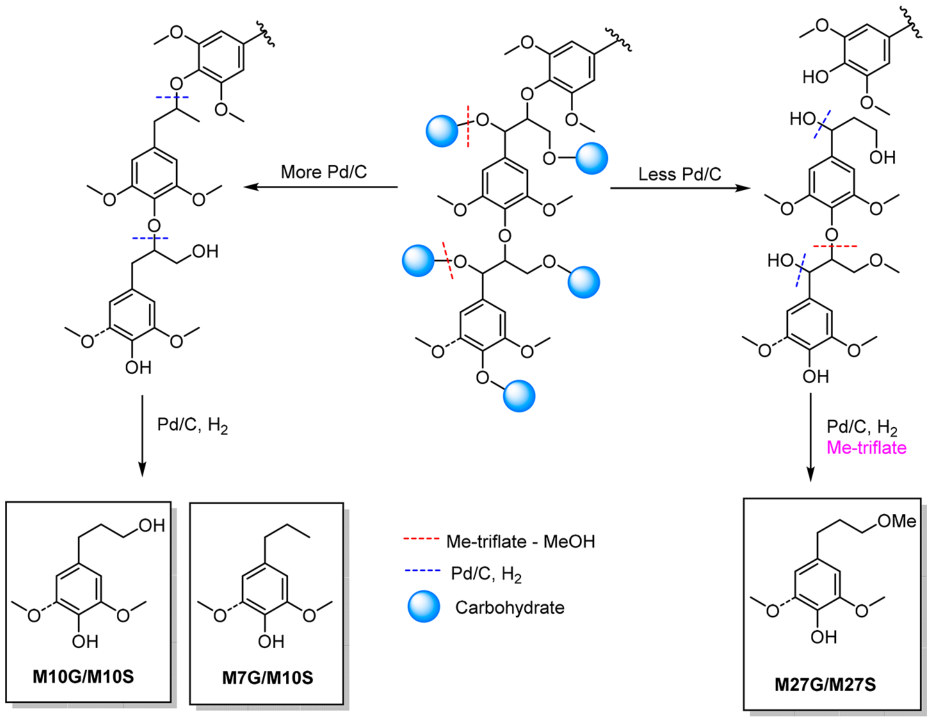


Figure 18. Reductive depolymerization of wood lignin into phenolic monomers over a tandem Pd/C and Al(III)-triflate catalyst system, at different Pd/Al ratios. Adapted with permission from ref 200. Copyright 2017 Royal Society of Chemistry.

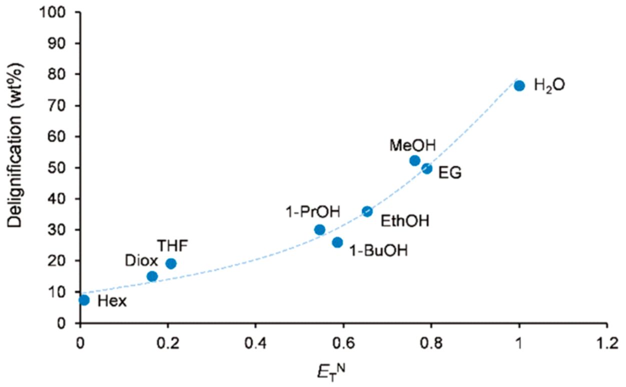


Figure 19. Birch delignification vs solvent polarity as described by the reichardt parameter (E_T^N). Reproduced with permission from ref 198. Copyright 2015 Royal Society of Chemistry.

alcohol solvent significantly enhanced the extraction of lignin, and the results were similar to methanol/water and ethanol/water solvent systems. By adding low amounts of water (≤50 vol %), the delignification strongly increased from 52 wt % to 80 wt %. Addition of more water however decreased the degree of delignification, down to 65 wt % for pure water. Thus a positive synergetic effect of mixing methanol and water with respect to the conversion of lignin was observed. The monomer yields showed similar trends with increasing water loading and reached a maximal value of 44 wt % at 30 vol % water content. Similar experiments were performed with ethanol/water mixtures as ethanol is less harmful and more readily available from biomass fermentation. The maximal degree of delignification for ethanol/water (82 wt %) was almost equal to that of methanol/water (80 wt %). Additionally, the composition and structure of the pulp was characterized showing that low water concentrations (≤30 vol %) preserved most of the carbohydrates as solid pulp; however, with water-rich (≥70 vol %) solvents, the majority of the hemicellulose fraction was removed, while the cellulose fraction was largely left unaltered.

The positive effect of adding water was also confirmed by Chen et al.[196] They developed the catalytic fractionation of beech sawdust using a Ni/C catalyst in a methanol−water cosolvent (Table 1, entry 16). The total monomer yield increased from 39.3 wt % to 51.4 wt % when 40 vol % water was added to pure methanol.

The ideal reductive catalytic fractionation process would proceed in pure water; however, redeposition of the dissolved lignin on the wood fiber surface presents a major problem, a phenomena only seldom discussed.[214] In this regard, the addition of an organic solvent plays an important role as it retards the redeposition of lignin onto the other biomass components after separation.[215] This is also likely the reason why higher product yields are obtained when an organic cosolvent is used.

2.2.5. Use of Hydrogen Donors Instead of Hydrogen Gas. Alcohols and acids that can be derived from renewable sources can serve as hydrogen source. A seminal method combining transfer hydrogenation and hydrogenolysis was developed by Rinaldi and co-workers using a commercial Raney Ni catalyst. In earlier studies, H-transfer reactions in 2-propanol for hydrogenolysis of lignin model compounds, organosolv lignin[216] and upgrading of bio-oil[217,218] were investigated in the presence of Raney Ni and solid acids. Then poplar lignocellulose was treated in the presence of Raney Ni in 2-propanol/water solution, and a lignin-derived oil and a solid carbohydrate residue was obtained. The lignin bio-oil, originating from native lignin mainly contained phenolic monomers and was efficiently hydrodeoxygenated under low-severity conditions. Interestingly, separation of Raney Ni could be achieved by simple magnetic forces. The pulp obtained by this method contained very low amount of lignin, and the authors proposed that it may

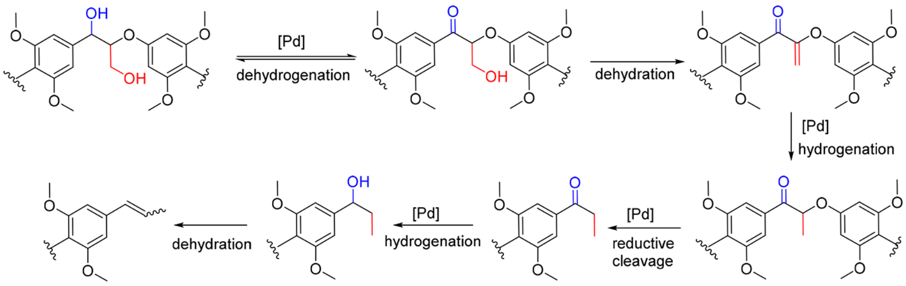


Figure 20. Proposed mechanism of aryl propene formation during Pd-catalyzed hydrogenolysis, established by model compound studies. Adapted with permission from ref 187. Copyright 2014 Wiley VCH.

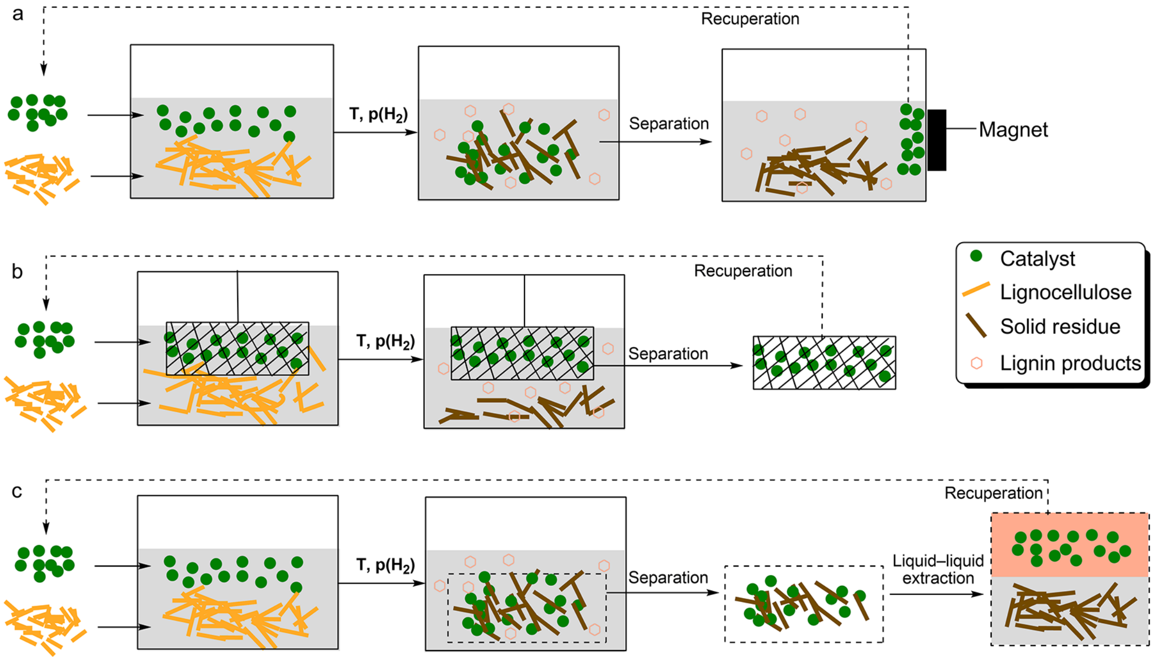


Figure 21. Solutions developed for the separation of catalysts from solid residue after reductive catalytic fractionation process. (a) Separation of a magnetic catalyst by application of magnetic field, (b) Using a microporous catalyst cage, and (c) Liquid–liquid extraction.

be suitable for further upgrading to the production of biofuels, chemicals, or papers.[219]

Song and co-workers[186] (Table 1, entry 6) developed an elegant method using Ni/C catalyst in the presence of alcohols as hydrogen donors. Under optimized conditions (200 °C, 6 h, 1 MPa Ar), the native birch-wood lignin was converted into 4-propylguaiacol (**M7G**) and 4-propylsyringol (**M7S**) with the best selectivity of 97% for both and the total monomers yields reached 54%. It was proposed that lignin is first fragmented into smaller lignin species through alcoholysis reactions, and then smaller fragments are converted into monomeric phenols over the Ni/C catalyst.

Formic acid can be easily obtained from hydrogenation of carbon dioxide[220] and is also generated as a byproduct from biomass degradation processes.[221] Recently it has attracted much interest in the area of green chemistry because of its potential as a hydrogen carrier and as means of utilizing carbon dioxide. Samec and co-workers developed the palladium-catalyzed transfer hydrogenolysis of primary, secondary, and tertiary benzylic alcohols by formic acid.[222] On the basis of this, a tandem organosolv and Pd-catalyzed transfer hydrogenolysis system was devised (Table 1, entry 7).[187] Surprisingly, 23% yield of 4-(1-propenyl)guaiacol (**M18G**) was generated from pine lignocellulose, and 49% yield of 4-(1-propenyl)syringol (**M18S**) was obtained from birch wood. The generation of aryl propene from lignin in wood could be explained by the mechanism proposed by the authors (shown in Figure 20). First, the ketone intermediate was formed by Pd-catalyzed dehydrogenation of the benzylic alcohol. The corresponding α,β-unsaturated ketone was then generated by dehydration reaction. Pd with chemisorbed hydrogen then catalyzed the following hydrogenation and reductive cleavage reaction. Finally, the corresponding aryl propene was generated by first hydrogenation of ketone and then dehydration of the hydroxyl group.

Besides using hydrogen donors, it is also possible to perform the reductive catalytic fractionation of lignocellulose under hydrogen-free conditions as proposed by Samec and co-workers.[193] In this system, part of the lignocellulose (hemicellulose) could be utilized as an internal source of hydrogen for the reductive lignin transformations. In this efficient RCF process, the total monomers yield was as high as 40% (**M7S**, 23% and **M18S**, 14%) in only 2 h at 210 °C, using Pd/C.

2.2.6. Recycling of Catalysts.

Recuperation of the heterogeneous catalyst[553] after reductive catalytic fractionation is a very important aspect, considering the overall economics of the process. It is highly desired to achieve efficient catalyst recycling and at the same time sufficiently high quality catalyst-free pulp, that is suitable for further applications. Several studies have reported good catalyst reusability by different separation processes which included using ferromagnetic catalysts (Figure 21a) like Ni/C[186] and Raney Ni,[212] using a microporous catalyst cage,[195,203] (Figure 21b) or catalyst recovery by liquid−liquid extraction[188,200] (Figure 21c).

Song and co-workers[186] (Table 1, entry 6) demonstrated that nickel-based catalysts are highly active and selective in the conversion of native lignin, and the best selectivity of 97% toward monomeric phenols was achieved at 50% conversion from birch wood lignin. The magnetic Ni/C catalyst could be easily separated by a magnetic bar and reused. Conversion of lignin remained as high as 50% for 4 consecutive reactions, indicating good stability and reusability of the Ni/C catalyst. The Raney Ni could be separated with the same method as well, and the isolated yield of lignin bio-oil remained at 23 ± 2% throughout eight recycling experiments.[212]

A different creative solution was developed in the group of Abu-Omar[195] that relies on the physical separation of the catalyst from the substrate by means of a microporous catalyst cage (Figure 21b). After reaction, over a Ni/C catalyst (Table 1, entry 15), nickel-free cellulose residue was obtained and the catalyst was reused in three consecutive reactions. However, the ability of the Ni catalyst to function as a hydrogenation catalyst decreased with each reuse, and this lead to the shift in monomer selectivity. Sels and co-workers[203] developed a related method using a reactor basket, filled with catalyst pellets ($Ni-Al_2O_3$, 1.2 × 3 mm). The commercial $Ni-Al_2O_3$ catalyst pellets in the basket could be easily separated after reaction, resulting in monomer-enriched lignin oil, a catalyst-free carbohydrate pulp, and the catalyst could be quantitatively recuperated. Compared with $Ni-Al_2O_3$ powder, the $Ni-Al_2O_3$ catalyst in the basket gave slightly lower monomer yield but similar selectivity. A systematic decrease in the phenolic monomer yield of ∼2% was osberved, which showed catalyst deactivation after each recycling step; however, a H_2-treatment after 5 runs almost completely recovered the performance of the spent catalyst. Tandem regeneration/recycling experiments, in which the $Ni-Al_2O_3$ pellets were treated with H_2 before each run, showed excellent performance without significant changes in both monomer yields and selectivity.

Liquid−liquid extraction of the catalyst from the solid residue was first reported by Sels and co-workers[188] (Table 1, entry 8). In their study, the Ru/C catalyst could be recovered from the decane phase, while the more polar carbohydrate pulp was located at the bottom of the methanol phase. The recycled catalyst showed a phenolic monomer yield of 48% which is similar to the fresh catalyst (50%). Good selectivity toward 4-propanolsyringol (**M10S**) and 4-propanolguaiacol (**M10G**) as well as a higher C5 sugar retention of 83% was observed using the recycled catalyst. However, the drawback of the liquid−liquid extraction was that only a part of the catalysts could be recovered (about 30% recovery).[198]

Considering the better solubility of metal triflates in water compared to common organic solvents, Hensen and co-workers[200] recovered Al(III)-triflate from the liquid products by using a solvent mixture of ethyl acetate and water (Table 1, entry 21). However, Al(III)-triflate could not be fully recovered by this workup procedure, and the total monomer yield in the next catalytic step decreased to 37 wt % from 52 wt %.

2.2.7. Utilization of the Solid Residue.

The advantages of reductive catalytic fractionation processes are mild reaction conditions and high selectivity for lignin-derived monomers. Another advantage is that the carbohydrate solid residue retains its value for the further upgrading to produce platform chemicals (Figure 22) as long as separation from the catalyst is sufficient.

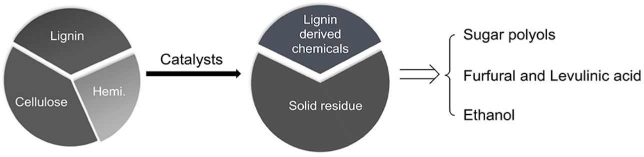


Figure 22. Possible applications of the solid residue after reductive catalytic fractionation.

Sels and co-workers[188] successfully converted the carbohydrate solid residue to sugar polyols in water by tungstosilicic acid with a maximal total yield of 74%. Abu-Omar and co-workers[195] targeted the platform chemicals furfural (55%) and levulinic acid (76%) by using iron-trichloride at 200 °C.

Furthermore, when Ni/Al_2O_3 pellets were used as catalyst[203] in a microporous cage, the carbohydrate solid residue was easily separated with the catalysts and then subjected to a saccharification and fermentation experiment resulting in a total yield of 73% bioethanol, showing great promise for the total utilization of lignocellulose. Román-Leshkov[199] subjected the obtained sugars to enzymatic digestion, reaching conversions above 90% in 96 h. All of the residual solids showed comparable digestibility, producing glucan and xylan with more than 80% yield. Samec et al.[193] treated the pulp with a commercially available enzyme mixture at 50 °C for 72 h, thereby the pulp could be converted to glucose. The shorter treatment time of the first catalytic fractionation step generally resulted in higher glucose yields. The authors also found that hardwood pulps normally resulted in higher glucose yield than softwood pulps. This was attributed to either the difference in pulp structure (higher lignin content in softwood pulp) or the absence of softwood-specific hemicellulose activity in the enzyme cocktail used.

Recently, this group reported that the pulp generated in a flow setup consisting of a percolation reactor filled with woody biomass and a fixed catalytic bed reactor filled with Pd/C was enzymatically hydrolyzed to glucose in 87 wt % yield without prior purification.[204]

2.3. One-Pot Catalytic Processes

One-pot catalytic processes are able to completely covert all components of lignocellulose to a range of chemicals, simultaneously. Ford and his research group introduced the use of copper-doped hydrotalcite-based porous metal oxides (PMO) for the broader use in catalytic conversion of various lignocellulose-derived materials.[223] First, the selective cleavage of the aromatic ether bond in a simple lignin model compound dihydrobenzofuran (DHBF) was achieved in supercritical methanol.[224] The Cu-doped PMO served multiple purposes, catalyzing substrate hydrogenolysis and hydrogenation as well as the methanol reforming and water gas shift reaction, allowing for hydrogen to be in situ derived from the solvent itself. Later, under similar reaction conditions (300 °C, ∼200 bar) poplar wood organosolv lignin was also successfully converted to very clean mixtures of substituted cyclohexanols.[130] Importantly, for the first time, no insoluble char was observed during the reaction. With this catalytic system, lignocellulose was fully and rapidly converted to a mixture of cellulose-derived (C2−C6) and lignin-derived (C9+) aliphatic alcohols without formation of char.[225]

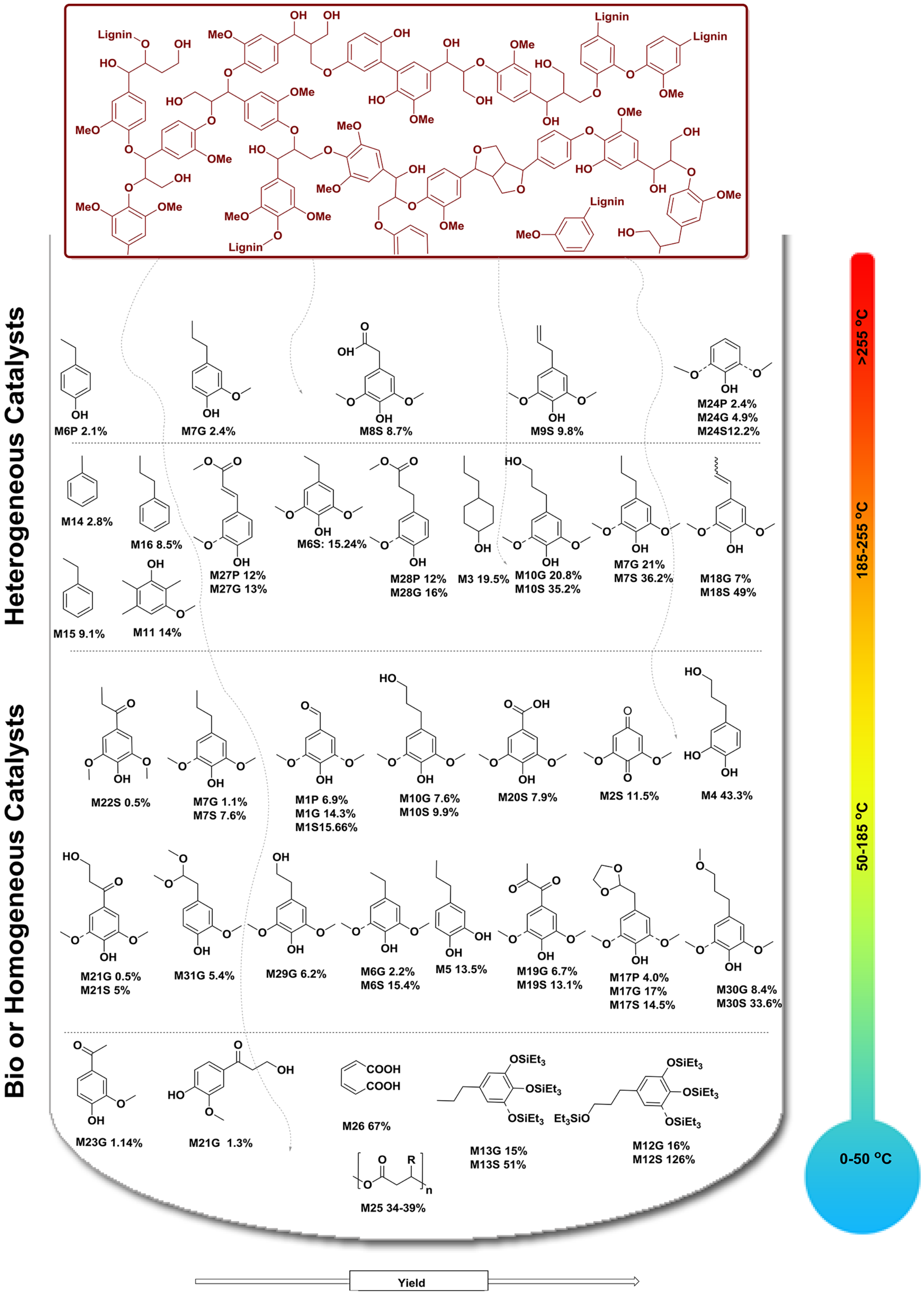


Figure 23. A summary of lignin-based monomers obtained via the different catalytic processes in section 2.

Zhang and co-workers[207] converted woody biomass directly into two groups of chemicals over a carbon-supported Ni−W_2C catalyst. The carbohydrate fraction was converted to ethylene glycol and other diols with a total yield of up to 75.6% while lignin underwent selective catalytic processing into monophenols (4-propanolphenols and 4-propylphenols) with a yield up to 46.5% (based on lignin) at 235 °C under 60 bar hydrogen. Catalyzed by layered $LiTaMoO_6$ in the presence of Ru/C in an aqueous phosphoric acid medium, different biomass resources (e.g., pine sawdust, corn stalk, corncob, wheat straw, and rice straw) were converted to gasoline alkanes, monophenols, and related hydrocarbons.[226]

A wide variety of raw lignocellulose could be used for the production of liquid alkanes by a one-pot catalytic process reported by Wang and co-workers. With the multifunctional Pt/$NbOPO_4$ catalyst, excellent mass and carbon yields were achieved in cyclohexane as solvent.[227] The same group also developed a selective procedure to obtain arenes via direct hydrodeoxygenation of organosolv lignin over a porous Ru/Nb_2O_5 catalyst. Remarkably, this catalytic system enabled the complete removal of the oxygen content from the lignin-derived aromatic monomers obtained from lignin.[159] The conversion of birch lignin was nearly quantitative, and the products consisted of C7−C9 hydrocarbons with a total mass yield of 35.5 wt % and arenes with an exceptional selectivity of 71 wt %. All these processes operated under relatively high temperature (>190 °C) and resulted in complex product mixtures.

2.4. Summary of Catalytic Processes

The catalytic methods targeting selective lignin depolymerization resulted in various defined building blocks, mainly aromatic chemicals, which are summarized on Figure 23 (the structure, full name, and code for each compound is also listed in Figure S1). Naturally, the degree of defunctionalization correlates with the reaction temperature, and the method of catalytic degradation have great influence on the structure of the obtained monomers. These monomers are mainly phenolic compounds with sufficient functionality to be further upgraded to value added chemicals.

It has to be mentioned that techno-economic calculations are available for a few products shown on Figure 23. For example, according to Global Market Insights, with the emerging expansion of the plastic industry, the muconic acid (**M26**) market is projected to grow from 36 million $ in 2016 to 60 million $ in 2024.[228] Also, adipic acid that can be obtained from lignin is currently manufactured on a very large scale (2700000 tonnes annually) with relatively low price (1600$/t) from petroleum.[229,54] However, the conventional adipic acid production involving nitric acid oxidation presents serious drawbacks related to NOx emissions.[229]

The selling price of petroleum-derived BTX components and phenol is currently low and difficult to compete with (benzene, 1.49$/kg; toluene, 1.38$/kg; xylene, 1.36$/kg; phenol, 1.54$/kg). However, if a cost competitive method would emerge for their production from lignin, there is huge potential (80000000 t annually for BTX and 8000000 t for phenol) without the danger of oversaturating the market.[37] 4-Alkylphenols may serve as replacements for petroleum-derived phenols in applications such as nonionic surfactants, lubricant additives, phenolic resins, polymer additives, and agrochemicals.[143,230] In order to produce these from structures shown in Figure 23 (e.g., **M6G**, **M6S**, **M7G**, and **M7S**), methods for selective demethoxylation are needed. Phenol could also be produced from 4-alkylphenols through new C−C bond cleavage reactions.[231] Catechol is an important chemical that can be used directly or as a precursor for the production of pesticides, or other fine chemicals such as perfumes and pharmaceuticals; however, the conventional phenol to catechol pathways[232] generally suffer from low selectivities.[233] An emerging pathway from lignin through guaiacol would provide a much more sustainable alternative. To this end, selective C−C bond cleavage and demethylation methods are required. Recent developments with regard to defunctionalization of lignin-derived aromatics to these simpler aromatics are discussed in section 3.

Another historically inexpensive petroleum-derived bulk chemical is styrene (1.9$/kg).[51] The demand for styrene shows a steady increase from 2.0 million metric tons (Mt) in 1970 to 3.2 million Mt in 1980 and 5.8 million Mt in 2004 in the United States alone.[234] A number of aromatic building blocks on Figure 23 could be potentially selectively defunctionalized to styrene; however, this will be the subject of future research.

The aromatic monomer 4-propylguaiacol (**M7G**) is frequently obtained by the lignin depolymerization strategies described in section 2. The price of such a typical monomer was recently found 1900$/t.[53]

Because lignin depolymerization is an emerging research area, selling prices for most obtained monomers are not yet available.

In the next section, we will explore the various possibilities for the further conversion of typical lignin-derived aromatic monomers to concrete products.

2.5. Conclusions

The large number of recent research papers summarized in section 2 suggests that lignin depolymerization has moved to the next level. A number of strategies exist that deliver interesting, emerging aromatic structures. It was generally recognized that recondensation phenomena either through lignocellulose processing or catalytic treatment seriously effect product yields, and a number of groups have focused on suppressing these side reactions. For example, near theoretical yields could be achieved by introducing formaldehyde during lignin isolation from lignocellulose,[105] or the stabilization of reactive intermediates during acidolysis of organosolv lignin[101,166,167] was described. Catalytic fractionation methods, especially under reductive conditions have significantly improved the product yields, notably obtaining only a limited number of defined products instead of complex mixtures.[40]

It is very difficult to provide a precise comparison of the novel catalytic methods developed for the depolymerization of organosolv lignin since the quality, molecular weight, solubility, and β-O-4 content of these starting materials differ strongly depending on the method of processing and isolation used by each research group. Therefore, standardization regarding method of isolation and reporting yields will be required to provide a better comparison of efficiency of the novel catalytic methods. A severe challenge at the moment is the lack of standard lignin samples of reproducible quality that would be suitable to benchmark novel methodologies. In addition, development of novel analytical methods and standardization of existing and emerging analytical techniques for understanding of the structure of lignocellulose and the resulting, frequently complex, product mixtures is desired.

Thus far, most catalytic methods have focused on tackling the fundamental challenge of selective bond cleavage in organosolv lignin or lignocellulose, focusing on the β-O-4 moiety. However, a significant knowledge gap exists regarding the cleavage of other types of linkages in lignin. In the future, more effort has to be devoted to the development of robust and recyclable catalysts which are tolerant to impurities. Novel catalytic systems should enable the full valorization of all lignocellulose components.

Upscaling of depolymerization methodologies as well as efficient methods for isolation and purification of the products, also in larger scale and efficient catalyst recycling should be investigated. Techno−economic analysis needs to be performed for these processes as well as possible products that may be derived from the emerging building blocks.

3. FUNCTIONALIZATION AND DEFUNCTIONALIZATION STRATEGIES

The lignin-derived monomers obtained in section 2 are less complex than lignin itself, however, keep some of the inherent

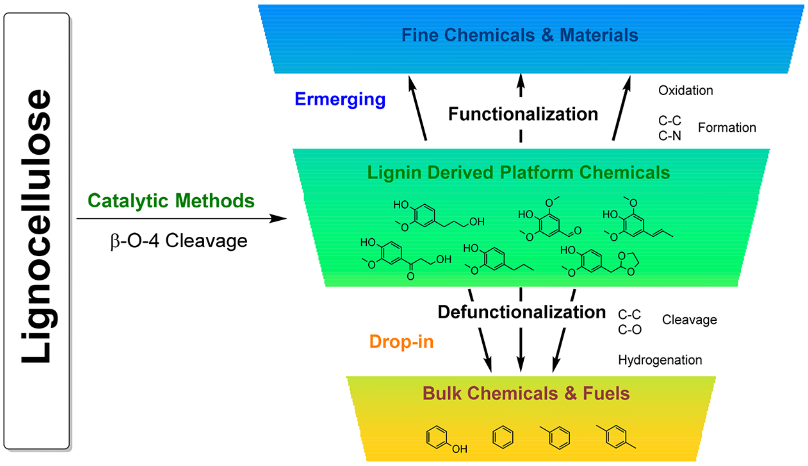


Figure 24. Summary of strategies for the conversion of lignin-derived monomers to emerging structures and bulk chemicals.

structural features of the renewable starting material. These structures will inspire new research directions in chemical catalysis that will focus on (a) selective functionalization to emerging building blocks and fine chemicals (b) selective defunctionalization to bulk chemicals (Figure 24).

Selective functionalization strategies should target atom economic and waste-free pathways for the direct conversion of aliphatic and aromatic alcohols to amines or the formation of new C−C bonds to obtain value-added products such as various polymer building blocks or pharmaceutical intermediates in few reaction steps, which will significantly contribute to achieving overall sustainability and meet green chemistry goals.[235] Novel and efficient defunctionalization methods hold the promise of producing simpler drop in molecules (e.g., BTX, phenol, catechol, and cyclohexane), which have large market potential. The advantage of producing compounds equivalent to those obtained from petrochemicals is that these structures are fully compatible with existing infrastructure.[236,237]

3.1. Functionalization Strategies

In this section, the possibilities for functionalization of aromatic monomers are detailed as such reactions have not yet comprehensively reviewed. Focus is devoted to catalytic methods able to transform moieties that constitute −OH as well as −OMe groups on the one hand and side chain functionalization of moieties on the other hand (Figure 25) related to compounds originating from catalytic depolymerization of lignin or lignocellulose (section 2).

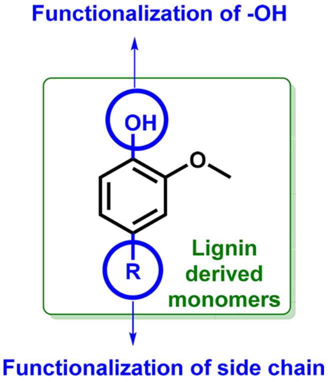


Figure 25. General strategies for functionalization of aromatic monomers obtained upon lignin depolymerization.

3.1.1. Functionalization of Guaiacyl-Type Substrates.

To detail the types of reactions able to functionalize phenol moiety in the presence of methoxy functionality, we have focused on guaiacol as model substrate. The guaiacol unit is the most abundant moiety in lignin-based monomers. However, compared to functionalization of phenol alone, methods for direct functionalization of phenol in the guaiacyl moiety are limited.

Direct Functionalization of the Phenol Moiety in Guaiacyl Type Substrates. Metal-free synthesis of aryl amines has been reported for the direct amination of phenols using aminating reagents in the presence of the stoichiometric amount of the base (Figure 26, route 1).[238] Later, cross-coupling of guaiacol with aryl boronic acids was achieved with nickel-based homogeneous catalysts. In this reaction, initially, guaiacol was reacted with 2,4,6-trichloro-1,3,5-triazine (TCT) to give the aryl C−O electrophile for the cross coupling with arylboronic acid (Figure 26, route 2).[239] Recently, Li explored the palladium-catalyzed direct cross-coupling of guaiacol with cyclohexylamine using sodium formate adding catalytic amount of acid (Figure 26, route 3). A tentative mechanism was proposed for this transformation.[240] Efficient O-arylation of the phenol moiety in guaiacol with aryl bromoarenes was reported using iron/copper-catalyst in DMF as a solvent at 135 °C (Figure 26, route 4).[241]

Functionalization of the Phenol Moiety in Guaiacyl Type Substrates via Derivatization. A strategy by which the free phenol group could undergo further catalytic transformation in a guaiacyl unit is through activation of the Ar−OH bond in the form of pseudohalogenides. Such strategy mitigates possible difficulties encountered due to the acidic hydroxyl group (pKA = 10) that frequently interferes with organometallic complexes and reduces the high dissociation energy of the Ar−OH bond in phenol. Even after derivatization, applying such pseudohalogenides in catalytic transformations may result in decreased reactivity compared to simple halogenides, due to the increased steric hindrance and electron density induced by the methoxy group.

Following this strategy, derivatives such as triflates, carboxylates, carbamate, and tosylates were prepared and subjected to various catalytic functionalizations, mainly relying on cross-coupling reactions that involve the formation of C−C and C−N bonds containing a guaiacol moiety. For instance, Buchwald reported Pd-catalyzed amination of aryl sulfonates under mild conditions using CS_2CO_3 as a base (Figure 27, route 1).[242] Later, a microwave-assisted, palladium-catalyzed coupling of aryl

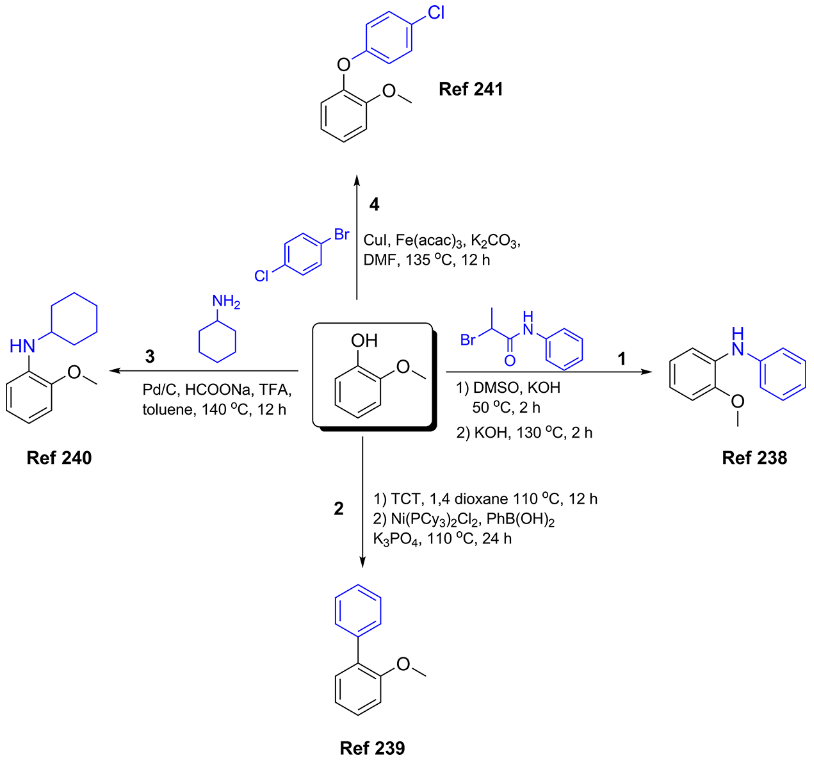


Figure 26. Direct functionalization of the phenol moiety in guaiacol.

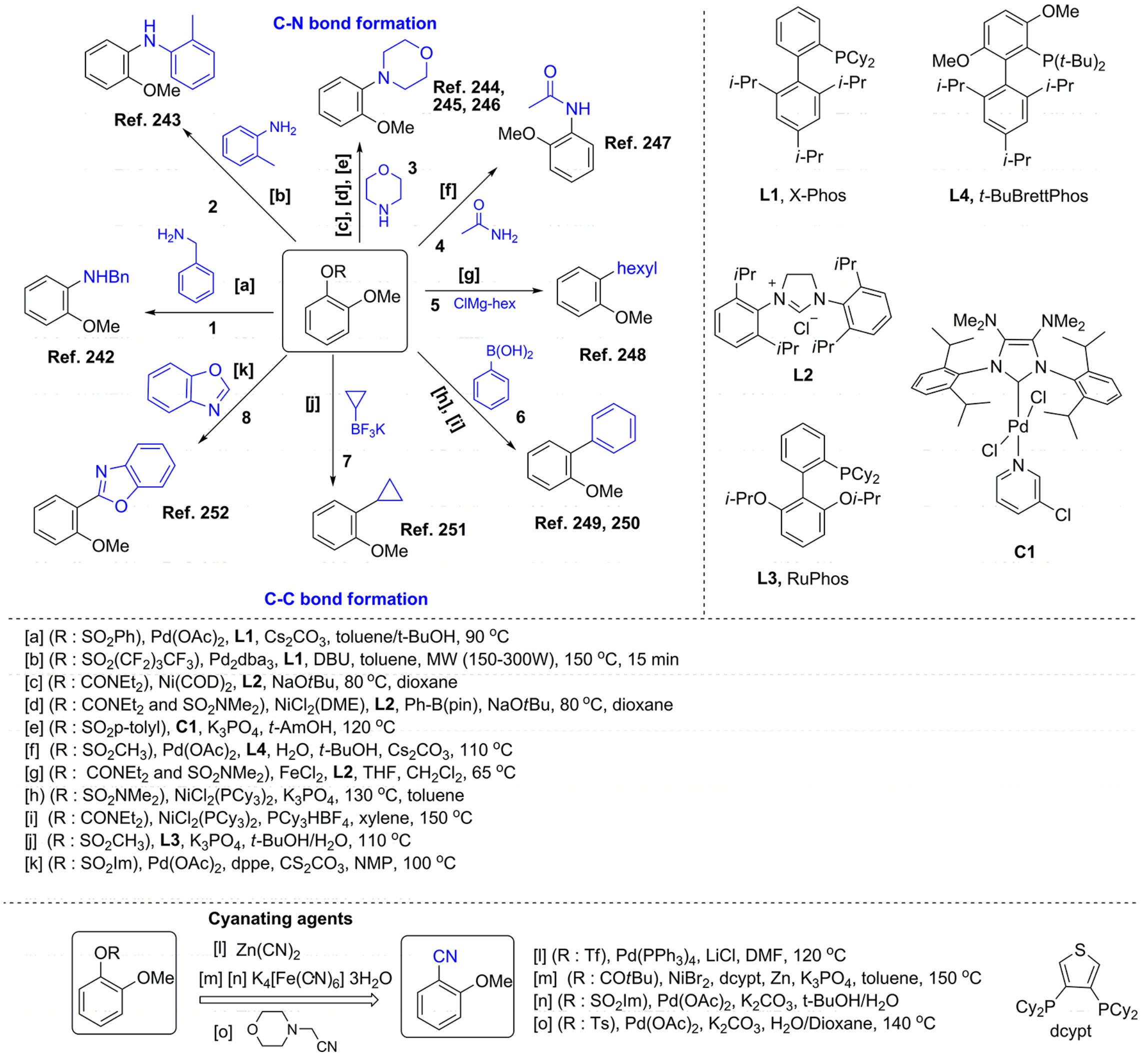
nonaflates and anilines were described using soluble and weak amine base (Figure 27, route 2).[243] In both cases, X-phos ligand showed good activity for the amination of guaiacol derivatives. Garg showed that aryl carbamates are attractive coupling partners for amination reactions using inexpensive and earth-abundant nickel catalyst (Figure 27, route 3, condition c).[244] Later, the same group developed the air-stable nickel precursor and NHC ligand system for the amination of aryl carbamates and sulfamates in the presence of Ph-B(Pin) as a reducing agent (Figure 27, route 3, condition d).[245] The Pd-PEPPSI catalyst was used for the cross-coupling of aryl tosylates with morpholine. In this work, an imidazol-2-ylidene ligand containing two dimethylamino groups enhanced both the electronic and steric properties of the carbine (Figure 27, route 3, condition e).[246] Interestingly, Pd-catalyzed cross-coupling reactions of amides and aryl mesylates yielded *N*-aryl amides (Figure 27, route 4).[247] The iron-catalyzed coupling of aryl sulfamates and carbamates with alkyl Grignard reagents was also reported, enabling carbon−carbon bond construction (Figure 27, route 5).[248] Extending possibilities for C−C formation reactions, the Suzuki-Miyaura coupling reactions of aryl sulfamates and carbamates with boronic acid was developed and reported independently by Garg and Snieckus with K$_3$PO$_4$ (Figure 27, route 6).[249,250] Interestingly, aromatic compounds comprising the small ring strained cyclopropyl moiety were constructed by palladium-catalyzed cross-coupling of mesylated guaiacol derivatives with potassium cyclopropyltrifluoroborate (Figure 27, route 7).[251] Notably, Ackermann et al. developed the palladium-catalyzed C−H activation coupling of benzoxazole with imidazole-sulfonates (Figure 27, route 8).[252]

Furthermore, 2-methoxybenzonitrile could be prepared by palladium-catalyzed cyanation of hindered aryl triflates and aryl tosylates in the presence of Zn(CN)$_2$[253] and K$_4$[Fe(CN)$_6$][254,255] as a cyanating agent, respectively. Nickel-catalyzed cyanation of phenol derivatives was described by Itami and Yamaguchi using metal-free and easy-to-handle cyanating agents, aminoacetonitriles, for this transformation. Interestingly, dicyclohexyl-substituted phosphine ligands showed good reactivity to achieve this conversion effectively.[256]

3.1.2. Functionalization of the Side Chain.

Alcohol 4-propanolguaiacol (**M10G**) is omnipresent in many lignin depolymerization methods. While catalytic methods involving **M10G** were not reported to the best of our knowledge, selected mild stoichiometric methods are known. Oxidative acetoxylation of **M10G** was carried out using hypervalent iodine reagents [phenyliodine(III) diacetoxy (PIDA)] via oxidative activation of arenol that converted into isolable orthoquinol acetates (Figure 28, route 1).[257] Alcohol **M10G** treated with 4-nitro benzaldehyde in the presence of AlCl$_3$ yielding 1,3,4,5-tetrahydrobenzo[c]oxepines (Figure 28, route 2).[258] Silica gel supported BF$_3$ catalyst were used for the selective acetylation of aliphatic alcohol in the presence of phenolic hydroxyl group by treatment with EtOAc (Figure 28, route 3)[259]

Furthermore, vanillin (**M1G**) can be obtained from lignin through various oxidative catalytic methods. Rhodium catalyst were used for the reductive amination of aldehyde with ammonia to form the corresponding primary amine under mild conditions (Figure 28, route 4).[260] The same amine could be obtained in the presence of palladium(0)-aminopropyl-mesocellular foam (Pd0-AmP-MCF) in toluene using HCOONH$_4$ (Figure 28, route 5).[261] Oxidation of the aldehyde group to the corresponding acids proceeds smoothly in the presence of Pd/C catalyst in aqueous methanol and sodium borohydride and potassium hydroxide at room temperature under air (Figure 28, route 6).[262] Another method to obtain the acid is thorugh Ag$_2$O/CuO-catalyzed oxidation by molecular oxygen (Figure 28, route 7).[263] 4-(1-Propenyl)guaiacol (**M18G**) is another encountered aromatic monomer from lignin depolymerization. It can be



[a] (R : SO_2Ph), $Pd(OAc)_2$, **L1**, Cs_2CO_3, toluene/t-BuOH, 90 °C
[b] (R : $SO_2(CF_2)_3CF_3$), Pd_2dba_3, **L1**, DBU, toluene, MW (150-300W), 150 °C, 15 min
[c] (R : $CONEt_2$), $Ni(COD)_2$, **L2**, NaO*t*Bu, 80 °C, dioxane
[d] (R : $CONEt_2$ and SO_2NMe_2), $NiCl_2(DME)$, **L2**, Ph-B(pin), NaO*t*Bu, 80 °C, dioxane
[e] (R : SO_2p-tolyl), **C1**, K_3PO_4, *t*-AmOH, 120 °C
[f] (R : SO_2CH_3), $Pd(OAc)_2$, **L4**, H_2O, *t*-BuOH, Cs_2CO_3, 110 °C
[g] (R : $CONEt_2$ and SO_2NMe_2), $FeCl_2$, **L2**, THF, CH_2Cl_2, 65 °C
[h] (R : SO_2NMe_2), $NiCl_2(PCy_3)_2$, K_3PO_4, 130 °C, toluene
[i] (R : $CONEt_2$), $NiCl_2(PCy_3)_2$, PCy_3HBF_4, xylene, 150 °C
[j] (R : SO_2CH_3), **L3**, K_3PO_4, *t*-BuOH/H_2O, 110 °C
[k] (R : SO_2Im), $Pd(OAc)_2$, dppe, CS_2CO_3, NMP, 100 °C

[l] (R : Tf), $Pd(PPh_3)_4$, LiCl, DMF, 120 °C
[m] (R : CO*t*Bu), $NiBr_2$, dcypt, Zn, K_3PO_4, toluene, 150 °C
[n] (R : SO_2Im), $Pd(OAc)_2$, K_2CO_3, t-BuOH/H_2O
[o] (R : Ts), $Pd(OAc)_2$, K_2CO_3, H_2O/Dioxane, 140 °C

Figure 27. Functionalization of the phenol moiety in guaiacol through protective groups, applying homogeneous catalysts.

oxidized to vanillin (**M1G**) by H_2O_2 using the catalyst combination *n*-Bu_4NVO_3/pyrazine-2-carboxylic acid (Figure 28, route 8).[264] 4-(1-Propenyl)guaiacol (**M18G**) can undergo oxidative cleavage by use of a special Co−porphyrin catalyst CoTPyP/TN and molecular oxygen as the oxidant to yield vanillin (**M1G**) (Figure 28, route 9).[265] 4-(1-Propenyl)guaiacol (**M18G**) was also shown to undergo an interesting para-hydroxyl group-directed remote benzylic C(sp^3)−H bond oxidation, by ligand and additive-free $Cu(OAc)_2$-catalyzed method and EG as solvent (Figure 28, route 10).[266] The double bond in this substrate is a promising moiety for the versatile functionalization of this aromatic building block by olefin metathesis. For instance, a cross-metathesis method in order to obtain the corresponding stilbene product was developed for the 4-(1-propenyl)guaiacol (**M18G**) which can be obtained from lignin after depolymerization. Notably, the reaction proceeds under solvent-free conditions and at low catalyst loading (0.01 mol %) within a couple of minutes (Figure 28, route 11).[267] In addition, acrylate cross-metathesis was developed for the synthesis of *α*,*β*-unsaturated esters (Figure 28, route 12).[268] Palladium catalysts surrounded on molecular sieves effectively catalyzed the selective hydrogenation of the alkene in 4-(1-propenyl)guaiacol (**M18G**) (Figure 28, route 13).[269] An efficient continuous-flow approach was used for the hydrogenation of 4-(1-propenyl)guaiacol (**M18G**) utilizing Wilkinson's catalyst (Figure 28, route 14).[270] Furthermore, an efficient method for the selective cleavage of C−C bond in this substrate was developed. Such reactions are important for the controlled chain shortening of lignin-derived monomers that are frequently bearing C3 chains, originating from the native structure of lignin. Ethenolysis reactions of 4-(1-propenyl)guaiacol (**M18G**) to styrene compounds was achieved with ruthenium NHC complex using 1,7-octadiene as a solvent under room temperature (Figure 28, route 15).[271]

3.2. Defunctionalization Strategies

With its intrinsic aromatic structure, lignin is by far the largest volume and most suitable renewable resource to substitute petro-aromatics. Although several lignin-derived products are already useful starting materials (e.g., vanillin **M1G**), the large scale implementation of other lignin-derived phenolic monomers, for instance as fuels or chemicals, requires further (bio)chemical upgrading. Microbial transformation with or without combination with a chemo-catalytic reaction step is one promising route. In this way, lignin fragments could be converted into adipic acid,[181,272] polyhydroxyalkanoates,[206,273] alkenoic acids,[206] and C9−C14 hydrocarbons.[273]

Catalytic hydrodeoxygenation (HDO) to alkanes and aromatics for direct use as liquid fuel or as feedstock for established petrochemical processes received increasing atten-

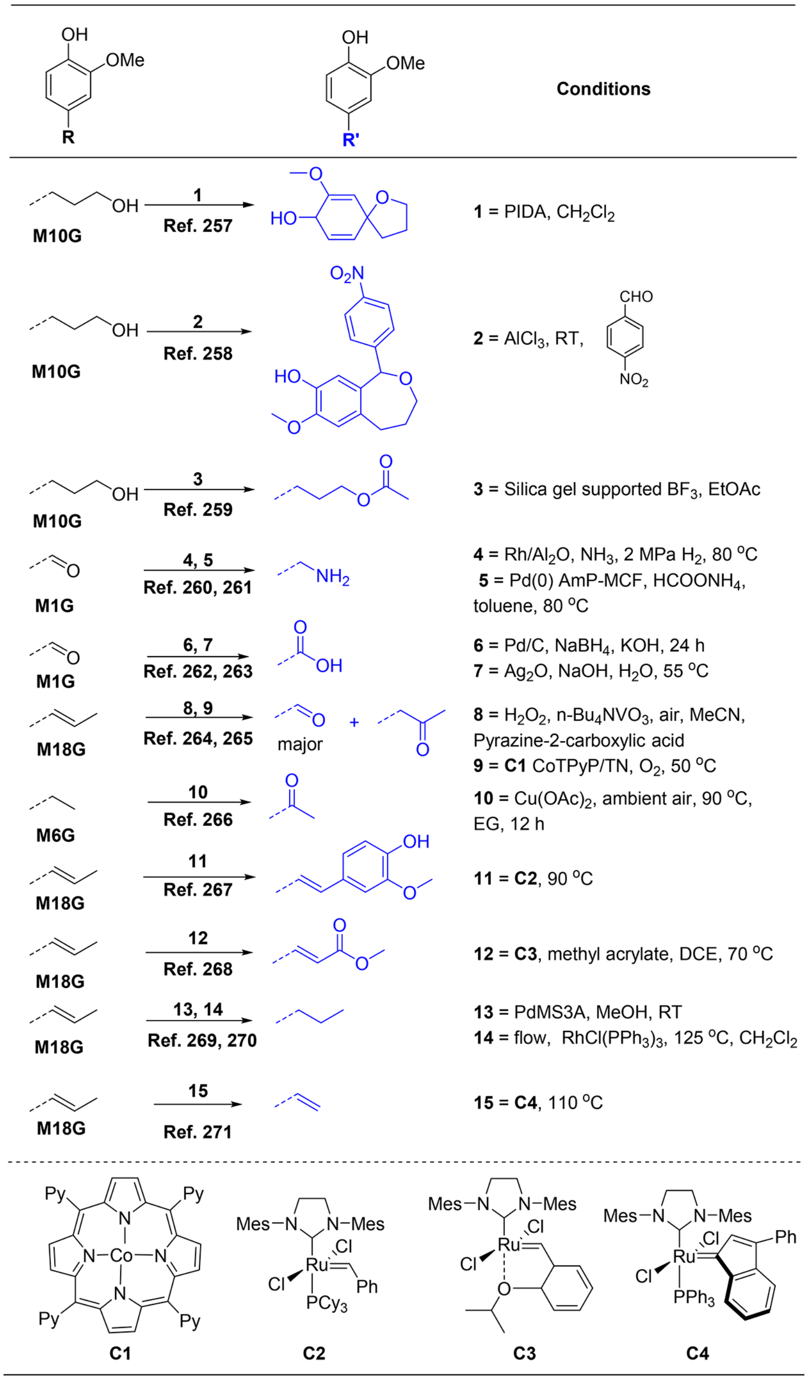


Figure 28. Catalytic strategies for the functionalization of the side chain of lignin-derived monomers.

tion (see Table 2). In Figure 29, the desired defunctionalization strategies applied on possible lignin-derived aromatics are summarized. These strategies have been primarily investigated with guaiacol and phenol as model compounds related to upgrading of biomass-derived pyrolysis oils, and studies have been summarized in several excellent reviews.[30,274−278] Herein, we will give a short discussion about the catalytic systems developed after 2010.

Selective hydrogenation of aromatic rings is one of the most important chemical processes as the generated aliphatic derivatives are crucial starting materials in synthesis of polymers, resins, dyes, and fine chemicals.[281] This reaction is normally operated under hydrogenation conditions with supported metal catalysts at high temperatures.[296] A suitable catalyst for the selective hydrogenation of the aromatic ring is Pd/C. Schutyser and co-workers[279] have shown that the selectivity for 2-methoxy-4-propylcyclohexanol could reach 90% when using lignin-derived 4-propylguaiacol (**M7G**) as substrate. Compared to Pd/C, a Ru/C catalyst gave slightly lower selectivity at 250 °C as the formation of cyclohexanol (19%) and cylcohexane (12%) as by products.[280] It was also found that a ZrO_2 supported Rh catalyst is also selective for the aromatic ring hydrogenation in guaiacol as model compound.[280] Beller and co-workers developed an intriguing method based on well-dispersed Ru nanoparticles supported on a nitrogen-doped carbon material. The method exhibited good-to-excellent activity in the selective

Table 2. Hydrogenation and Hydrodeoxygenation of Lignin-Derived Monomers

catalyst	reactor	T (°C)	P (bar)	solvent	substrate	conv. (%)	product (sele. %)[a]	ref
Pd/C	batch	300	40	hexadecane	4-propylguaiacol	~99	2-methoxy-4-propylcyclohexanol (90)	279
Rh/ZrO_2	batch	250	40	decane	guaiacol	100	2-methoxycyclohexanol (89)	280
Ru/C	batch	250	40	decane	guaiacol	100	2-Methoxycyclohexanol (60)	280
Ru@NDCs	batch	60	10	isopropanol	4-propylguaiacol	N. R.[c]	2-methoxy-4-propylcyclohexanol (86)[b]	281
Ru@NDCs	batch	60	10	isopropanol	vanillin	N. R.	4-hydroxy-3-methoxycyclohexanecarboxaldehyde (81)[b]	281
Pt/C	batch	200	20	H_2O	guaiacol	~80	cyclohexanol (~68)	282
Ru/C	batch	200	20	H_2O	guaiacol	~75	cyclohexanol (~70)	282
RuZrLa	batch	200	40	H_2O	guaiacol	100	cyclohexanol (91.6)	283
RuZrLa	batch	200	40	H_2O	4-propylguaiacol	100	propylcyclohexanol (89.5)	283
RuZrLa	batch	200	40	H_2O	4-propylsyringol	100	propylcyclohexanol (86.9)	283
RuZrLa	batch	200	40	H_2O	syringol	100	propylcyclohexanol (90.8)	283
Ru/C + MgO	batch	160	15	H_2O	guaiacol	98	cyclohexanol (79)	284
$Ru\text{-}MnO_x/C$	batch	160	15	H_2O	guaiacol	>99	cyclohexanol (72)	285
$Ru\text{-}MnO_x/C$	batch	160	15	H_2O	syringol	>99	cyclohexanol (70)	285
Co/TiO_2	batch	200	10	dodecane	eugenol	100	propylcyclohexanol (99.9)	286
Co/TiO_2	batch	200	10	dodecane	guaiacol	100	cyclohexanol (98)	286
Co/TiO_2	batch	200	10	dodecane	syringol	100	cyclohexanol (99.9)	286
$NiCo/Al_2O_3$	batch	200	50	H_2O	guaiacol	96.0	cyclohexanol (70.9)	287
Ni/CeO_2	batch	300	40	hexadecane	guaiacol	100	cyclohexanol (81)	288
Ni/CeO_2	batch	300	40	hexadecane	4-propylguaiacol	100	propylcyclohexanol (82)	288
$Ni/SiO_2\text{−}Al_2O_3$	batch	250	10	hexadecane	4-propylguaiacol	100	propylcyclohexanol (85)	279
RANEY@ Ni	batch	80	atm[d]	isopropanol	guaiacol	100	cyclohexanol (95)	218
RANEY@ Ni	batch	80	atm	isopropanol	syringol	95	cyclohexanol (92)	218
RANEY@ Ni	batch	80	atm	isopropanol	4-propylguaiacol	100	propylcyclohexanol (80)	218
RANEY@ Ni	batch	120	atm	isopropanol	4-allylsyringol	100	propylcyclohexanol (78)	218
RANEY@ Ni	glass H-cell	75	atm	H_2O	guaiacol	~99	cyclohexanol (79)	289
Ru/ACC	glass H-cell	80	atm	isopropanol	guaiacol	~53	cyclohexanol (~72)	290
Ni/SiO_2 (64.2%)	batch	320	170	no solvent	guaiacol	96.7	cyclohexanone (~55)	291,292
$NiCu/CeO_2\text{−}ZrO_2$	batch	320	170	no solvent	guaiacol	94.2	cyclohexanone (~60)	291,292
Raney Ni and nafion/SiO_2	batch	300	40	H_2O	guaiacol	100	cyclohexane (86)	137
Raney Ni and nafion/SiO_2	batch	300	40	H_2O	syringol	100	cyclohexane (57)	137
Raney Ni and nafion/SiO_2	batch	300	40	H_2O	4-propylguaiacol	95	propylcyclohexane (91)	137
Pd/C and H_3PO_4	batch	250	50	H_2O	4-propylguaiacol	99	propylcyclohexane (65)	136,142
Pd/C and H_3PO_4	batch	250	50	H_2O	eugenol	100	propylcyclohexane (71)	136,142
Pd/C and H_3PO_4	batch	250	50	H_2O	4-allylsyringol	92	propylcyclohexane (58)	136,142
Pt/C and H_3PO_4	batch	200	20	H_2O	guaiacol	~78	cyclohexanol (~85)	282
Pd/C and HZSM-5	batch	200	50	H_2O	guaiacol	100	cyclohexane (85)	139
Pd/C and HZSM-5	batch	200	50	H_2O	4-propylguaiacol	97	propylcyclohexane (90)	139
Pd/C and HZSM-5	batch	200	50	H_2O	eugenol	97	propylcyclohexane (90)	139
Pd/C and HZSM-5	batch	200	50	H_2O	4-allylsyringol	95	propylcyclohexane (80)	139
Ru/HZSM-5	batch	200	50	H_2O	guaiacol	99.9	cyclohexane (93.6)	293
Ru/HZSM-5	batch	200	50	H_2O	syringol	76.2	cyclohexane (57.2)	293
Ru/HZSM-5	batch	200	50	H_2O	4-propylguaiacol	99.6	propylcyclohexane (89.5)	293
Ru/HZSM-5	batch	200	50	H_2O	4-allylsyringol	99.9	propylcyclohexane (85.4)	293
$Rh/SiO_2\text{−}Al_2O_3$	batch	250	40	decane	guaiacol	100	cyclohexane (57)	280
$Ru/SiO_2\text{−}Al_2O_3$	batch	250	40	decane	guaiacol	100	cyclohexane (60)	280
Ni/HZSM-5	batch	250	50	H_2O	guaiacol	100	cyclohexane (74)	138
Ni/HZSM-5	batch	250	50	H_2O	4-propylguaiacol	98	propylcyclohexane (84)	138
Ni/HZSM-5	batch	250	50	H_2O	eugenol	100	propylcyclohexane (80)	138
Ni/HZSM-5	batch	250	50	H_2O	4-allylsyringol	93	propylcyclohexane (78)	138
$Ni/SiO_2\text{−}ZrO_2$	batch	300	50	dodecane	guaiacol	100	cyclohexane (96.8)	294
Ni/SiO_2 (55.5%)	batch	320	170	no solvent	guaiacol	97.5	cyclohexane (~62)	291,292
$NiCu/Al_2O_3$	batch	320	170	no solvent	guaiacol	80.2	cyclohexane (~52)	291,292
$NiCu/SiO_2$	batch	320	170	no solvent	guaiacol	87	cyclohexane (~62)	291,292
$NiCuLa/ZrO_2\text{−}SiO_2$	batch	320	170	no solvent	guaiacol	85.6	cyclohexane (~63)	291,292

Table 2. continued

catalyst	reactor	*T* (°C)	*P* (bar)	solvent	substrate	conv. (%)	product (sele. %)[a]	ref
Ru/CNT	batch	220	50	dodecane/H_2O	guaiacol	N. R.	cyclohexane (92)[e]	295
Ru/CNT	batch	220	50	dodecane/H_2O	4-propylguaiacol	N. R.	propylcyclohexane (94)[e]	295
Ru/CNT	batch	220	50	dodecane/H_2O	eugenol	N. R.	propylcyclohexane (94)[e]	295
Ru/CNT	batch	220	50	dodecane/H_2O	4-allylsyringol	N. R.	propylcyclohexane (80)[e]	295

[a]Numbers in brackets are selectivity determined by GC. [b]Isolated yield. [c]N. R. means not reported. [d]atm means atmospheric pressure at room temperature. [e]Number in brackets means GC yield.

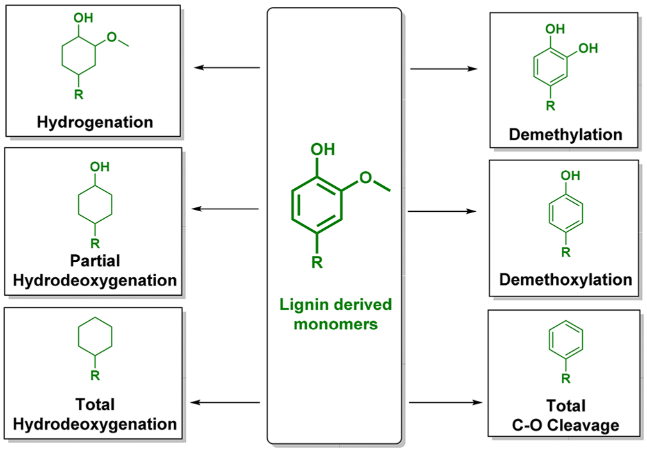


Figure 29. Strategies for defunctionalization of lignin-derived monomers.

hydrogenation of arenes without promoting extensive hydrodeoxygenation.[281] This method was also efficient in the hydrogenation of realistic lignin-derived aromatic compounds while preserving the phenyl- and benzyl C−O bonds.

Another interesting route for defunctionalization of lignin-derived monomers is the selective hydrodeoxygenation to oxygenated products such as cyclohexanols that should involve a combination of hydrodemethoxylation and aromatic ring hydrogenation with retention of the hydroxyl group. Cyclohexanol is an important precursor of polymer building blocks like caprolactam, caprolactone, and adipic acid.[297,298] Alkyl-substituted cyclohexanols could open a new way for synthesizing alkylated variants of these polymer building blocks since the presence of alkyl groups allows for tuning the polymer's physical properties such as crystallinity, melting point, elasticity, etc.[279,288] Both noble and non-noble metal catalysts have been used and high cyclohexanol selectivity was mainly achieved with Pt,[282] Ru,[282−285,290] Co,[286,287] and Ni[218,279,287−289] based catalysts. Methods using Pt/C and Ru/C give similar selectivity (68% vs 70%) in the hydrogenation/deoxygenation of guaiacol at 200 °C.[282] Furthermore, a bifunctional RuZrLa catalyst showed significant activity and selectivity for the hydrogenation/deoxygenation of both guaiacol and lignin-derived monomers.[283] Over 88% yield of cyclohexanols were obtained from lignin-derived methoxyphenols after hydrotreatment at 200 °C for 4 h in water. Nakagawa and co-workers successfully used a Ru catalyst combined with MgO at significantly decreased reaction temperature.[284] Addition of MgO to the reaction media suppressed the unselective C−O dissociation, and cyclohexanol and methanol were obtained in high yield (>80%) at 160 °C. However, MgO was not stable during the reaction when using water as solvent and acidic substrates. An optimized catalyst system, namely Ru-MnO_x/C,[285] was found to be an easy-to-handle alternative to promote selective demethoxylation. This catalyst gave cyclohexanol from guaiacol in higher yield than Ru/C combined with MgO.

Several groups focused on using less expensive, Co- or Ni-based catalysts, which are familiar to industry. Liu et al.[286] investigated a series of cobalt-based catalysts on various supports for the catalytic conversion of lignin-derived phenols to cyclohexanols. Among these catalysts, Co/TiO_2 showed the best HDO activity and high yield of propylcyclohexanol (>99.9%) was achieved under 1 MPa H_2, 200 °C for 2 h. Zhou and co-workers[287] studied the catalytic activity of γ-Al_2O_3 and ZSM-5 (Si/Al = 25, 38) supported non-noble metal (Co and/or Ni) catalysts for the HDO of guaiacol. The introduction of Co into Ni/γ-Al_2O_3 could enhance the acidity, reducibility, and metal particle dispersion of the catalyst, which resulted in increase of catalytic activity. The maximum guaiacol conversion was observed when water was used as solvent with a selectivity of 70.9% of cyclohexanol. Sels et al. developed several supported Ni catalysts, such as Ni supported on CeO_2 for the conversion of lignin-derived guaiacols into the corresponding cyclohexanols in yields above 80%.[288] Furthermore, using commercial base metal catalyst Ni/SiO_2−Al_2O_3 a propyl-cyclohexanol yield of 85% was obtained at 250 °C.[279] However, the drawback of using Ni/SiO_2−Al_2O_3 was shown to be methane formation.

Raney nickel is widely used in current industrial processes owing to its low cost, easy preparation, and high activity.[299] Wang and Rinaldi pioneered the use of isopropanol as H-donor and solvent in combination with Raney Ni for the defunctionalization of lignin monomers.[218] Under low-severity conditions (80−120 °C), excellent yield (78%−95%) of cyclohexanols was obtained.

Another promising strategy to achieve high yield of cyclohexanols at mild conditions was the use of Raney Ni as electrode in electrocatalytic hydrogenolysis/hydrogenation.[289] Selective cleavage of aryl ether (C−O) bond followed by reduction of the aromatic ring at ambient pressure and 75 °C was observed in aqueous solution. Another example of a hydrogenation/hydrodeoxygenation strategy was using a Ru/ACC electrocatalyst.[290] Similar electrochemical efficiencies for reducing guaiacol, phenol, and syringol were seen; however, temperature was found to influence the electrochemical efficiency. Guaiacol reduction increased from 8% at 25 °C to 17% at 50 °C but then dropped back to 10% at 80 °C. Solution pH also affected catalyst activity and product selectivity, with acidic conditions favoring guaiacol conversion, electrochemical efficiency, and cyclohexanol selectivity.

Despite their importance as precursor for the polymer intermediate caprolactone,[300] cyclohexanones are rarely reported products in one-pot catalytic conversion of lignin-derived monomers. Cyclohexanones can be obtained from cyclohexanols by dehydrogenation reaction using Cu/ZrO_2[288] or as an intermediate in the isomerization of the partial-hydrogenation product cyclohexenol (ketone/enol tautomerism).[292] When testing the performance of several Ni-based catalysts obtained by coprecipitation and impregnation techniques in the hydro-

Table 3. From Lignin-Derived Monomers to Catechol, Phenol, and Benzene by Heterogeneous Catalysts

catalyst	reactor	T (°C)	P (bar)	solvent	substrate	conv. (%)	product (sele. %)	ref
α-MoC_{1-x}/AC	batch	340	atm	H_2O	guaiacol	36	catechol (94)	302
MoO_2/AC	batch	340	atm	H_2O	guaiacol	33	catechol (93)	302
MoN/SBA15	batch	300	50	decalin	guaiacol	44	phenol (26)	303
MoN-A	batch	300	50	decalin	guaiacol	95	phenol (90)	304
1Mo/C	fixed-bed	350	40	no solvent	guaiacol	74.1	phenol (78.5)	305
$NiMo/Al_2O_3$	packed-bed	450	20.7	no solvent	4-propylguaiacol	~95	4-propylphenol (~70)	306
α-MoC_{1-x}/AC	batch	340	atm	tetralin	guaiacol	53	phenol (84)	302
$MoWBO_x/AC$	fixed-bed	400	40	methanol	vanillic acid + syringic acid	100	p-hydroxybenxoic acid (71.6)	307
MoC_x/ C	batch	300	5	hexane	guaiacol	99	phenol (76)	308
MoC_x/ C	batch	300	5	hexane	syringol	91	phenol (37)	308
$NiMo/Al_2O_3$	packed-bed	450	20.7	no solvent	4-propylguaiacol	~95	4-propylphenol (~70)	306
Re/ZrO_2	batch	300	50	decalin	guaiacol	~50	phenol (~35)	309
WP/SiO_2	packed bed	300	50	no solvent	guaiacol	60	phenol (100)	310
Au/TiO_2	batch	300	65	toluene	guaiacol	100	phenol (49.6)	311
CoMoS	fixed bed	300	40	no solvent	guaiacol	50	benzene (42)	312
$CoMoS/TiO_2$	fixed bed	300	40	no solvent	guaiacol	~95	benzene (~60)	313
10Mo/C	fixed-bed	400	40	no solvent	guaiacol	100	benzene (83.5)	305
Ni_2P/SiO_2	fixed-bed	300	1.4	no solvent	guaiacol	99.5	benzene (71.9)	314
Ni_2P/SiO_2	packed bed	300	50	no solvent	guaiacol	80	benzene (60)	310
Ru/C	fixed-bed	400	40	no solvent	guaiacol	100	benzene (69.5)	305
$Ru/LaCO_3OH$	batch	240	2	H_2O	guaiacol	95.6	benzene (~79)	315

deoxygenation of guaiacol, Bykova et al.[292] found that large amount of cyclohexanone can be obtained at 320 °C from 1-cyclohexen-1-ol through keto−enol tautomerism.

Another defunctionalization strategy is the selective cleavage of C−O bonds (either demethylation or demethoxylation of full defunctionalization) without hydrogenation of the aromatic ring and yielding catechols, phenols, and benzenes, respectively, which are important aromatic compounds. These processes are generally operated at high temperatures (>300 °C), frequently in continuous flow reactors to avoid hydrogenation of aromatic ring.

Total hydrodeoxygenation of bioderived phenols to hydrocarbons is the most effective method for upgrading of bio-oils.[30,274,275,277] Many studies were conducted to develop catalysts with high catalytic activity and stability, low hydrogen consumption, and high selectivity toward direct removal of oxygen with the aim to convert oils originating from catalytic pyrolysis processes.[2,301] Most of the studies use guaiacols and syringols as the model compounds and guide for the potential upgrading of lignin-derived monomers.

Lercher and co-workers developed a series of catalytic methods for the one-pot hydrodeoxygenation through multistep reactions consisting of hydrogenation, dehydration, or hydrolysis and hydrogenation of functionalized aromatics to alkanes, which use the combination of a hydrogenation catalyst (Raney Ni, Pd/C or Pt/C) with a homogeneous/heterogeneous acid (H_3PO_4, Nafion, or HZSM-5).[136,137,139,142] Excellent cycloalkane yields, above 80%, were reported from lignin-derived monomers in the case of Pd/C and HZSM-5. Another strategy is the use of solid acid support for the development a bifunctional catalyst such as Ru supported on HZSM-5, which exhibited excellent hydrodeoxygenation activity toward the conversion of lignin-derived phenolic monomers.[293] It was shown that both the presence of Brønsted acid site supplied by HZSM-5 for dehydration and the metal Ru for hydrogenation were crucial to achieve good selectivity. Several lignin-related C6−C9 phenolic monomers could be converted to cyclohexanes in high yield at 200 °C. The high activity of this catalyst was attributed to the strongly acidic site on the surface of HZSM-5 as other acidic support like SiO_2−Al_2O_3 gave much lower yield (~60%) with Ru and Rh at even higher temperature (250 °C).[280] Other than noble metal catalysts, bifunctional Ni catalyst also showed excellent activity for hydrodexoygenation of lignin-derived monomers. However, higher temperature (250−320 °C) and pressure (50−170 bar) were normally required.[291,292,138,294]

Most of the systems for HDO of phenols were conducted in a single solvent such as water or *n*-decane. Biphasic systems have notable advantages in protecting the products from further degradation by extraction/separation into another phase. In 2015, Fu and co-workers[295] found that biphasic systems with the combination of water and dodecane used showed superior advantages over monophasic systems in HDO reactions. By means of a Ru/CNT catalyst designed by this group, full conversion of eugenol and 98% alkane selectivity (94% propylcyclohexane and 4% propylcyclopentane) was achieved at 220 °C and 50 bar H_2.

Catechol is an important chemical that can be used directly or as a precursor for the production of pesticides or other fine chemicals such as perfumes and pharmaceuticals.[233] So far, only a few synthetic procedures exist for transformation of substituted phenols into catechols; however, these normally suffer from low selectivity, in particular for meta-substituted phenols.[232] Instead of using phenols, a more sustainable route from lignin via guaiacol and subsequent demethylation to catechol would be desired. A method for demethylation of aryl methyl ethers using iodocyclohexane in DMF under reflux condition was described by Zuo et al.[316] who obtained catechol with 91% isolated yield in 4 h from guaiacol. Waghmode et al. developed a method for selective cleavage of aryl methyl ethers in the presence of a protic acid (HBr) and a catalytic amount of phase-transfer catalyst (Aliquat-336).[232] Another method that provided full conversion of guaiacol and 89% yield of catechol was developed reported by Yang et al. This system relied on heating guaiacol in hydrochloric acid solution at 280 °C under 10 bar hydrogen.[317] Generally, the selective demethylation of guaiacols with heterogeneous catalysts is very challenging due to the more favorable demethoxylation

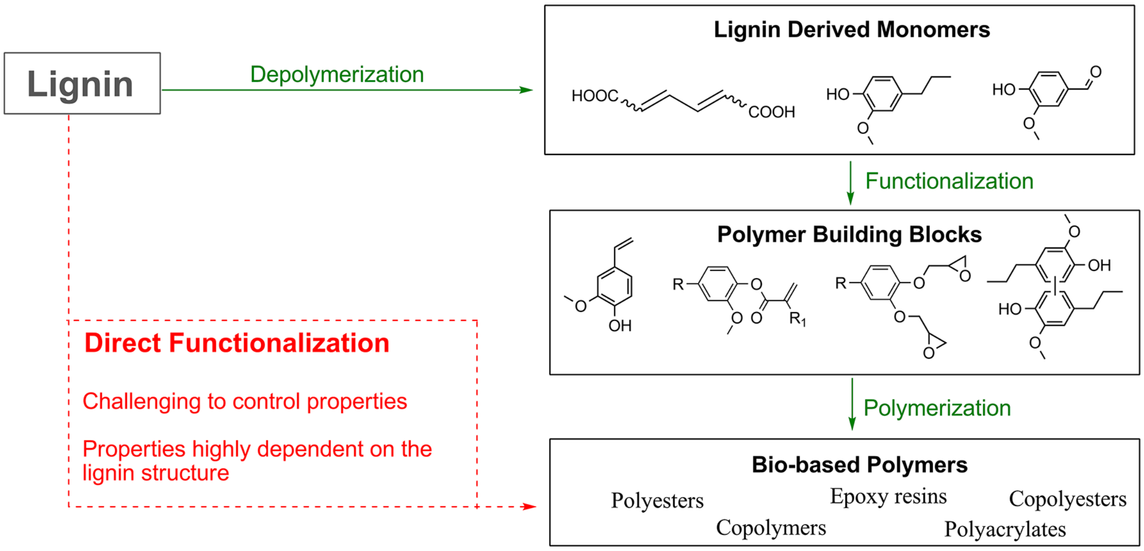


Figure 30. General strategies for production of polymers from lignin.

reaction that generally yields phenol as the main product. As shown in Table 3, the heterogeneous catalyst α-MoC_{1-x}/AC is a unique choice for obtaining catechol in high selectivity, albeit at lower conversion values.

4-Alkylphenols are interesting candidates to serve as replacements for petroleum-derived phenols in several applications[143,230] and can also be used as the intermediates for the production of phenols.[231] Several groups have studied the possibilities to obtain phenols by demethoxylation of guaiacols (Table 3) including the most widely applied molybdenum-based catalysts[302−308] as well as Re/ZrO_2,[309] WP/SiO_2,[310] and Au/TiO_2;[311] however, these often suffer either from low activity or low selectivity.

Benzene could be produced from guaiacol by total C−O bond cleavage generally through phenol as intermediate. Molybdenum-based catalysts including CoMoS,[312] $CoMoS/TiO_2$[313] and 10Mo/C[305] and Ni_2P-supported catalysts[310,314] were successfully applied in this reaction to give high benzene selectivity. This reaction could also be successfully performed with an increase in reaction temperature to 400 °C by using Ru/C as catalyst.[305]

Notably, in combination of Raney Ni with HZSM-5, Rinaldi and co-workers[217] pioneered the selective formation of fully defunctionalized aromatics from model compounds and pyrolysis oil components, via a unique transfer hydrogenation/dehydration/rearomatization sequence under mild conditions.

Recently Zhao and co-workers[315] synthesized a hydrothermally stable $Ru/LaCO_3OH$ catalyst in which Ru nanoparticles were partially encapsulated by $LaCO_3OH$ by a strong metal−support interaction. This conferred high catalyst stability and activity for the hydrogenolysis of several biomass-derived model compounds. Under aqueous conditions at 240 °C and 0.2 MPa H_2, 75.8% yield of benzene was obtained from guaiacol at nearly full substrate conversion. Notably, high conversion (>95%) and >70% benzene selectivity was found even after eight runs, highlighting the exceptional stability of this catalyst.

3.3. Conclusions

Several selective functionalization and defunctionalization strategies were reported that could be potentially applied in the downstream processing of lignin-derived monomers. However, a significant knowledge gap exists due to the predominant use of model compounds that are significantly simpler in structure than the monomers currently found from lignin depolymerization methods (Figure 23). This necessitates the study of the existing methods using more complex substrates as well as the development of novel methods that would allow for good functional group tolerance.

Regarding the functionalization of the phenol moiety in guaiacol derivatives, new catalysts are desired that would allow one to directly install C−C and C−N bond starting from aromatic alcohol moieties (especially in the vicinity of a methoxy substituent) since known transformations generally use protecting groups (Figure 27) which decrease the overall atom economy of such reactions. In addition, new catalysts are needed for the direct functionalization of an aromatic methoxy group, which is highly abundant in lignin-derived monomers. Regarding 4-propanolguaiacol (**M10G**) that can be obtained in high yield from lignin, the functionalization of the aliphatic alcohol in the presence of a phenol needs to be investigated, since the availability of such methods is very limited.

Several powerful methods have been identified for the selective defunctionalization of simpler lignin-derived aromatics that will be further evaluated and potentially upscaled. Future research should focus on the development of non-noble metal catalysts that might operate at milder reaction conditions as well as the development of one-pot, tandem depolymerization and defunctionalization strategies to obtain bulk chemicals directly from lignin.

4. LIGNIN-DERIVED MONOMERS TO BIOBASED POLYMERS OR POLYMER BUILDING BLOCKS

The world plastics production has markedly increased from 230 Mton/year in 2005 to 322 Mton/year in 2015.[318,319] Nearly 50−55% of this quoted polymer production volume is attributed solely to polyethylene and polypropylene, which currently are not easily or cost effectively bioderivable,[320] although second generation bioethanol serves as promising future alternative. Interestingly, biobased polyethylene can be produced via ethylene by ethanol dehydration (Braskem Company, plant production capacity of 200000 tons per year started in 2010 in Brazil),[321] even though this currently appears most feasible in places where the cost of sugars is low, such as Brazil.[322] Several commercial examples of biobased polymers are available but

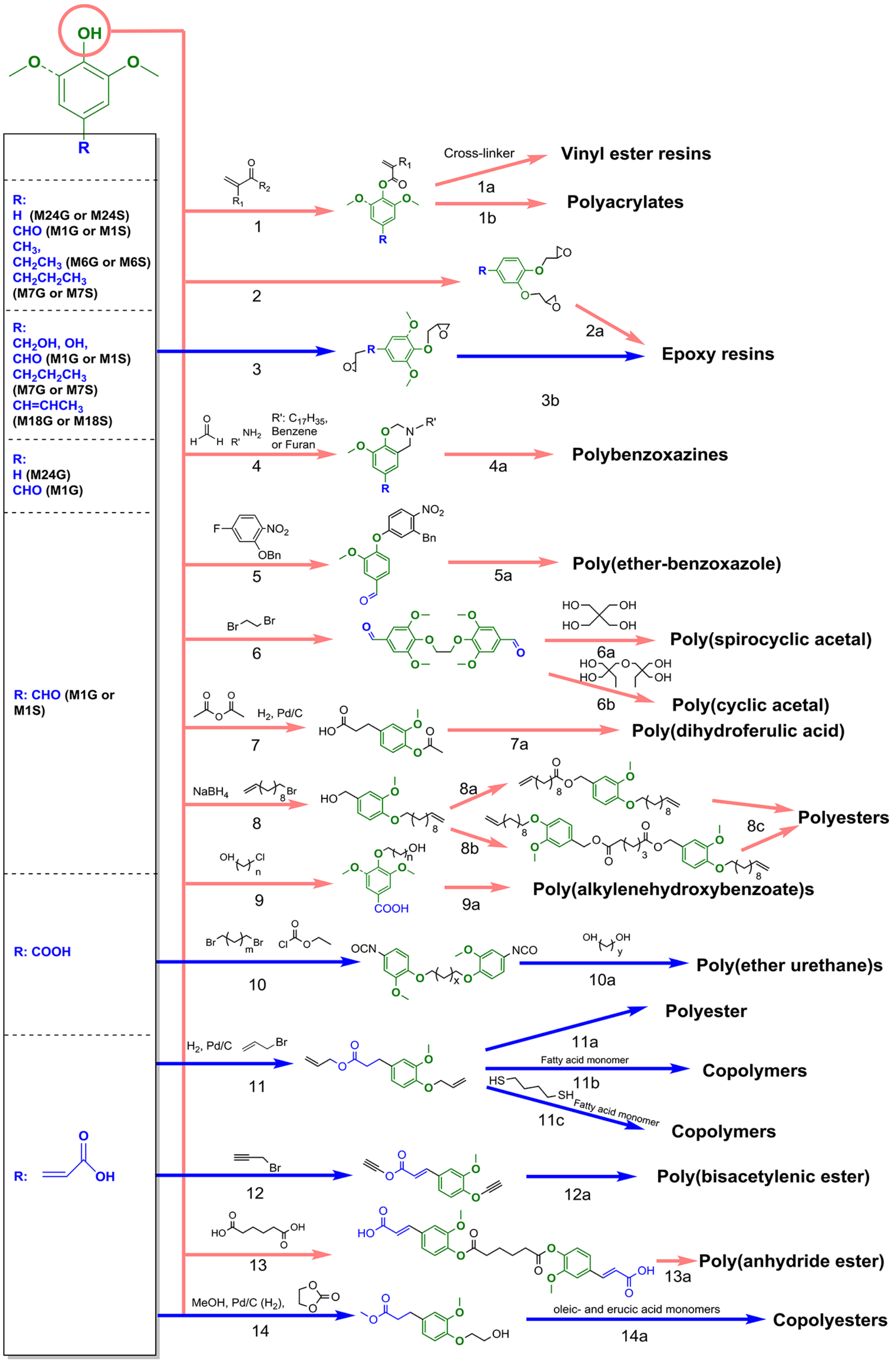


Figure 31. Polymers produced from lignin-derived monomers by functionalization of only the phenol moiety or both the phenol moiety and the side chain.

related mostly to different kind of polymers such as starch plastics,[323] poly(lactic acid) (PLA, Natureworks LCC), polyhydroxyalkanoate (PHA, Metabolix and Archer Daniels Midland Company), polyamide 11 (PA11, Arkema), partially biobased epoxy resins (Solvay Epiceroland DowGTE technologies), or polyethylenefuranoate (PEF, Avantium, pilot scale).[324] In spite of these existing examples, only a small fraction of the worldwide manufacture of polymers is bioderived (1.7 Mton/year in 2014).[325] Thus, new strategies are needed in order to facilitate the production of polymers from renewable resources.[326]

To this end, the search of suitable biobased starting materials for polymer production and, specifically, the development of biobased polymers from lignin or lignin-derived monomers has drawn an enormous interest in recent years.[325,327]

Lignin can be directly used for the production of polymers[325,327−330] (e.g., polyurethanes, phenol−formaldehyde resins, polyesters, and phenolic and epoxy resins) typically by

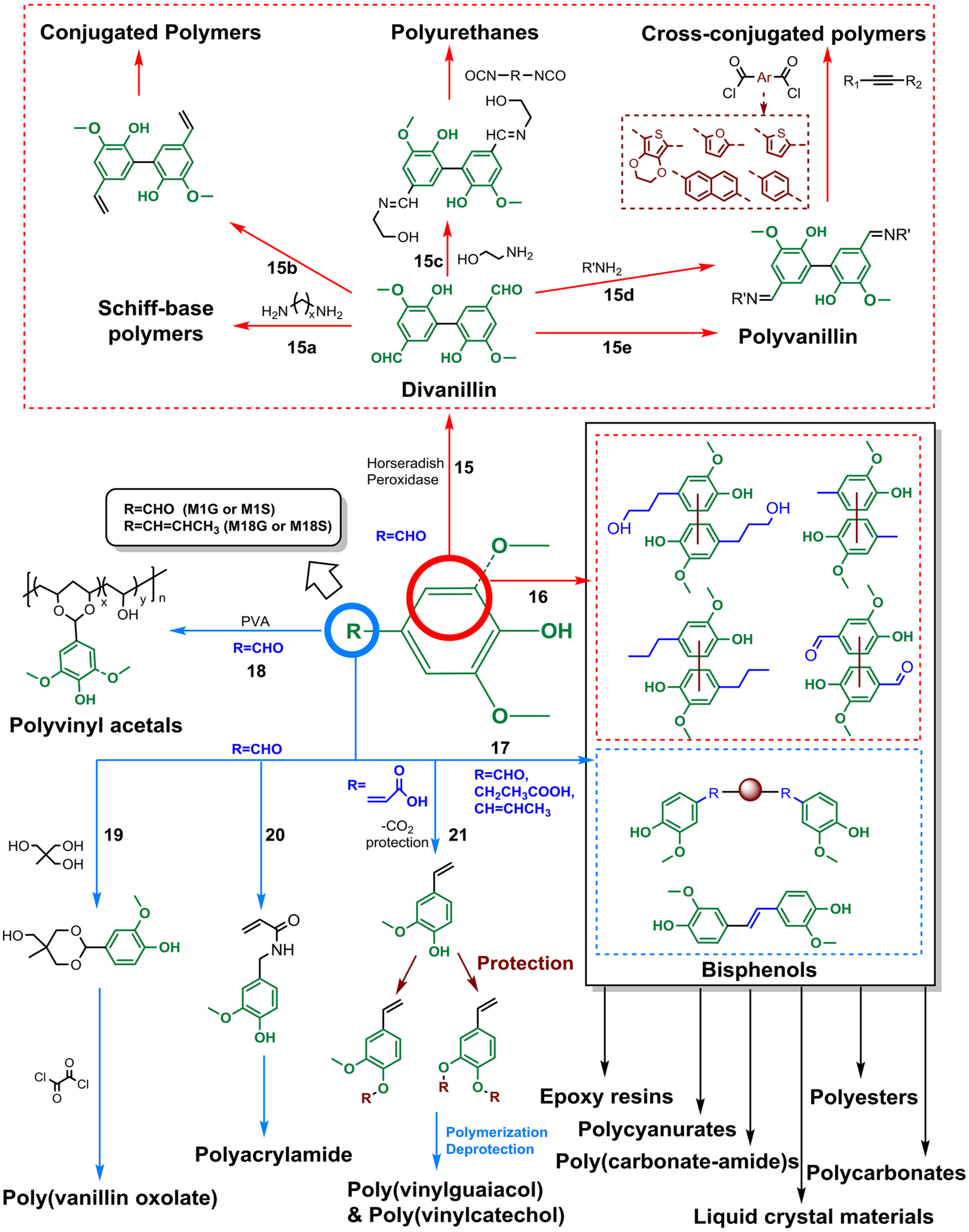


Figure 32. Polymers produced from lignin-derived monomers by functionalization of the aromatic ring or only the side chain.

functionalization of the hydroxyl groups in its structure or used as copolymers, blends, and composites.[331,332] The limitations of these applications are related to the relatively ill-defined structure/composition of the starting material, where the properties of the obtained polymers may depend on the origin of lignin, method of extraction, and fragmentation processes present during synthesis and functionalization (Figure 30).[333] Another limitation is that lignin is often used in minor amounts for these blends and composites since the main building blocks of these polymers still originate from petroleum.

Lignin-derived monomers, however, are well-defined small molecules, frequently aromatic in nature.[332] This aromatic structure provides valuable properties such as rigidity, hydrophobicity, as well as resistance against fire, essential for many applications. They are preferably obtained through a mild lignin depolymerization methodology, retaining most of the functionality present in the natural feedstock, which results in a highly modular structure and various possibilities for further functionalization. Indeed, numerous novel structures and polymers have been produced in the recent years.[327,328,330,334] Herein, we will give a summary of methods that were used to transform lignin-derived monomers to polymers. Further, we specifically describe the properties of reported polymers that were produced recently (2016−2017). The properties of polymers published before 2016 are summarized in the excellent review by Cramail and co-workers[333] and others.[327,330,335]

4.1. From Lignin-Derived Aromatic Monomers to Polymers

Figure 31 and Figure 32 show the various possibilities of functionalization of lignin-derived aromatic monomers (discussed in section 2), including modification of the phenol functionality and aromatic ring functionalization. In addition, the side chain can participate in several reactions depending on its nature, which will be influenced by the applied depolymerization method.

4.1.1. Modification through the Phenol Functionality and/or Side Chain. Several polymer materials were reported by modifying the phenol group only (Figure 31). For example by functionalization with acrylates (route 1), several polyacrylates (route 1b) were obtained from vanillin (**M1G**), guaiacol (**M24G**), or 4-alkylguaiacols[336−338] or vinyl ester resins (route 1a) by using a cross-linker.[339−342] Furthermore, the synthesis of epoxy resins was reported using vanillin (**M1G**), vanillic acid (**M20G**), vanillyl alcohol,[343−347] or 4-(1-propenyl)guaiacol (**M18G**)[348] from direct functionalization of both phenol and the side chain (route 2 and 3). Abu-omar and co-workers produced several novel biobased epoxy nanocomposites from 4-propylguaiacol (**M7G**) by functionalization of phenol and −OMe group.[349,350] Next, benzoxazines were produced with a one-pot method from phenolic derivative, primary amine, and formaldehyde (route 4), which underwent ring-opening polymerization (route 4a) to polybenzoxazines.[351−354] Biobased poly(ether benzoxazoles) could be obtained through reacting vanillin (**M1G**) with 5-fluoro-2-nitrophenol followed by hydrogenation and thermal treatment (route 5 and 5a).[355] Aromatic dialdehydes prepared by the reaction of lignin derivatives with 1,2-dibromoethane using sodium hydroxide and potassium iodide in water (route 6) were condensed with pentaerythritol (route 6a) and ditrimethylolpropane (route 6b) to produce a new class of cyclic polyacetal ether thermoplastics.[356] Poly(dihydroferulic acid), which exhibits thermal properties functionally similar to those of polyethylene terephthalate (PET), could be synthesized from vanillin (**M1G**) and acetic anhydride (route 7 and 7a).[357] Firdaus et al.[358] prepared bis-unsaturated esters from **M1G** and fatty acids (route 8). Then all the monomers were polymerized via the acyclic diene metathesis (ADMET) or thiol−ene methodologies (route 8c). Polyalkylenehydroxybenzoates and poly(ether urethane)s were produced by functionalization of only the phenol group (route 9 and 9a)[359] or both phenol and carboxyl groups (route 10 and 10a)[360] in vanillic acid. Although ferulic acid (**FA**) is not included in the product table from depolymerization strategies, we have also included related routes. Various polyesters could be produced from **FA**.[361] For instance, **FA** could be transformed to a α,ω-diene derivative in a two-step sequence (route 10), with subsequent preparation of the respective polyesters via ADMET reaction (route 11a). Following the same method, several copolymers were also produced but reacting with fatty acid monomers (route 11b) or via thiol−ene addition with 1,4-butanedithiol (route 11c). After reaction with propargyl bromide by using **FA**, a bisacetylenic monomer was obtained (route 12), and it was polymerized by the oxidative coupling polymerization to obtain a novel polyetherester (route 12a).[362] Uhrich and co-workers reported the synthesis of polyanhydride esters. In this study, a diacid monomer was first synthesized (route 13) and then polyanhydride esters were obtained by polycondensation with triphosgene (route 13a). Meier and co-workers[363] synthesized a series of novel copolyesters with different ratios of aliphatic (obtained from oleic and erucic acid via thiol−ene addition) and aromatic (hydroxyethylated methyl ester derivative of ferulic acid) monomers (route 14 and 14a).

4.1.2. Modification through the Aromatic Ring or Side Chain. *Divanillin.* Divanillin, which can be easily synthesized by oxidative dimerization of vanillin by horseradish peroxidase (route 15),[364] is a useful intermediate for synthesis of other polymer building blocks. For instance, Razzaq and co-workers reacted divanillin with alkyl diamines (1,2-diaminoethane, 1,3-diaminopropane, and 1,6-diaminohexane) in ethanol; after reflux the Schiff base polymers with a degree of polymerization between 25 and 32 were obtained (route 15a).[365] Divanillin was converted to α,ω-dienes and then a conjugated polymer was obtained by ADMET polymerization (route 15b).[366] Vanillin is also a useful chain extender after its dimerization and further modification with ethanolamine in the synthesis of biobased polyurethanes (route 15c).[367] These vanillin-derived diimines were converted into conjugated pyrrole-based polymers by a transformation exploiting a catechyl-substituted phosphonite-mediated multicomponent polymerization with commercial diacid chlorides and simple alkynes or alkenes (route 15d).[368] Importantly, this study reported, for the first time, a cross-conjugated polymer composed of both components of lignocellulosic biomass by using vanillin and furan-based acid chlorides. Polyvanillin, which is a functionalized polymer using totally renewable resources can be simply synthesized by electrochemical reductive polymerization of divanillin in aqueous sodium hydroxide (route 15e).[369]

Sustainable Bisphenols. To generate thermoplastics such as polycarbonates and thermosetting resins from lignin-derived monomers, bisphenols are usually required. There are two strategies to produce bisphenols using lignin-derived monomers as starting materials. The first is a coupling on the aromatic ring of two phenolic monomers with formaldehyde,[349,370−373] by enzymatic dimerization[366,374] or electrophilic aromatic condensation[375] (route 16). An alternative strategy is the functionalization of the side chain, which includes formation of stilbenes[267,376,377] or coupling of two phenolic monomers with a cross-linker[378−382] (route 17). After obtaining the bisphenol precursor, a series of polymers including polycarbonates,[370,376] epoxy resins,[378,380,382] polyesters,[374,379,383] polycyanurates,[370,372,376] poly(carbonate−amide)s,[384] and liquid crystal materials[381] could be produced with simple modification of the bisphenol structure.

Diverse Side Chain Modifications. Polymers with only functionalization of the side chain are also possible. Miller and co-workers reported a series of polyvinyl aromatic acetals, which were obtained from the condensation of commercially available poly(vinyl alcohol) (PVA) and sustainable aromatic aldehydes including vanillin (**M1G**), syringaldehyde (**M1S**), and other 11 aldehydes (route 18).[385] Polymeric nanoparticles based on poly(vanillin oxalate) (PVO), were developed by Lee and co-workers (route 19).[386] These nanoparticles presented great potential as novel antioxidant therapeutics and drug delivery systems. Roger and co-workers synthesized the acrylamide derivative from vanillin by a three step process, and then the obtained acrylamide monomer was polymerized by free radical polymerization (route 20).[387] Decarboxylation of ferulic acid results in 4-vinylguaiacol, which was easily and quantitatively transformed into novel-biobased styrene monomers by Take-

Table 4. Thermomechanical Properties of Lignin Derivative-Based thermosets

entry	resins	lignin derivatives	T_g (°C)	T_{dec} (°C)	curing procedure	ref
1	epoxy resins	4-(1-propenyl)guaiacol (**M18G**)	78–120[a]	T_{max} = 322–412[e]	150 °C for 1 h	348
2	epoxy resins	mixtures of phenolics	99–113[b]	T_{max} = 261–303[d]	(1) 110 °C for 1 h (2) 150 °C for 1 h	343
3	epoxy resins	4-propylguaiacol (**M7G**)	40–139 (T_α)[c]	$T_{5\%}$ = 193–297[d]	(1) 55 °C for 2 h (2) 75 °C for 2 h (3) 95 °C for 2 h	349
4	epoxy resins	hydrogenolysis products derived from softwood lignin (mixture used)	59–135[a]	$T_{5\%}$ = 220–325[d]	(1) 40 or 80 °C for 24 h (2) 120 °C for 24 h (3) 150 °C for 24 h	394
5	epoxy resins	vanillyl alcohol and guaiacol (**M24G**)	100–158 (T_α)[c]	T_{max} = 352–392[d]	(1) 90 °C for 5 h (2) 160 °C for 2 h	375
6	epoxy resins	vanillyl alcohol and guaiacol (**M24G**)	81–103[c]	T_{max} = 345–365[f]	(1) 90 °C for 5 h (2) 160 °C for 2 h	395
7	epoxy resins	4-hydroxybenzaldehyde, vanillin (**M1G**), syringaldehyde (**M1S**), 4- methylguaiacol, 4-propylguaiacol (**M7G**), 4-methylcatechol	82–167 (T_α)[c]	$T_{5\%}$ = 220–269[d]	(1) r.t. for 8 h (2) 60 °C for 4 h (3) 80 °C for 4 h	396
8	epoxy network	4-propylguaiacol (**M7G**) + deprotected lignin	130–141 (T_α)[c]	$T_{5\%}$ = 273–297[d]	(1) 55 °C for 2 h (2) 75 °C for 2 h (3) 95 °C for 2 h	397
9	epoxy resins	vanillin (**M1G**)	166–214[a]	$T_{5\%}$ = 286–356[e]	(1) 160 °C for 2 h (2) 200 °C for 2 h (3) 230 °C for 2 h	382
10[g]	epoxy resins	lignin-derived C2-acetals	67–134[d]	N. R.	N. R.	378
11	cyanate ester resins	4-propylguaiacol (**M7G**)	193–231[h]	$T_{5\%}$ = 375–389[d]	(1) 150 °C for 1 h (2) 210 °C for 24 h (3) 280 °C for 4 h	370
12	vinyl ester resins	phenyl methacrylate, 2-methoxyphenyl methacrylate, and 4-propyl-2-methoxyphenyl methacrylate	125–155 (T_α)[c]	T_{max} = 392–427[d]	(1) 90 °C for 4 h (2) 180 °C for 2 h	341
13	poly-vanillin methacrylate	vanillin methacrylate	102[a]	250–480 °C[d,j]	65 °C for 6 h	340
14[i]	polymer on the methacrylate-modified Fe_3O_4 NPs	vanillin methacrylate	N. R.	N. R.	N. R.	342

[a] DSC under nitrogen. [b] DSC under air. [c] DMA. [d] TGA under nitrogen. [e] TGA under air. [f] TGA under argon. [g] Curing made directly during DSC analysis and occurring around 140 °C. [h] TMA under nitrogen. [i] Microshperes used as adsorbents, thermal properties not reported. [j] Decomposition temperature range.

shima and co-workers[388] (route 21). Herein the phenolic functions in 4-vinylguaiacol and 4-vinylcatechol were protected with silyl groups and subjected to controlled radical polymerization to give a series of polymers with controlled molecular weights.

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4.2. Properties of Polymers Obtained from Lignin-Derived Monomers

4.2.1. Lignin-Derived Thermosets. *Epoxy Thermosets.* A thermoset polymer is a material undergoing degradation with increasing temperature instead of behaving like a fluid.[389] Thermosets represent less than 20% of plastic production[390] and are usually synthesized from a polymeric chain reacting with a cross-linker in order to provide a three-dimensional structure.[391] These polymers are extremely interesting due to the possibility of easily varying their properties, which not only depend on the nature and molecular weight of the polymer material but also on the cross-linking density that is adjustable. Thus, a broad range of different properties can be potentially reached.[391] In fact, themosets have been employed in several applications such as packaging, electronics, coatings, adhesives, and composites thanks to their usually high modulus, strength, and good thermal and chemical resistance.[392] Among the various classes of thermosets, epoxy resins have been broadly investigated. These materials represent approximately 70% of the market of thermosets due to their superior chemical and heat resistance, adhesion, and mechanical properties.[390]

Several aromatic structures mentioned in section 2 (e.g., Vanillin **M1G**, 4-propylguaiacol **M7G**, and 4-(1-propenyl)-guaiacol **M18G**) can be obtained from lignin and lignocellulose. Interestingly, they can be employed to produce several polymers. For instance, François et al.[348,393] used 4-(1-propenyl)guaiacol (**M18G**) to synthesize its diglycidylether (DGE-isoEu) (Figure 31, route 3) which was subsequently cured in the presence of several anhydride and acid hardeners (e.g., maleic anhydride, MA) to prepare thermosetting resins (Figure 31, route 3b). After obtaining DGE-isoEu in 92% yield, epoxy resins were synthesized by heating mixtures of DGE-isoEu (Table 4, entry 1) with curing agents and 2-ethyl-4-methylimidazole (EMID) as catalyst. Nanoindentation measurements showed an instantaneous and relaxed modulus ranging from 4.15 to 5.54 GPa and a hardness parameter that varies between 230 and 400 MPa, values of the same order of magnitude as petroleum-based resins. Fache et al.[343] employed model mixtures of depolymerization products of lignins from both softwood and hardwood directly to prepare epoxy resins (Figure 33). First, the phenolic functionalities were subjected to Dakin oxidation followed by glycidylation to produce a mixture of epoxy monomers. Subsequently, the resins where prepared using isophorone diamine (IPDA) as hardener, obtaining a homogeneous glassy material after curing (Table 4, entry 2). The thermo-mechanical properties determined by dynamic mechanical analysis (DMA) showed characteristics of high-performance epoxy thermosets.

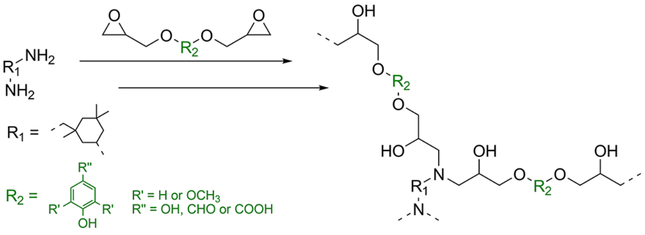

Figure 33. Synthesis of cross-linked thermosets by epoxy/amine reaction and epoxy polymers from model mixtures of G- and GS-type monomers. Adapted with permission from ref 348. Copyright 2016 Royal Society of Chemistry.

Zhao et al.[349] used 4-propylguaiacol (**M7G**) to synthesize several starting monomers differing in molecular weight orientation of functional group and number of epoxy groups to explore systematically the differences in the final material properties (Figure 31, route 2; Figure 32, route 16). They demonstrated that the epoxy resins obtained from the new monomers in the presence of diethylenetriamine (DETA) improved in thermomechanical properties increasing the cross-linking density (Table 4, entry 3). In particular, the use of an oligomer derived from modification of 4-propylguaiacol (**M7G**) through phenol−formaldehyde reaction led to the highest cross-linking density with an α-relaxation temperature (T_α) of 139 °C and a high degradation temperature ($T_{5\%}$ = 297 °C in contrast with 193−245 °C). Importantly, T_α value is slightly higher than the 137 °C of traditional DGEBA/DETA epoxy resins (diglycidyl ether of bisphenol A/epoxy prepolymer cured with diethylenetriamine), showing the possible effective replacement in terms of this parameter.

Van de Pas and Torr[394] used the oil from mild hydrogenolysis of pinewood to react with epichlorohydrin to give epoxy prepolymers (Figure 34). After fractionation in diethyl ether, they obtained two fractions named hydrogenolysis epoxy prepolymers (LHEP) and oligomeric lignin hydrogenolysis epoxy prepolymers (LHOEP). Blending these with bisphenol A diglycidyl ether (BADGE) or glycerol diglycidyl ether (GDGE) and curing with DETA or IPDA they obtained epoxy resins. Interestingly, the use of BADGE or GDGE and different curing agent leads to a pronounced effect on the final thermomechanical properties (Table 4, entry 4). In particular, this study evidenced that blending LHEP and LHOEP with BADGE and curing with IPDA gave mechanical properties similar to the industrial BADGE control resin while increased flexural modulus and strength were observed if cured with DETA. However, lower T_g (68−104 °C) were detected in this case, indicating that IPDA enhanced the resin thermal properties reaching T_g of the order of 100−135 °C. When LHEP and LHOEP were blended with GDGE, similar mechanical properties were detected while T_g around 60 °C were obtained, indicating a restriction in the use of these materials to lower temperature applications.

Hernandez et al.[375] prepared bisguaiacol through condensation of vanillyl alcohol and guaiacol (**M24G**) to then obtain diglycidyl ether of bisguaiacol (Figure 32, route 16). Furthermore, three single aromatic diglycidyl ethers were synthesized from vanillyl alcohol, gastrodigenin, and hydroquinone. Once cured with a diamine (4,4′-methylenebiscyclohexanamine), they found a positive influence of methoxy and methylene moieties on the thermomechanical properties of the final material. The methoxy groups improved the modulus of cured resins; however, a lower T_g (100−124 vs 131−149 °C) was found (Table 4, entry 5). Subsequently, the diglycidyl ethers of gastrodigenin, vanillyl alcohol, bisguaiacol, and hydroquinone were employed by Mauck et al.[395] to be reacted with the cellulose-derived 5,5-methylenedifurfurylamine as curing agent and obtain epoxy amine thermosets (Table 4, entry 6). These new highly bioderived thermosetting epoxy and amine resins were characterized by good thermogravimetric and thermomechanical properties comparable with a commercial BPA-epoxy resin demonstrating the possibility of its replacement.

Zhao et al.[396] prepared a series of triphenylmethane-type polyphenols (TPs) from guaiacols [4-methylguaiacol and 4-propylguaiacol (**M7G**)] and aldehydes [4-hydroxybenzaldehyde (**M1P**), vanillin (**M1G**) and syringaldehyde (**M1S**)] (Figure 35).

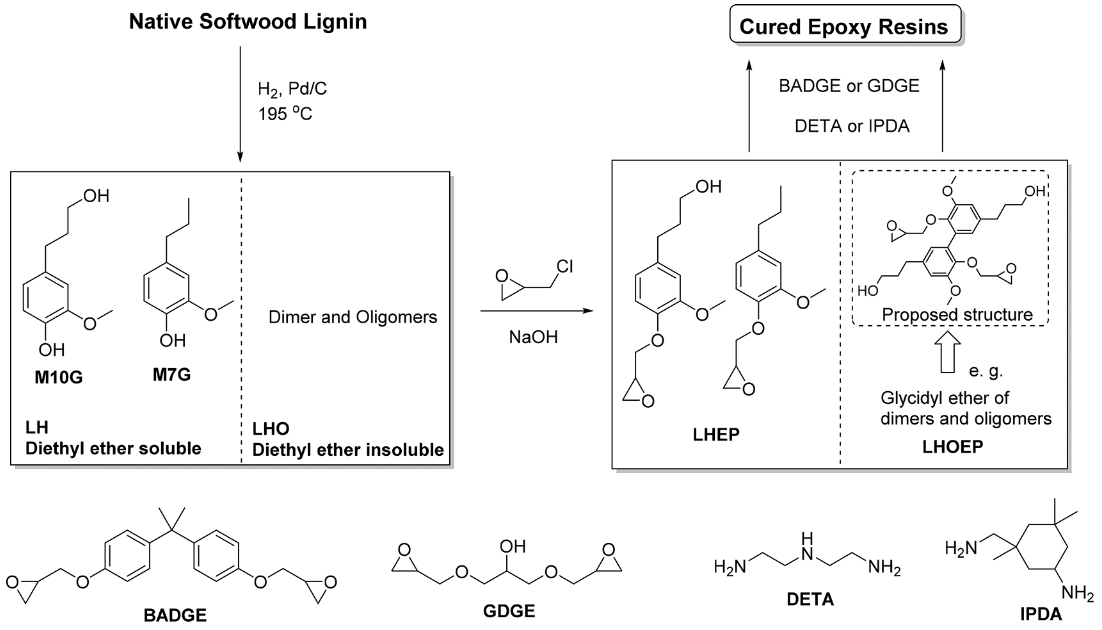

Figure 34. Approaches to prepare cured epoxy resins from lignin hydrogenolysis products and the cured epoxy resin specimens. Adapted from ref 394. Copyright 2017 American Chemical Society.

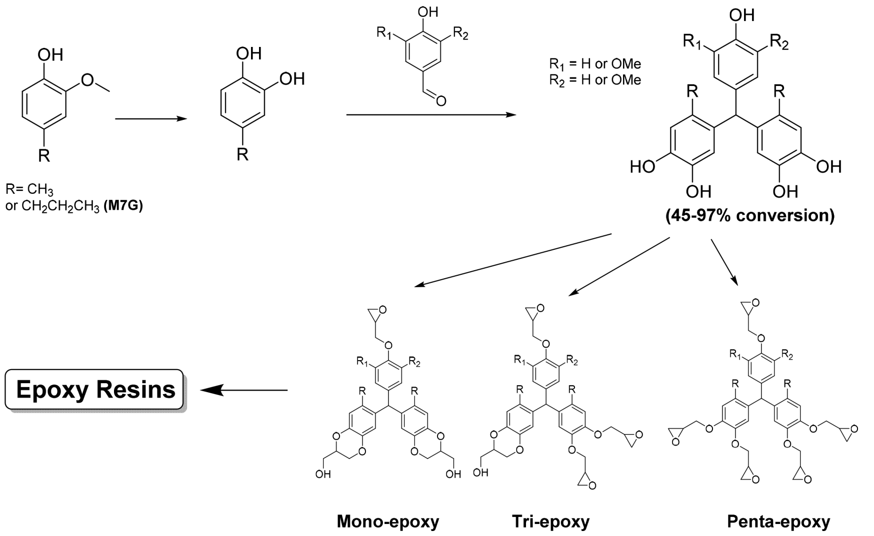

Figure 35. Synthesis route of fully renewable triphenylmethane-type polyphenols and corresponding polymers from lignin-derived aldehydes and para-substituted guaiacols. Adapted from ref 396. Copyright 2017 American Chemical Society.

Afterward, the polyphenol was epoxidized and cured or reacted with a modified linoleic acid followed by epoxidation and curing to obtain the final resin (Table 4, entry 7). Interestingly, the presence of the long chain of linoleic acid acted as plasticizer decreasing both T_α and storage modulus from 167 to 82 °C and from 12.3 to 3.6 GPa, respectively. They also prepared epoxy resin, employing both lignin-derived phenols (LDPs) and lignin itself.[397] This procedure involved demethylation of lignin followed by the addition of 4-propylguaiacol (**M7G**) and formaldehyde solution to make a deprotected lignin incorporated novolac polyphenol (DLINP). Consequently, the DLINP was reacted with epichlorohydrin and cured with diethylenetriamine (DLINEN). Interestingly, the obtained polymer (DLINENs) were characterized by thermal and mechanical properties similar to the neat polymer prepared exclusively with LDPs in terms of degradation temperature ($T_{5\%}$ = 273−287 °C vs 297 °C) and glass-relaxation temperature (T_α = 130−141 °C vs 139 °C) (Table 4, entry 8).

Wang et al.[382] reported the synthesis of vanillin-based epoxy resins characterized by flame retardant properties thanks to phosphorus introduction using the coupling agent [4,4-diaminodiphenylmethane (DDM)] or *p*-phenylenediamine (PDA) (Figure 32, route 17) to produce materials with similar or improved mechanical and thermal properties compared with the commercial DGEBA (Table 4, entry 9).

Kaiho et al.[378] studied the synthesis of lignin-based epoxy resins with controlled glass transition temperature starting from selectively depolymerized lignin containing a C2-acetal structure. The C2-acetals were subjected to (1) transacetalization with tetraol di(trimethylolpropane) (DTMP) to introduce a flexible structure or (2) generation of a phenylnaphthalene structure via aldol condensation and intramolecular annulation to introduce a

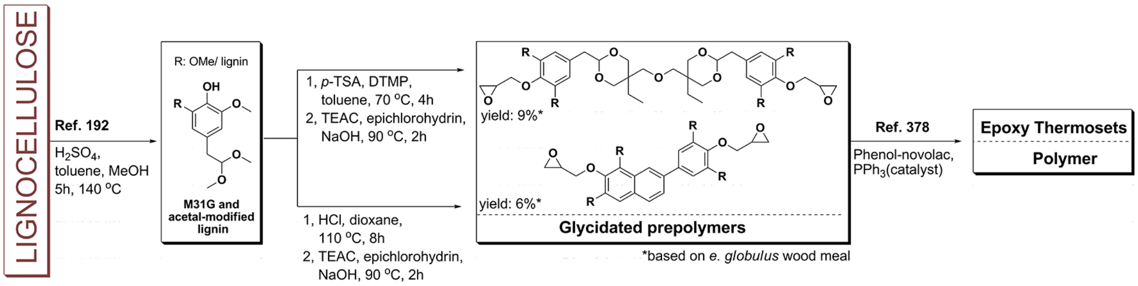

Figure 36. Synthesis of lignin-based epoxy resins by using lignin-derived monomer (**M31G**) and acetal-modified lignin.

rigid structure (Figure 36). Afterward, the phenolic hydroxyl group underwent glycidylation providing the corresponding reactive epoxide. Subsequently, phenol novolac and triphenylphosphine (TPP) were mixed with the monomer producing the final epoxy resins (Table 4, entry 10). Notably, the resin containing DTMP showed lower flexural strength and impact strength compared to the phenylnaphthalene.

Other Lignin-Derived Thermosets. Koelewijn et al.[370] proposed the synthesis of cyanate ester thermosets starting from 4-propylguaiacol (**M7G**) (Figure 32, route 16). Specifically, they prepared *m,m′*-bisguaiacols from methyl-, ethyl-, and propylguaiacols studying the effect of the alkyl chain systematically (Table 4, entry 11). Importantly, the highest decomposition and glass transition temperature were detected with 4-propylguaiacol (**M7G**). Bassett et al.[341] studied the effect of impurities in reactive diluents prepared from lignin model compounds on the properties of commercial vinyl ester resins (VER) (Figure 31, route 1a). VER are in fact usually blended with diluents like styrene to reduce resin viscosity for liquid molding processing and increase polymer performance.[398] Thus, the lignin-derived diluents (phenyl methacrylate, 2-methoxyphenyl methacrylate, and 4-propyl-2-methoxyphenyl methacrylate) were tested as possible styrene replacement (Table 4, entry 12). The use of pure compounds led to a material with properties comparable to the industrial one while the impure VER markedly deteriorated the material.

Zhang et al.[340] employed vanillin methacrylate as monomer to produce polymeric microspheres containing reactive aldehyde groups. Interestingly, they demonstrated the effective functionalization with glycine obtaining Schiff-base chelating microspheres which were proven to be efficient as adsorbent of Cu^{2+} used as a representative of heavy metal ions (over 130 mg/g) (Table 4, entry 13). Subsequently, the same group prepared the same microspheres introducing methacrylated-Fe_3O_4 NPs as magnetic moiety enabling an easy separation from liquid medium.[342] Interestingly, the microspheres were proven to be effective adsorbents for paraanisidine (representative for amines) and proposed as suitable materials for immobilizing enzymes (Table 4, entry 14).

4.2.2. Lignin-Derived Thermoplastic Polymers.

A thermoplastic polymer is a material which behaves as a fluid above a specific temperature.[335] Thermoplastic materials are employed in several applications depending on their chemical nature and thus final properties. Important industrial examples are polyamides (PA, nylon), polypropylene (PP), polyethylene (PE), poly(vinyl chloride) (PVC), polystyrene (PS), poly(methyl methacrylate) (PMMA, Plexiglas), and poly(ethylene terephthalate) (PET) which are polymers frequently used for fibers, containers, automotive parts, insulators, furniture, foams, packaging, medical equipment, and so on. However, their synthesis is usually based on fossil fuel-derived monomers which results in the strong necessity of finding alternative routes.[327] As mentioned in section 2, vanillin (**M1G**), guaiacol, and syringyl-derivatives and ferulic acid can be derived from lignin or lignocellulose in high yields. Remarkably, they have been also broadly investigated in order to produce materials characterized by thermo-mechanical properties comparable to those of traditional petroleum-based polymers.

Zhou et al.[338] prepared high glass-transition temperature methacrylate polymers from vanillin (**M1G**) and syringaldehyde (**M1S**) via four methacrylate monomers [syringaldehyde methacrylate (SMA), syringaldehyde acrylate (SA), vanillin methacrylate (VMA), and vanillin acrylate (VA)] that underwent free radical polymerization providing the corresponding polymers (PSMA, PSA, PVMA, and PVA) (Figure 31, route 1b). Remarkably, the final materials presented improved or similar thermal properties compared to biobased polylactic acid (PLA), petroleum-based polystyrene (PS), and polymethylmetacrylate (PMMA). In particular, glass transition temperature was found to be much higher in the new syringaldehyde-derived polymers compared to the traditional PLA, PS, and PMMA (95−180 °C vs 48−110 °C) (Table 5, entry 1). Furthermore, all the prepared materials presented an increased initial degradation temperature (T_{onset}) compared to PLA and PMMA (300−320 vs 296 and 280 °C, respectively).

Holmberg et al.[399] employed guaiacyl methacrylate (GM), creosyl methacrylate (CM), 4-ethylguaiacyl methacrylate (EM), and vanillin methacrylate (VM) from guaiacol (**M24G**), creosol, 4-ethylguaiacol (**M6G**), and vanillin (**M1G**), respectively (Figure 31, route 1) to obtain the equivalent polymers (PGM, PCM, PEM, and PVM) via reversible addition−fragmentation chain transfer (RAFT) polymerization (Figure 31, route 1b). Interestingly, they also reported the synthesis of two heteropolymers with different amounts of the four monomers mining a biomass-derived oil. Remarkably, the authors reported measurably differences in glass transition (T_g = 111−139 °C), thermal degradation ($T_{\max}$ = 281−327 °C), and viscoelastic properties (zero-shear viscosity, η_o = 730−25000 kPa s), depending on the starting monomer or on the relative composition in the heteropolymers (Table 5, entry 2). Following this research, the same group[337] then used syringyl methacrylate and related monomers to prepare homo- and heteropolymers (Figure 31, route 1b) with controllable glass transition temperature ranging from 114 to 205 °C and zero-shear viscosities ranging from ∼0.2 kPa·s to ∼17000 kPa·s at 220 °C, highlighting the wide applicability of these systems (Table 5, entry 3).

Takeshima et al.[388] utilized 4-vinylguaiacol derived from ferulic acid to synthesize polyvinylguaiacol and polyvinylcatechol via controlled radical polymerization using various protecting groups (Figure 32, route 21). The solubility of polymers before and after deprotection in several solvents as well as the glass

Table 5. Thermomechanical Properties of Lignin Derivative-Based Thermoplastics

entry	lignin-derived monomers	polymerization method	final polymers	M_n (g/mol)	Đ	T_g (°C)	T_m (°C)	T_d (°C)	ref
1	syringaldehyde (M1S) and vanillin (**M1G**)	free radical polymerization	lignin-based (meth)acrylate polymers	7600–14600	1.89–4.07	95–180[a]	N. R.	T_{max} = 340–360[c]	338
2	guaiacol (**M24G**), creosol, 4-ethylguaiacol (**M6G**), vanillin (**M1G**)	RAFT polymerization	(meth)acrylate polymers	15000–41000	1.12–1.39	111–139	N. R.	T_{max} = 281–327	399
3	syringyl methacrylate	RAFT polymerization	poly(syringyl methacrylate); SM-containing heteropolymers	11000–38000	1.32–1.74	114–205[b]	N. R.	$T_{onset(initial\ degradation)}$ = 256–303[d]	337
4	ferulic acid (**FA**)	RAFT+ living radical polymerization	poly(vinylcatechol) and poly(vinylguaiacol)	2200–41500	1.06–1.59	21–190[e]	N. R.	N. R.	388
5	syringic acid (**M20S**), vanillic acid (**M20G**), ferulic acid (**FA**), and *p*-coumaric acid	ring-opening polymerization (ROP)/polycondensation	N. R.	1500–60700	1.6–6.3	(−48)–113[e]	36–354	$T_{5\%}$ = 209–343[c]	400
6	vanillin (**M1G**)	N. R.	divanillin-ethanol amine conjugate-based polyurethane	N. R.	N. R.	(−68.08)–(−67.2)[a]	N. R.	$T_{5\%}$ = 329.59–341.54[c]	367
7	vanillic acid (**M20G**) and syringic acid (**M20S**)	N. R.	poly(ether urethane)s	32100–36100	1.6–1.9	49–74[a]	N. R.	$T_{10\%}$ = 304–308[c]	360
8	12 aromatic aldehydes including vanillin and syringaldehyde	N. R.	polyvinyl acetals	22300–46000	N. R.	114–157[e]	N. R.	$T_{95\%}$ = 185–308[c]	385
9	4-propylguaiacol (**M7G**)	N. R.	polycarbonates	2503–5182	N. R.	99–125[a]	205–305[a]	$T_{5\%}$ = 346–376[c]	370
10	vanillin (**M1G**)	N. R.	poly(ether-o-hydroxyamide) and following cyclodehydration to poly(-ether benzoxazole)	N. R.	N. R.	N. R.	N. R.	>400[c]	355
11	vanillin-based monomers	phosphonite-mediated multicomponent polymerization	vanillin-derived fluorescent polymers	3000–12700	1.8–2.3	N. R.	N. R.	N. R.	368

[a] DSC under nitrogen. [b] DSC under air. [c] TGA under nitrogen. [d] TGA under air. [e] Atmosphere not specified.

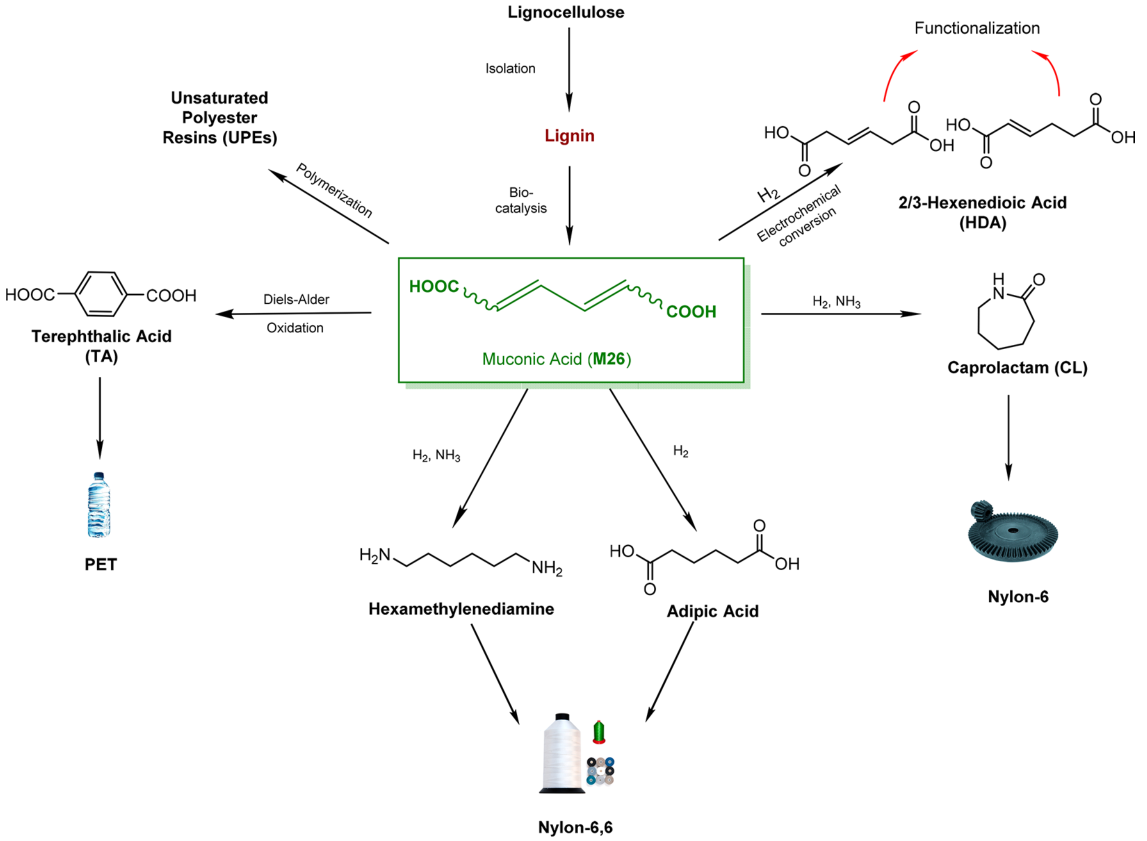

Figure 37. Strategies for transformation of muconic acid to biobased polymers or polymer building blocks.

transition temperature were reported, the latter varied in a wide range [from 21 to 190 °C being the lowest for poly(bis-(triethylsilyl)-protected vinylcatechol) (poly(TES_2VC))] showing that trialkylsilyl groups tend to decrease the T_g of the polymers by enhancing the mobility of the polymer chain (Table 5, entry 4).

Miller and co-workers[400] prepared several polymers via copolymerization of lactones (L-lactide or ε-caprolactone) and bioaromatics (hydroxy-acid derived from syringic acid (**M20S**), vanillic acid (**M20G**), ferulic acid (**FA**), and *p*-coumaric acid) through concurrent ring-opening polymerization/polycondensation strategies to obtain new materials with promising properties. In fact, the introduction of bioaromatics in poly(lactic acid)(PLA) was reported to increase the T_g from 50 to 62−107 °C and to improve the thermal stability [$T_{95\%}$ from 207 °C (PLA) up to 323 °C]. An analogous effect was verified introducing bioaromatics in polycaprolactone (PCL) [T_g from −60 °C (PCL) to −48−105 °C and $T_{95\%}$ from 255 °C (PCL) up to 325 °C] (Table 5, entry 5).

Gang et al.[367] used a dimerized and modified vanillin (**M1G**) [divanillin-ethanol amine conjugate (DVEA)] to partially replace the traditional 1,4-butanediol as chain extender to produce polyurethanes (PU) with increased percentage of biocontent (Figure 32, route 15c). Notably, the final materials containing DVEA presented similar strength and thermal stability but improved Young's modulus (8.02−9.67 MPa vs 7.53 MPa of control PU) and strain (644.82−770.86% vs 522.57% of control PU) (Table 5, entry 6).

Kuhire et al.[360] synthesized biobased-aromatic diisocyanates [bis(4-isocyanato-2-methoxyphenoxy)alkane and bis(4-isocyanato-2,6-dimethoxyphenoxy)alkane] from vanillic acid (**M20G**) and syringic acid (**M20S**) to prepare polyether urethanes by reaction with aliphatic diols (1,10-decanediol and 1,12-dodecanediol) (Figure 31, route 10) and found that thermal stability was mainly determined by the stability of urethane linkages. The highest T_g and degradation temperature ($T_{10\%}$) values corresponded to the use of vanillic acid instead of syringic acid which involved a higher number of methoxy groups that increased the conformational barrier to chain rotation (Table 5, entry 7).

Rostagno et al.[385] studied the synthesis of polyvinyl aromatic acetals from the condesation of commercially available poly(vinyl alcohol) (PVA) and sustainable aromatic aldehydes [12 aromatic aldehydes including vanillin (**M1G**) and syringaldehyde (**M1S**)] (Figure 32, route 18). Importantly, the T_g values in the obtained polymers reached 114−157 °C compared to 75 °C of PVA. Remarkably, the possible degradation of two of the polymers prepared (namely 63.3% and 54% acetalization) was tested in aqueous acidic medium (pH = 1, 2, 3,and 5) verifying that even though they were not degraded at pH = 5, they were efficiently hydrolyzed at pH = 1, 2, and 3 (conditions in the stomach of mammals, fish, and birds) with regeneration of biodegradable PVA and benign aromatic small molecules (Table 5, entry 8).

Koelewijn et al.[370] synthesized a bisphenolic polymer precursor [*m,m′*-methylenebis(4-n-propylguaiacol) (*m,m′*-BGF-4P)] from 4-propylguaiacol (**M7G**) which displayed a markedly reduced potency to activate human estrogen receptor in comparison with commercial bisphenols (Figure 32, route 16). Notably, this molecule was employed as precursor to obtain a thermoplastic polycarbonate (PC3) which was compared with the corresponding polycarbonates from *m,m′*-bis(4-methylguaiacol) (named PC1) and *m,m′*-bis(4-ethylguaiacol) (named PC2) and with the commercial PC-BPA. Importantly, PC3 is reported to have the slowest tendency to crystallize and improved

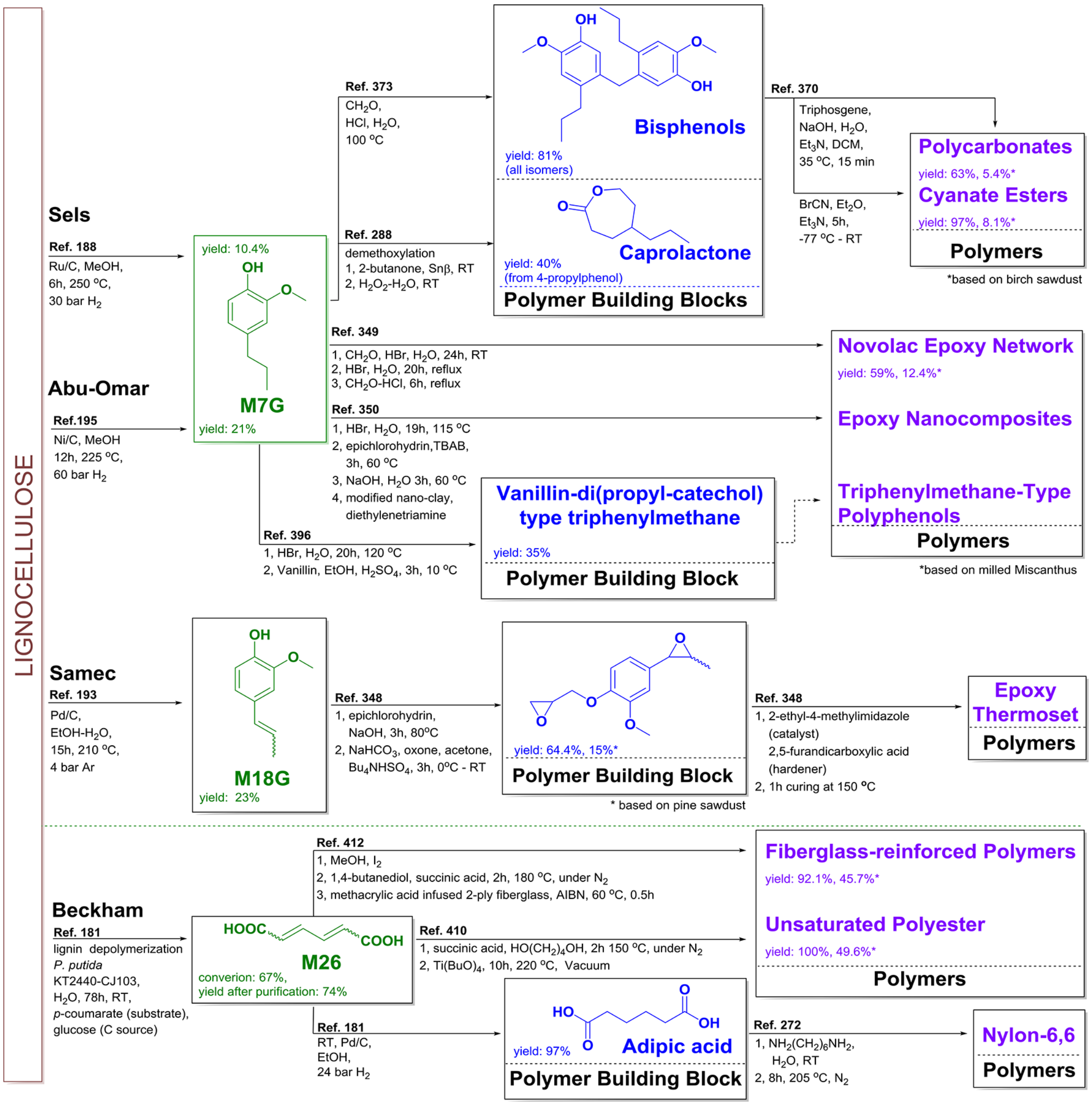

Figure 38. Polymer materials obtained in feasible starting from lignin.

solubility in common solvents even though its glass transition temperature resulted to be lower than PC-BPA, PC1, and PC2 (99 °C vs 145−150, 125, and 116 °C, respectively) (Table 5, entry 9).

Sun et al.[355] investigated the synthesis of polyether benzoxazole (PEBO) from modified vanillin (Figure 31, route 5a). In particular, this polymer was obtained from a precursor poly(ether *o*-hydroxy amide) (PEHA) by cyclodehydration with following analysis of thermo-mechanical properties. Interestingly, no evident glass transition was observed possibly due to the rigid benzoxazole structure in PEBO. Moreover, an improved Young's modulus and tensile strength was reported compared to commercial equivalent polymers (Table 5, entry 10).

Kayser and co-workers[368] studied the synthesis of cross-conjugated fluorescent polymers from vanillin-based monomers with tunable properties (Figure 32, route 15d and Table 5, entry 11). In particular, optical properties such as UV/vis absorbance and fluorescence were investigated showing that these lignin-based polymers were blue-emitting compounds and structural modifications modulated this emission. These materials were stated to be of potential relevance in polymer-based LED production.

4.3. From Lignin-Derived Muconic Acid to Polymers or Polymer Building Blocks

As mentioned in section 2.1, muconic acid (**M26**) is considered an important biomass-derived chemical. As shown in Figure 37, **M26** can be converted to a wide range of commodity chemicals currently produced from fossil resources such as adipic acid, caprolactame, and terephthalic acid.[401]

Adipic acid is a bulk chemical of which approximately the 85% is converted together with hexamethylenediamine (HMDA) to obtain nylon-6,6 where the remainder was used for polyurethanes and adipic esters.[402,403] Thus, the result of catalytic conversion of **M26** to these two chemicals is particularly appealing. In this context, **M26** plays an important role since its possible conversion to both adipic acid and HDMA was demonstrated. Niu et al.[404] reported an efficient cis,cis- **M26** hydrogenation to adipic acid by using Pt/C as catalyst. An excellent 97% yield of adipic acid was obtained at room temperature after 2.5 h. Vardon et al.[272] investigated the

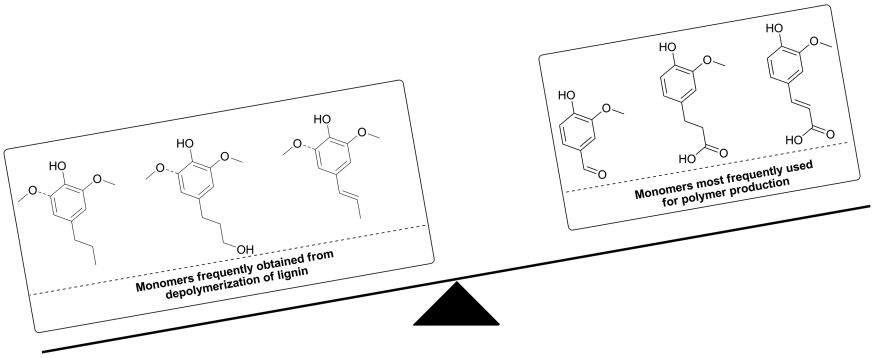

Figure 39. Monomers frequently originating from lignin depolymerization methods (left) and monomers very frequently used for polymer production (right).

separation and purification of **M26** after biological synthesis and achieving a purity of 99.8% which is pure enough for further polymer synthesis. Catalysts screening in batch reactor for hydrogenation of **M26** to adipic acid by using different supported metal catalysts (Pt, Ru, Rh, and Pd on activated carbon or SiO_2) found that Rh/C showed the best activity and stability. A complete conversion and 99.8% purity could be achieved as well even in a trickle bed reactor. Interestingly, they were able to polymerize the synthesized adipic acid with HMDA and obtained a polymer which has similar properties to nylon derived from petrochemical adipic acid. Instead of using hydrogen gas, Matthiesen et al.[551] investigated the electrocatalytic hydrogenation of cis,cis-**M26** by hydrogen generated in situ from water. They demonstrated that trans,trans-**M26**, trans-3-hexenedioic acid, and adipic acid can be produced depending on metal and conditions chosen. However, high selectivity could be obtained mostly for trans-3-hexenedioic acid (up to 95% by using Pb at a conversion of ~75%). Adipic acid was only observed when using Ni with less than 10% selectivity.

Caprolactam which is usually used to produce nylon-6 fibers and resins[405] is another relevant chemical which can be derived from of **M26**. Frost et al.[406] provided a valid synthesis from the three isomers of **M26** (cis,cis-, cis,trans-, and trans,trans-) using Pd/Al_2O_3 in dioxane at 250 °C. After 2 h, the highest yield (55%) was reached from cis,cis-**M26** at a conversion of 79%. Terephthalic acid (TA), another bulk chemical mainly used to produce polyethylene terephthalate (PET),[407] can be obtained from **M26** as reported by Burk et al.[408] In particular, the trans,trans-**M26** or cis,trans-**M26** can be converted to terephtalic acid in a two-step process via Diels−Alder reaction with acetylene at 200 °C followed by oxidation in air or oxygen. The Diels−Alder reaction between muconate and acetylene proceeds via cyclohexa-2,5-diene-1,4-dicarboxylate as intermediate, which is subsequently exposed to air or oxygen to rapidly convert to TA. In 2016, Lu et al.[409] proposed a synthetic route from trans,trans-**M26** to diethyl terephthalate (DET) through a cascade reaction combining esterification, Diels−Alder cycloaddition, and dehydrogenation by using ethanol and ethylene as reactant. Basically, the esterification step improves the solubility of reaction products in ethanol and modifies the electronic properties of trans,trans-**M26** promoting the Diels−Alder reaction with ethylene. Various metals were tested for the hydrogenation step, achieving the highest yield in DET (80,6%) with Pd/C at 200 °C.

Apart from its use as a precursor, **M26** can be exploited as a monomer itself. For instance, Rorrer et al.[410] studied its application as unsaturated polyester resins (UPEs) which are considered interesting materials suitable for coatings, drug delivery systems, tissue engineering, and insulating materials.[411] In particular, they incorporated cis,cis-**M26** into four succinate-based polyesters showing how thermal properties such as the glass transition temperature of the polymer can be tuned depending on **M26** loading. Furthermore, they demonstrated the applicability of these polymers fabricating a material characterized by a shear modulus typical of fiberglass composites. Subsequently, the same authors synthesized a family of copolymers incorporating maleic anhydride, fumaric acid, cis,cis-muconate ester, and trans,trans-muconate ester into poly(butylene succinate) at various loadings. Then, the obtained copolymers were cross-linked with styrene, methacrylic acid, and a blend of methacrylic and cinnamic acid in the presence of woven fiberglass mats to produce a series of fiberglass-reinforced polymers (FRPs).[412] When UPEs and methacrylic acid were used for the preparation of the composites, a greater UPE resin/fiberglass compatibility was observed compared to when styrene was employed even though the final FRP was characterized by lower shear and storage moduli. To overcome this problem, a certain amount of cinnamic acid (20% mol) was incorporated, resulting in a significant improvement of these properties and enabling a fully renewable system.

4.4. Conclusions

The possibility of producing polymers from lignin-derived aromatics has generated significant advances in polymer chemistry. Most groups have utilized pure and well-defined starting materials obtained from commercial sources for the synthesis of novel polymers, especially thermosets and thermoplastics that have shown comparable or even better properties than those conventional materials. Several researchers were engaged in the development of both lignin depolymerization methods as well as the synthesis of lignin-derived polymers. Related examples summarized in Figure 38 show that a number of interesting polymer materials can be obtained in feasible quantities starting from lignin.

However, a discrepancy still exists regarding the monomers used for the synthesis of polymers (Figure 39). Novel methodologies are needed that would deliver higher yields of aromatic compounds, which have been widely studied as starting materials for polymer synthesis. In turn, the actual monomers that can be obtained in high yield offer new possibilities for the synthesis of emerging materials and polymers.

Furthermore, catalytic methods typically deliver mixtures of aromatic compounds, which can be directly used for polymer synthesis, thereby eliminating tedious purification steps; however, reproducibility regarding the starting material and the composition of these product mixtures should be clarified. And last, the biobased polymers are not automatically biodegradable, therefore more insight into the biodegradability, toxicity, and properties of the novel polymers is desired.

5. COMPOUNDS WITH PHARMACOLOGICAL ACTIVITY FROM LIGNIN-DERIVED MONOMERS

Phenols, lignans, and neolignans are a large group of natural products derived from the pool of compounds originating from the Shikimate pathway.[413] They possess a wide range of biological activities and have been used for a long time both in ethnic[414,415] as well as lead compounds for the development of new drugs.[416] Furthermore, such structural moieties can be found in already existing pharmaceuticals as well as compounds with pharmacological activity. From a synthetic point of view, these molecules can be synthesized from lignin-derived monomers, since these already contain the required functional groups on the aromatic ring and side chain.

5.1. Natural Products Synthesized from Lignin-Derived Monomers

5.1.1. 4-(1-Propenyl)-syringol, 4-(1-Propenyl)-guaiacol and Isomers. Lignin-derived trans-4-(1-propenyl)-syringol ***E*-M18S** that could be directly obtained through Pd-catalyzed transfer hydrogenolysis of birch lignocellulose in ethanol in high yield (49%)[187] serves as suitable starting material for the synthesis of polysphorin (**PN1**) in 2 steps.[417] **PN1** was isolated from *Piper polysphorum C* in China and from the leaves and stems of *Rhaphidopora decursiva* in Vietnam[418] and shows in vitro antimalarial activity.[419] The ***E*-M18S** can be converted in one step to neolignan Eusiderin K (**PN2**) that can be methylated to Eusiderin J (**PN2-Me**).[420] Primarily due to the 1,4-benzodioxane moiety, **PN2** and **PN2-Me** show cytotoxic and hepatoprotective activity[421] and have been isolated from *Virola elongata* or *Licaria chrysophylla*.[422,423]

M18G is a starting material for the synthesis of variety of natural products. For instance, the sodium salt of ***E*-M18G** can be converted to (−)-virolin (**PN3**) that was isolated from the leaves of *viola surinamensis*[424] and shows activity against parasites in mice.[425]

Licarin A (**PN4**), present in various tropical or subtropical plants or nutmeg,[426−428] exhibits a wide range of beneficial pharmacological effects,[429−431] including free-radical scavenging[432] and cytotoxicity against tumor cells.[433] **PN4** can be easily synthesized in one-step through an enzymatic oxidative coupling of ***E*-M18G** with outstanding 98% yield.[434] Licarin A can be further converted to (±)-acuminatin (**PN4-Me**),[435] a natural product isolated from various *Piper* plant species[436,437] displays a variety of biological activities.[436,438,439]

5.1.2. Syringaldehyde and Related Compounds. Syringaldehyde (**M1S**) is a lignin-derived lignin monomer, which can be nearly quantitatively methylated to the corresponding derivative with 96% yield.[440,441] (−)-Rhaphidecursinol B (**PN5**), first isolated from *Rhaphidophora decursiva* Schott (Araceae),[419,442] can be obtained from methylated syringaldehyde (**M1S**) in only three steps.[443] **PN5** was found active against *Plasmodium falciparum*, the parasite responsible for the most severe form of malaria.[444,445] Another antimalarial agent prepared from **M1S** and the TBS ether of sinapyl alcohol is Nitidanin (**PN6**)[446] that was isolated from the tropical plant *Grewia Bilamellata* Gagnep (Tiliaceae).[447]

Daphneticin (**PN7**) was isolated as a racemic compound from the roots and stems of *Daphne tangutica*.[448] The plant is used extensively in Chinese traditional medicine as a remedy for the treatment of rheumatism and toothache and also shows cytotoxicity against Walker-256-Carcinoma Ascites cells.[449] **PN7** can be obtained in 9 steps from **M1S**.[450]

The high yield (82%) cobalt/Schiff base-catalyzed oxidation of **M1S** was presented by Bozell and co-workers to 2,6-dimethoxy-1,4-benzoquinone (**M2S**), which can be isolated from direct lignin oxidation as well.[451,452] This compound is starting material for the 6 step synthesis[453] of Ladanein (**PN8**), an antiviral flavone identified from *Lamiaceae* extracts.[454] Interestingly, **PN8** has shown potential against enveloped viruses such as the hepatitis C (HCV), as a safe flavonoid-based alternative.[455,456]

5.1.3. C2-Aldehydes and Alcohols. The acetal of C2 aldehyde **C2AldG** was obtained in high yield by acidolysis in conjunction with ethylene glycol treatment of lignin.[166] Interestingly, **C2AldG** was found as a key ingredient in the synthesis of quebecol [2,3,3-tri-(3-methoxy-4-hyroxyphenyl)-1-propanol] (**PN9**), which was isolated in 2011 from maple syrup and named after the world largest maple syrup producer region, Quebec.[457] Maple syrup is obtained by thermal evaporation of the sap[458] collected from the sugar maple (*A. saccharum*) tree, and maple syrup extracts have antioxidant, antimutagenic, and anticancer properties.[459,460] Quebecol, a compound derived from natural resources and consumed for decades without showing any toxicity shows activity against various cancer cell lines including the human breast adenocarcinoma (MCF-7).[461] Thus far, a sufficient quantity of pure quebecol could not be isolated to conduct detailed biological evaluation, but a patent exists that shows its synthesis from lignin-derived building blocks involving **C2AldG** as well as vanillin (**M1G**).[462]

Alcohol **C2AlcS** should be easily obtained by reduction of the syringyl derivative of **C2AldG**, and it has been reported as product from lignin depolymerization. Raphanuside (**PN10**) can be found in *Descurainia sophia*[463] and was used for anticough and antiasthmatic purposes and moreover show anticancer activity, and it can be synthesized from **C2AlcS** in eight steps.[464,465]

5.1.4. Dihydroferulic Acid and Derivatives. 4-Propanolguaiacol (**M10G**) is a building block that can now be obtained in high yield in one step from lignocellulose, owing to the novel catalytic lignocellulose fractionation strategies.[185,194] These methods have also reported the corresponding dihydroferulic acid methyl ester (**M28G**) is tangible quantities.[195] **M28G** can be converted to dihydroferulic acid (**C3AcidG**) through hydrolysis.[466] These compounds are versatile starting materials for the synthesis of a variety of natural products as summarized below.

(−)-Arctigenin (**PN11**) is a phenylpropanoid isolated from a variety of plants which shows phagocytic activity on leukemia cells[467−469] and synergistic effects in combination with cisplatin against several cancer cell lines.[470,471] Furthermore, the cytotoxicity of doxorubicin in combination with (−)-arctigenin against several multidrug-resistant cells showed improved results.[472] Other effects are also known.[469] The synthesis of **PN11** was reported from 3,4-dimethoxycinnamic acid in a convergent nine-step synthesis resulting in 19% overall product yield.[473] This synthesis route proceeded through the methylated[474,475] analogue of alcohol **M10G**, and **M10G-Me** could be directly used as the starting material.

(+)-Imperanene (**PN12**) is a novel phenolic compound that has been isolated from *Imperata cylindrical* and used extensively in traditional Chinese medicine as diuretic and anti-inflammatory agents.[476] From the reported synthesis, it is recognized that **M28G** can directly be used, giving an overall yield of 17%.[477]

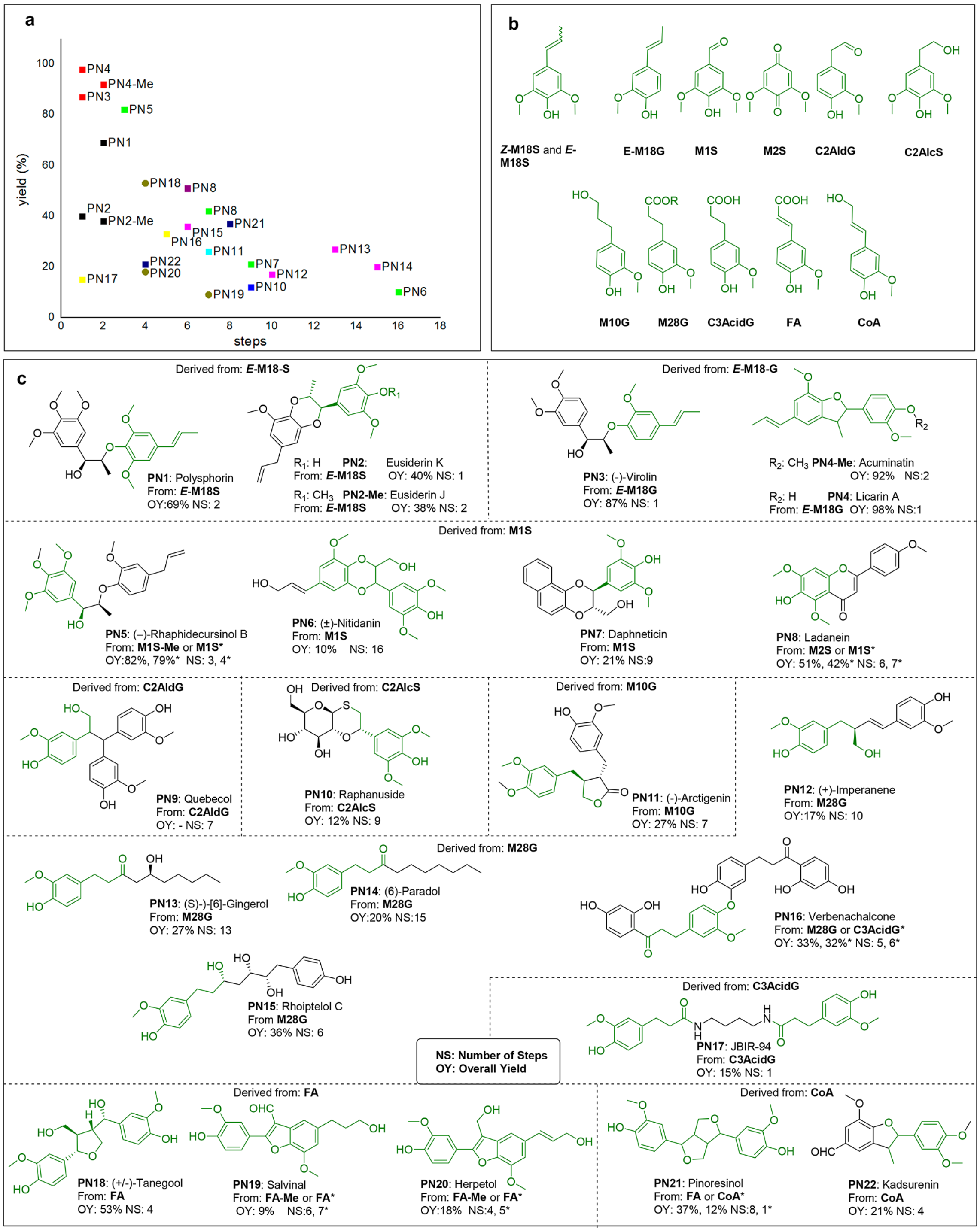

Figure 40. Summary of structures of natural products obtained from lignin-derived monomers. (a) Number of steps required to synthesize the natural products versus overall yield of the process. (b) Monomers used as starting material. (c) Chemical structures of natural products separated by dotted line based on different starting material.

Ginger is a widely used spice and a food supplement throughout the world, and widely applied in traditional Chinese and Japanese medicine.[478] Its major ingredient, (+)-(*S*)-[6]-gingerol (**PN13**), has been found to exhibit diverse pharmacological activities such as antioxidant, anti-inflammatory, antitumor, and antibacterial effects.[479] (*S*)-[6]-Gingerol can be synthesized from ferulic acid (**FA**) in 15 steps and from **M28G** in 13 steps, with overall 27% yield.[480] (6)-Paradol (**PN14**) shows anti-inflammatory effect and can be synthesized from **PN13** in a two-step procedure.[481]

Rhoiptelol C (**PN15**) was first isolated from the fruits of *Rhoiptelea chiliantha*.[482] The molecule shows strong phenol oxidase inhibitor effect and has potential for future use in the development of environmentally friendly pesticides.[483] **PN15** was synthesized in eight steps from vanillin and can be obtained from **M28G** in 6 steps.[484]

Verbenachalcone (**PN16**) was isolated from *Verbena littoralis* (Verbenaceae) and displays a biological effect as enhancer of nerve growth factor (NGF) in specific cells[485] and can be synthesized from **C3AcidG** in 6 steps with 32% yield or from **M28G** in 33% overall yield in five steps.[486]

Streptomyces strains are producing a wide variety of compounds that serve as antibiotics, including the recently reported JBIR-94 (**PN17**).[487] This phenolic compound can be synthesized from ferulic acid in four steps and from dihydroferulic acid **C3AcidG** in only one step with 15% yield without any protecting group.[488]

5.1.5. Ferulic acid and Its Derivatives, Monolignols.

Ferulic acid (**FA**) is usually obtained by extraction[489,490] but was also seen as product in lignin depolymerization mixtures.[491] Although a direct, high yield production of **FA** from lignin is not known at the moment, we will include a few examples of natural products that can be obtained from ferulic acid.

Tanegool (**PN18**) can be found in various plants including *Magnolia fargesii*, *Taxus yunnanensis*, or *Patrinina villosa* originating mainly in East Asia and North America.[492,493] It shows diverse pharmacological activity, including a great potential in the prevention of Alzheimer's disease.[494] **PN18** can be synthesized from **FA** in four steps in 53% overall yield based on recovered starting material.[495]

Ferulic acid (**FA**) can be quantitatively esterified.[167] Salvinal (**PN19**), first isolated from *Salvia mitorrhiza*, can also be obtained from the methyl ester of **FA** through a six-step synthesis route.[496] In traditional Chinese medicine, water extracts have been used to treat acute myocardiac infarction and angina pectoris.[497]

Herpetol (**PN20**) featuring a benzofuran skeleton was isolated from *Herpetospermum caudigerum* and possesses anti-inflammatory and free radical scavenging properties.[498] It can be synthesized in four steps from the methyl ester of **FA** with 18% overall yield.[496]

Similarly to ferulic acid, monolignols are also not direct products from common lignin depolymerization routes. However, the structural variants of the natural products shown below, synthesized from monolignol **CoA**, have been observed on lignin acidolysis studies as part of mixtures.[166]

The substance (+)-pinoresinol (**PN21**) is a compound present in the lignan fraction of several plants, such as the seeds of the species *Forsythia* or sesame (*Sesamum indicum*).[499,500] In a traditional human diet, extra virgin olive oil is an excellent source of pinoresinol up to a concentration of 100 mg/kg.[501] Pinoresinol has cytotoxic activity against human colon cancer cell lines (SW480 and HCT116).[502] It had been synthesized in one step from coniferyl alcohol **CoA** in 12% yield[503] or in an eight-step synthesis in 37% yield from **CoA**.[495]

(7*S*,8*S*)-Kadsurenin M (**PN22**) is a Chinese traditional drug used as a remedy for inflammation and rheumatic conditions.[504] It was synthesized from vanillin (**M1G**) in five steps. In the procedure, methylated derivative of **CoA** was an intermediate which was converted in three steps to **PN22**; the procedure does not report on the yields of each steps.[505] Guaiacol type phenylalkylalcohol-phenols can be chemoselectively quantitatively methylated;[474,475] and the methylated **CoA** compound can be chlorinated with 95% yield,[506] based on **CoA** the synthesis would take four steps with 21% overall yield.

Structures and overall yields of natural products obtained from lignin-derived monomers described in this section are summarized in Figure 40.

5.2. Pharmaceutical Products from Lignin-Derived Monomers

Actual pharmaceutical products (**PD**) can also be obtained from lignin-derived monomers (***E*-M18G**, **M1S**, **C3AcidG**) and ferulic acid (**FA**). Tofisopam (marketed under brand names Emandaxin and Grandaxin) (**PP1**) is an anxiolytic agent without addiction potential and without the sedative-hypnotic side effects generally associated with the use of 1,4-benzodiazepines.[507,508] According to the 2017 report of the European Medicines Agency (EMA), the lead producer of **PP1** in the EU is Hungary.[509] Methylated ***E*-M18G** can be dimerized to 4-(1-propenyl)-guaiacol (**M18G**) by an acid-catalyzed cycloaddition reaction.[510] It can be further converted by oxidation to the corresponding diketone with 88% yield.[511] The diketone is then transformed to Tofisopam by hydrazine hydrate in a single step.[512] The calculated yield for the four steps starting from ***E*-M18G** is 40%. The original patent used the same synthesis strategy.[513,514]

Trimethoprim (**PP2**) is a classical antibacterial agent that serves as selective inhibitor of bacterial dihydrofolate reductase.[515] It is used alone or in combination with sulfamethoxazole to treat a wide range of bacterial infections in humans and poultry. According to the 2017 report of the European Medicines Agency (EMA), the lead producer of **PP2** in the EU is Estonia.[509] **PP2** was sold in more than 140 tons as a veterinary antimicrobial agent in the countries of EU, Iceland, and Switzerland in 2014.[509] More than 80 tons of **PP2** were sold in 2010 for human treatment in the U.S. alone,[516] and in the same year in China, more than 3000 tons[517] of **PP2** were produced for the global market, which shows a huge demand due to antimicrobial and antimalarial applications. **PP2** can be synthesized from the methylated derivative of syringaldehyde (**M1S-Me**) with overall 85% yield in three steps.[517] **M1S** can be nearly quantitatively (96%)[440,441] transformed to the methylated derivative, and based on this, the overall yield of **PP2** from **M1S** is 82% in four steps.

Donepezil (**PP3**) is a drug used in the treatment of Alzheimer's disease. Since its first approval by the FDA in 1996, this blockbuster drug generated more than 2 billion USD sales in 2010, just in the U.S. After the original patent expired in 2010, generic competitors made **PP3** less expensive and more accessible for patients in 5 and 10 mg doses.[518] According to the 2017 report of the European Medicines Agency (EMA), the lead producer of **PP3** in the EU is the United Kingdom.[509] Several synthetic procedures exist for the synthesis of **PP3**.[519,520] In a short synthetic route, dihydroferulic acid **C3AcidG** can undergo ring closure, and upon methylation it can be turned into 5,6-dimethoxy-2,3-dihydro-1H-inden-1-one (DMI) with 63% yield from **FA** in three steps.[521] **PP3** can be obtained upon a one-step catalytic alkylation of DMI, according to the procedure developed by Glorius et al. with 40% yield which means 25% overall yield in this four step synthesis from **FA**.[522]

PP4 (lead EU producer, Hungary[509]) is used in combination with other APIs such as carbidopa, constituting the least expensive (less than 319$ annual treatment cost) Parkinson's disease medication.[523] Parkinson's disease is affecting more than 2 million people in our world, and it is projected to grow to 2.89 million cases worldwide by 2022.[521] Several synthesis routes have been established to synthesize **PP4**.[524] The most well-known example is the Monsanto process which utilizes asymmetric hydrogenation.[525,526] Another interesting approach to get **PP4** is based on the demethylation of **FA** to caffeic acid with 62% yield.[527] Caffeic acid can aminate in the presence of NH_3 with a plant-derived phenylalanine ammonia-lyase enzyme to yield L-DOPA (**PP4**) close to 100% yield and excellent enantioselec-

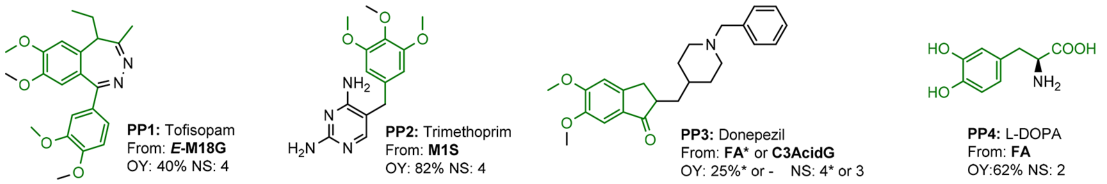

Figure 41. Summary of structures of pharmaceutical products obtained from lignin-derived monomers.

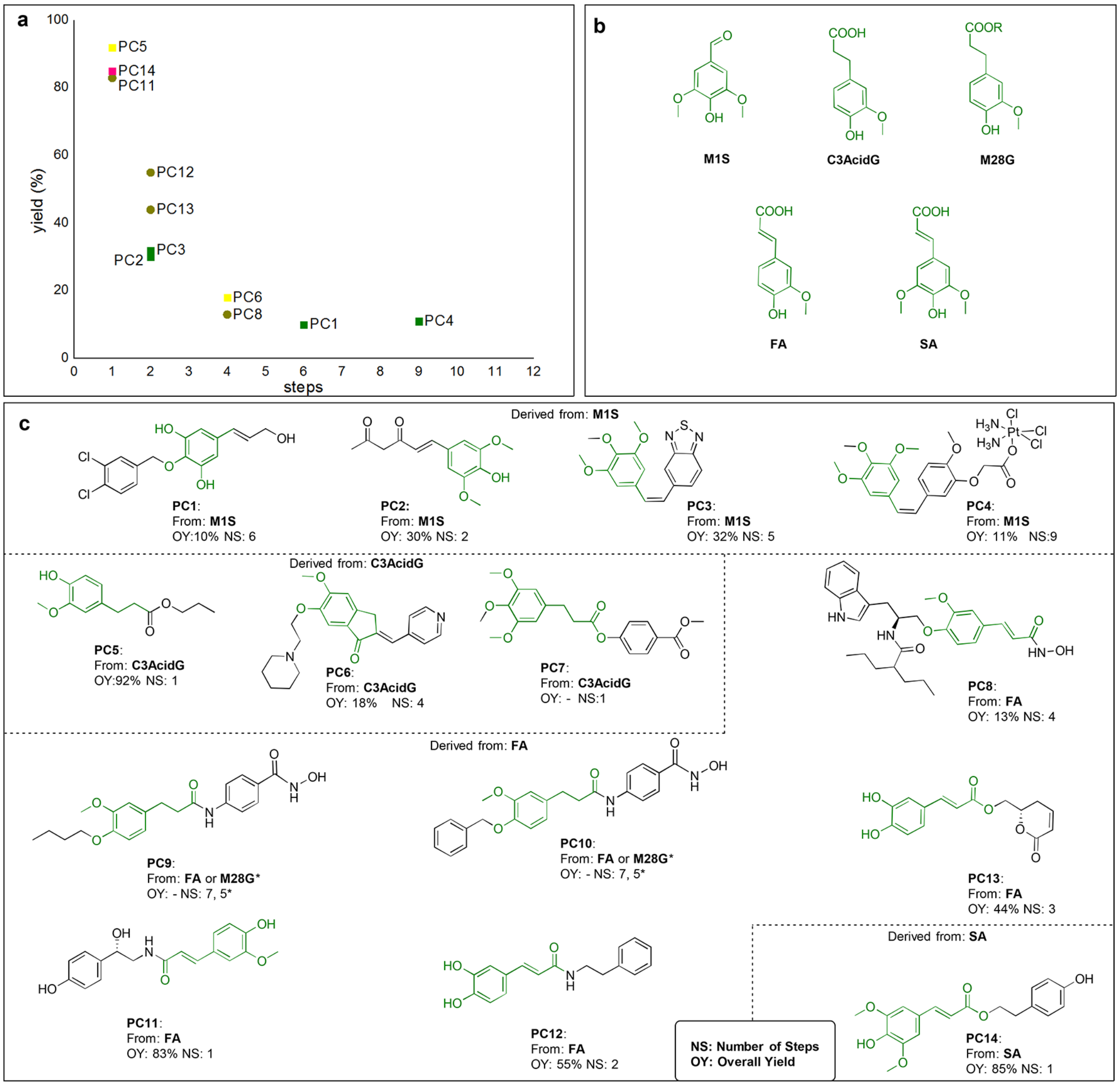

Figure 42. Summary of structures of drug lead compounds obtained from lignin-derived monomers. (a) Number of steps required to synthesize the drug lead compounds versus overall yield of the process. (b) Monomers used as starting material. (c) Chemical structures of drug lead compounds separated by dotted line based on starting material.

tivity, which means 62% overall yield for the two-step procedure.[528]

Structures and overall yield of all these pharmaceutical products are summarized in Figure 41.

5.3. Drug-Leads from Lignin-Derived Monomers

Drug-leads are chemical compounds that possess favorable pharmacological and biological effects (Figure 42). Their properties can usually be tuned by chemical modifications to yield drug candidates before those enter into clinical trials.[529] However, the probability for a drug candidate to succeed as an active pharmaceutical ingredient is typically low, which significantly contributes to the development cost.[530]

5.3.1. Syringaldehyde and Related Compounds.

Drug lead candidate **PC1** exhibited significant cytotoxicity to several human tumor cell lines in the micromolar range and showed 20 times more potency than the control cisplatin. **PC1** was synthesized from **M1S** in 6 steps with 10% yield.[531]

Curcumin, 1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadien-3,5-dione, is the primary bioactive compound isolated from turmeric, the dietary spice made from *curcuma longa*. Curcumin is a potent anti-inflammatory and antiproliferative agent.[532] Moreover no cancer cell type has yet been found where curcumin lacks antiproliferative effects, and this effect is selective toward tumor cells showing minimum effect on normal cells.[533]

Next to the natural analogues (e.g., demethoxycurcumin and bisdemethoxycurcumin), numerous derivatives have been synthesized in an attempt to find "super curcumin".[534] It was found that **PC2** showed higher antiproliferative affect than curcumine.[535] **PC2** can be synthesized from **M1S** in two steps with 30% yield.

Combretastatin derivatives also show antitumor activity, and the Z isomer of **PC3** was the most potent derivative in the paper presented by Riant et al.[536] It was synthesized from methylated **M1S** in four steps with 33% yield. **M1S** can be quantitatively (96%) methylated[440,441] which means five steps to **PC3** from **M1S**.

The Z isomer of platinum containing combretastatin derivative **PC4** also show antitumor activity with higher cytotoxicity but with lower toxicity and lower resistance than cisplatin in HepG-2 cancer cells.[537] It can be synthesized in eight steps from the methylated **M1S** with 11% overall yield. **M1S** can be quantitatively (96%) methylated,[440,441] which means nine steps from **M1S** with overall yield around 11%.

5.3.2. Dihydroferulic and Dihydrosinapic Acid Derivatives.

The propylester of dihydroferulic acid (**PC5**) is able to totally inhibit the growths of *Aspergillus fumigatus* and *Aspergillus flavus* in the concetration as low as 6.4 mM. It was synthesized in one step from **C3AcidG** with 92% yield.[538]

The inhibitory activity of **PC6** on acetylcholinesterase enzyme was 14-fold of that of donepezil (**PP3**).[539] It can be synthesized from **C3AcidG** in four steps with 18% yield.

AV170 (**PC7**), derivative of dihydrosinapic acid **C3AcidS**, exhibited the most pronounced reduction in peptide hydrolysis activity and was four times more effective for certain applications compared to the previously reported beta-lactone inhibitors (gold standard); this might open possibilities to obtain new antimicrobial agents.[540] The compound was purchased, but the yield from **C3AcidS** is inaccessible.

5.3.3. Ferulic and Sinapic Acid Derivatives.

Ferulic acid (**FA**) can serve as the starting material for the synthesis of several lead compounds. For example, **PC8** exhibited potent in vitro and in vivo antitumor activity, which was synthesized from **FA** with 13% yield in four steps.[541] Derivatives **PC9** and **PC10** have been shown to be nearly as potent as the positive control drug Zolinza in in vitro histone deacetylase (HDACs) activity assays. Inhibition of HDACs is considered as a potent strategy for cancer therapy. **PC9** and **PC10** can be synthesized from **FA** in seven steps or from **M28G** in five steps with unpublished yields.[542] Furthermore, the amide (**PC11**) that is selectively cytotoxic to white blood cancer cells has been synthesized from **FA** in one step with 83% yield.[543]

Ferulic acid **FA** can be demethylated to caffeic acid,[527] which can undergo condensation with phenyethylamine to yield a promising drug candidate, the insulin sensitizer[544] and antioxidant[545] KS370G (**PC12**) with 88% yield.[546]

FA can be demethylated to caffeic acid with 62% yield.[527] Some simplified analogues of the natural product (−)-tarchonanthuslactone showed anticancer activity in different cell lines, including the highly drug-resistant human pancreatic carcinoma cell line.[547] Caffeic acid derivative **PC13** was the most active compound from the tested analogues.

(−)-Oleocanthal is a bioactive compound isolated from virgin olive oil. Tyrosol sinapate (**PC14**) is a semisynthetic analogue of (−)-oleocanthal. Tyrosol sinapate (**PC14**) which shows several biological effects including anticancer activity.[548] It can be synthesized from **SA** in one step with 85% yield.

5.4. Conclusions

Compared to polymers, pharmaceuticals are produced on much lower scales, therefore the possibility to source them from renewables is considered much less important. Nonetheless, lignin-derived, highly functionalized aromatics appear to be possible entry points into the synthesis of pharmaceuticals; however, this approach must show clear advantages over existing methods. Such a goal is for example the possibility to significantly reduce waste (improve atom economy and E factor)[235,237] by minimizing the number of reaction steps in total syntheses.

Due to their inherent structure and natural origin, several aromatics are very common starting materials for the synthesis of natural products (e.g., **FA**, monolignols). These however are not directly obtained by lignin depolymerization methods. Several monomers, on the other hand, especially those obtained by reductive depolymerization methods (e.g., alkyl-guaiacols or phenols), are not generally encountered starting materials for the synthesis of natural products, pharma intermediates, or drug candidates.

Some of the transformations described in section 5 proceed in biorenewable and/or environmentally benign solvents. For example, **PN4** was synthesized in the mixture of water and methanol, **PP2** in methanol, **PC2** was synthesized in ethyl acetate while **PC5** in propanol. For the synthesis of Tanegool (**PN18**), 2,2,2-trifluorethanol, acetone, and hexanes were used; the latter could be replaced with heptane. The THF used in several syntheses such as **PC14** could be substituted with 2-Me-THF[549] or CPME.[550] However, most of the synthesis routes in the examples detailed above utilize traditional solvents such as dichloromethane (DCM) or dimethylformamide (DMF). Effort should be devoted to search for biobased solvent alternatives possibly also from lignin, as this would have significant environmental benefits.

6. CONCLUDING REMARKS

In this review, a comprehensive overview of catalytic processes that are capable of delivering products in high yield and good selectivity from preisolated lignin or lignocellulose as starting material was provided. This gives insight into the creative solutions that were found to tackle the great challenges related to the robust and refractory structure of this intriguing aromatic biopolymer, especially in the past 5 years. Most of the new catalytic methods have focused on the selective cleavage of C−O bonds in the most abundant β-O-4 moieties. Considering this strategy, and the natural abundance of β-O-4 linkages, high theoretical efficiencies were already reached. In order to further improve product yields, new research should focus on the development of selective catalysts for cleaving moieties that are mutually connected by two bonds and via stronger C−C linkages. Several of the new methods have recognized the importance of suppressing recondensation reactions, which typically lead to decreased product yields especially when acid or base and elevated temperatures are used. Also in these cases, high theoretical efficiencies were reached, and further challenges will involve addressing engineering solutions for possible upscaling and in depth mechanistic understanding. Several research groups have identified the significance of the processing parameters (temperature, additives) for lignin fractionation, as a major factor influencing product yield and selectivity. Future challenges will relate to the implementation of these novel lignin isolation methods in existing biorefinery schemes. The elegant, catalytic lignocellulose fractionation methods pioneered by several groups have overcome the undesired modification of the native lignin structure and found well-defined products in improved yields. Future research in this area will focus on solving challenges related to catalyst separation from the cellulose and hemicellulose and their valorization.

A summary of well-defined products (Figure 23), including interesting, unexpected structures (**M7-M10**, **M17**, **M18**, **M20**, and **M21**), originating from the novel catalytic methods developed recently, will provide a starting point for designing new lignin-based products, revisiting the idea of lignin-derived platform chemicals. While phenol or BTX are still highly interesting targets, future research should also focus on defining new strategies for the valorization of these emerging, more functionalized structures, for the production of tangible products. Given the large scale and importance of the field of biobased polymers, it would be highly desired to find novel applications that take advantage of the inherent complexity of lignin-based aromatics, especially to add extra functions or improve existing properties.

About a decade ago, "cracking" the recalcitrant lignin structure appeared to be a daunting task, which was met with considerable skepticism on the one hand and enthusiasm on the other. Today, owing to the remarkable achievements in catalysis research, it became possible to derive well-defined compounds from lignin in acceptable quantities, among which several structures will emerge as future lignin-derived platform chemicals, and there is a much clearer understanding of the challenges that still need to be tackled in order to enable the full implementation of lignin as sustainable starting material for the production of drop-in chemicals, polymers, or emerging functional materials. This will require close collaboration across multiple disciplines and a dialogue between academia and industry. Without any doubt, the new, exciting developments achieved thus far project a bright future for lignin valorization for years to come.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.chemrev.7b00588.

Structure, codes, and names of identified lignin monomers (Table S1) (PDF)

AUTHOR INFORMATION

Corresponding Author

*E-mail: k.barta@rug.nl.

ORCID

Katalin Barta: 0000-0002-8046-4248

Author Contributions

‡B.F. and A.d.S. contributed equally.

Notes

The authors declare no competing financial interest.

Biographies

Zhuohua Sun received his bachelor's degree in applied chemistry in 2011 from Heilongjiang University, Harbin. Then he moved to State Key Laboratory of Fine Chemicals in Dalian University of Technology. He carried out research on preparation of graphene supported catalysts and biomass transformation with Raney Ni catalysts under the supervision of Dr. Zeming Rong and obtained his Master's Degree in chemical engineering in 2014. In September 2014, he joined the research group of Katalin Barta as a Ph.D. student. His research interest lies in the development of novel heterogeneous catalysts and methods for the catalytic conversion of lignocellulosic biomass.

Bálint Fridrich was born in Budapest, Hungary. He obtained his bachelors's degree in Chemical Engineering in 2015 and master's degree from the Budapest University of Technology and Economics in 2016 with highest distinction. During his university studies he worked on the "Conversion of non-edible biomass waste streams to optically active platform molecules" in the research group of Prof. László T. Mika. He then moved to the Leibnitz Institute of Catalysis (LIKAT) in Rostock, Germany to work in Prof. Matthias Beller's group as a visiting student. Starting from November 2016, he is in the group of Katalin Barta, exploring the topic ''Sustainable catalysis for value-added chemicals from biomass''. Bálint received several scholarships, including a Fellowship granted by the Hungarian Republic (2015) and National Talent Program (2017) from the Hungarian Ministry of Human Capacities. He was recently awarded with the Pro Scientia Medal from the Hungarian National Scientific Student Council. In his free time, he enjoys road cycling and geography, and also likes travelling, exploring museums and libraries.

Alessandra De Santi was born in Viareggio, Italy, in 1992. She obtained her bachelor's degree in Chemistry for Industry and Environment from the University of Pisa (Italy) in 2014. As an undergraduate, Alessandra's work was developed under the guidance of Dr. Elisa Passaglia (ICCOM-CNR U.O.S. of Pisa) focusing on modification of cationic and anionic clays and their dispersion at nanoscale in polylactic acid matrix. In 2017, Alessandra received her master's degree in Industrial Chemistry from the University of Pisa. Her master's research project dealt with the catalytic conversion of biobased molecules such as furfural and was performed as part of a joint project under the supervision of Prof. A. M. Raspolli Galletti (University of Pisa) and Prof. H. J. Heeres (University of Groningen). In 2017, Alessandra joined the group of Katalin Barta as Ph.D. student and her research focuses on the catalytic conversion of lignin and lignocellulose.

Saravanakumar Elangovan was born in Ramanathapuram and grew up in Thogur, a small village in Tamilnadu, India. He completed his M.Sc in chemistry at St. Joseph's college, Trichy and worked as a research associate in Syngene International Ltd, Bangalore, India. In 2012, he moved to France to perform an International Master program in Molecular Catalysis and Green Chemistry at the University of Rennes. He then started his PhD studies under the guidance of Prof. Christophe Darcel and Prof. Jean-Baptiste Sortais at the University of Rennes and with Prof. Matthias Beller and Dr. Kathrin Junge at Leibniz Institute for Catalysis (LIKAT), Rostock, Germany. His doctorate was focused on well-defined iron and manganese catalysts for reduction and dehydrogenation reactions. He is currently a postdoctoral researcher at the Stratingh Institute for chemistry, University of Groningen, in the group of Katalin Barta working on several research directions related to sustainable catalysis and green chemistry.

Katalin Barta is Associate Professor at the Stratingh Institute, University of Groningen. She studied chemistry at ELTE Budapest (Hungary) and carried out her master's research in alternative solvents in the group of István T. Horváth. She was also Erasmus research student at the University of Leeds. Then she moved to RWTH-Aachen (Germany), to pursue her PhD research under the guidance of Walter Leitner in asymmetric catalysis and ligand design. During postdoctoral research (2008-2010) with Peter Ford at University of California, Santa Barbara she worked on the conversion of renewable resources. After, she was Associate Research Scientist (2010-2012) at Yale University, the Center for Green Chemistry and Engineering (New Haven, USA) with P. T.

Anastas where she worked on catalytic conversion of renewable resources, with special focus on lignin valorization. She established her independent research group at the Stratingh Institute for Chemistry, the University of Groningen in 2013. Combining various fields, the research interests in the Barta group are broadly in Sustainable and Green Chemistry, focusing on the development of novel homogeneous and heterogeneous catalytic strategies for the conversion of all main components of lignocellulose, utilizing Earth abundant metals.

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