

## Review

## Lignin Functionalization for the Production of Novel Materials

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**Lignin, a major constituent of lignocellulosic biomass, is the largest natural source of aromatic molecules and thus is an attractive feedstock for renewable chemical production. Direct incorporation of isolated lignin into materials has long been researched due to the idea's simplicity and the scheme's potentially high atom economy. However, due to its high chemical reactivity lignin is difficult to isolate without having it undergo uncontrolled condensation and repolymerization, which greatly hinder its ease of incorporation into polymers and other materials. Therefore, controlled chemical modifications have been and are being developed to increase lignin's compatibility with existing materials. This review presents the latest advances in lignin extraction and functionalization and their potential for improving the production of lignin-based materials.**

**Lignin: A Renewable Feedstock for Aromatic-Based Products**

Due to increasing concerns of rising concentrations of atmospheric carbon dioxide, many countries have established programs and strategies to mitigate climate change [1–3]. These concerns are notably leading to demands for sustainable alternatives to crude oil and are encouraging the scientific community to explore new renewable feedstocks for producing energy and materials [4]. In this context, lignocellulosic biomass is an especially promising feedstock to replace carbon-based products because it already contains partially reduced multicarbon molecules [5].

Lignocellulosic biomass, comprising cellulose, hemicellulose, and lignin, has been widely used for hundreds of years and while it has been industrially fractionated to cellulose for over a century [6,7], the isolation and purification of hemicellulose and lignin on an industrial scale is still under development. Until now, lignin has been mostly used as a source of renewable energy by the pulp and paper industry, where lignin-containing black liquors derived from pulping processes are still largely burned to recover inorganics and energy for the mills [8]. However, as the production of lignin exceeds the demand for its use as a fuel and as interest for renewable chemical has increased [9], increasing attention is being given to **lignin valorization** (see [Glossary](#)) into new chemicals and materials, since it is by far the most abundant natural source of renewable aromatic molecules on earth. Given the prominence of aromatic functionalities in important chemical sectors such as fragrances, flavors, polymers, coatings, and resins, these areas have all explored the use of lignin [10,11]. Although lignin has an extraordinary potential as a renewable feedstock, its use poses several challenges including its isolation and valorization. First, due to the biosynthetic process, its structure is variable especially across different types of plant species, in terms of monomer composition as well as in the type and order of the chemical bonds that hold these monomers together [12]. Second, the functional groups present in lignin make it a very reactive compound under most extraction conditions, limiting its further upgrading. Lignin's original structure is incredibly difficult to maintain intact during most pulping and isolation procedures [13]. Moreover, despite significant improvements in the past decade, the qualitative and especially quantitative determination of lignin's structural features remains challenging [14,15]. Nevertheless, recent improvements in both lignin analytics and lignin functionalization have created new

## Highlights

Lignin is the largest natural source of aromatic molecules and thus represents a promising renewable chemical feedstock.

Lignin has a complicated chemical structure and generally undergoes rapid condensation during its isolation from biomass. Condensation makes lignin more recalcitrant to further upgrading and to incorporation into materials.

New analytical techniques are allowing a better understanding of native and isolated lignin's structure, which in turn is allowing the development of improved isolation methods that minimize or prevent condensation.

As a result of better analytics, improved chemical modification techniques are being performed on the lignin backbone to introduce new functional groups that were not present in the native structure. The functionalization of lignin allows improved blending of lignin with polymers and the development of new biobased materials.

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opportunities for the production of controlled lignin structures and the incorporation of these structures into materials, which we describe later.

### Lignin's Structure and Its Challenging Characterization

Most of the mass of lignocellulosic biomass is found in the macro- and micro-fibrils of the rigid walls of its plant cells, which essentially comprise three biopolymers: cellulose, hemicellulose, and lignin (Figure 1) [16]. The cellulose is in the form of bundled fibrils that are bound together by the hemicellulose and lignin giving the overall rigidity to the cell wall. Lignin is formed during radical coupling of phenylpropanoid units, such as *p*-coumaryl, coniferyl, and sinapyl monolignols [17]. The consequence of this is a random copolymer comprising syringyl (S), guaiacyl (G), and *p*-hydroxyphenyl (H) subunits [18], although the monomer composition varies across wood species. Softwoods like pine or spruce are composed mainly of guaiacyl units, while hardwoods such as birch or eucalyptus contain both guaiacyl and syringyl functionalities but with a higher fraction of syringyl units. *para*-Hydroxyphenyl monomers, together with the syringyl and guaiacyl units, are mostly found in grass lignin [19].

Additional structural heterogeneity comes from the **radical biosynthesis of lignin**, not described in this review, but widely described in the literature [12,20]. The driving force for the synthesis of lignin is the formation of monolignol radicals, which have several resonance structures leading to the formation of several different C–O and/or C–C linkages [21–23] (see potential model structures in Figure 2).

Due to the complexity, heterogeneity, and variety that is present in lignin, elucidating its structure and associated properties is a nontrivial task [24]. One of the main recurring issues is that lignin is difficult to isolate from its other components without modifying its structure. This leads to a trade-off where lignin must either be characterized in the presence of other biomass constituents or analyzed in a modified form. One example of these recurring issues is faced during gravimetric isolation techniques such as the **Klason method**, which is known to lead to significant lignin degradation due to the high acidity that is used [25]. Moreover, the high acidity necessary for the isolation of lignin can also lead to polysaccharide degradation and the formation of **humins** that are sometimes erroneously included with the lignin (often termed 'pseudolignin').

A few types of isolated lignin can overcome these challenges. Among the most important are milled wood lignin (MWL) and cellulolytic enzyme lignin (CEL). The first is based on fine ball-milling of wood followed by extraction of the lignin using a solution of water and dioxane. The second also begins with ball-milling, but this is followed by several treatments with cellulase enzymes that can hydrolyze the polysaccharides leaving behind the lignin as a solid residue. However, these methods have several limitations. Notably, the extraction of lignin is less efficient compared with chemical methods, leaving some lignin behind, while the intensive ball-milling has the effect of partially depolymerizing lignin and inducing chemical modifications on its structure [26,27].

Analysis of isolated lignins can thus be complicated by these structural modifications, which make the analytical results difficult to trace back to the native lignin structure. To overcome the need for lignin extraction, many researchers have focused on analyzing native lignin embedded in plant cell walls via nuclear magnetic resonance (NMR) spectroscopy. However, these techniques require the reduction of plant material to a gel-like structure through ball-milling and then finding suitable solvents capable of solubilizing whole-cell walls without yielding chemical modifications [28]. Due to lignin's complex structure, the information provided by <sup>1</sup>H NMR is often limited because the signals of the various protons overlap. 2D NMR, and particularly **heteronuclear single quantum coherence (HSQC) NMR**, leads to much more straightforward identification

### Glossary

#### Heteronuclear single quantum coherence (HSQC) NMR:

bidimensional (2D) NMR experiments where every signal on the spectrum corresponds to a proton (H) covalently attached to a heteronucleus (C). This experiment is especially useful when the peaks of the molecule analyzed overlap in a simple <sup>1</sup>H NMR or <sup>13</sup>C NMR experiment.

#### Heteronuclear single quantum coherence zero (HSQC<sub>0</sub>) NMR:

experiments that comprise a series of HSQC NMR spectra (see earlier) recorded with different time intervals between the excitation of the sample and the acquisition of the signal. The series of experiments make possible the extrapolation of the intensity of the peak at 'time zero' (when there is no decay), which corrects for the effects of different decay rates between signals. Different decay rates for different chemical functionalities are the principle difficulty associated with quantification in HSQC NMR. This difference creates variable proportionality between the peak volume and a given chemical functionality's concentration. With this experiment, peaks corresponding to the different protons covalently attached to a carbon atom can be assigned like a simple HSQC, but their peak volume becomes proportional to the respective quantity of protons covalently attached to a carbon.

**Humins:** complex polymeric material, insoluble in a large variety of solvents, that can be formed from the degradation reactions of sugars.

**Klason lignin quantification:** a method developed by Johan Peter Klason for the hydrolysis of biomass. In this method lignocellulosic biomass is treated first with concentrated and then with dilute sulfuric acid to solubilize and then depolymerize the polysaccharide fraction. The acid hydrolysis removes cellulose and hemicellulose leading to the formation of mostly simple sugars and yields lignin and ash as a solid residue. The sample is then calcined leaving behind only the ash, leading to a gravimetric quantification of lignin.

**Lignin valorization:** conversion of extracted lignin into a product with added value (e.g., monomers, polymers, fine chemicals, small aromatic molecules).

**Organosolv process:** a process for the isolation of the different biomass components that involves the use of an

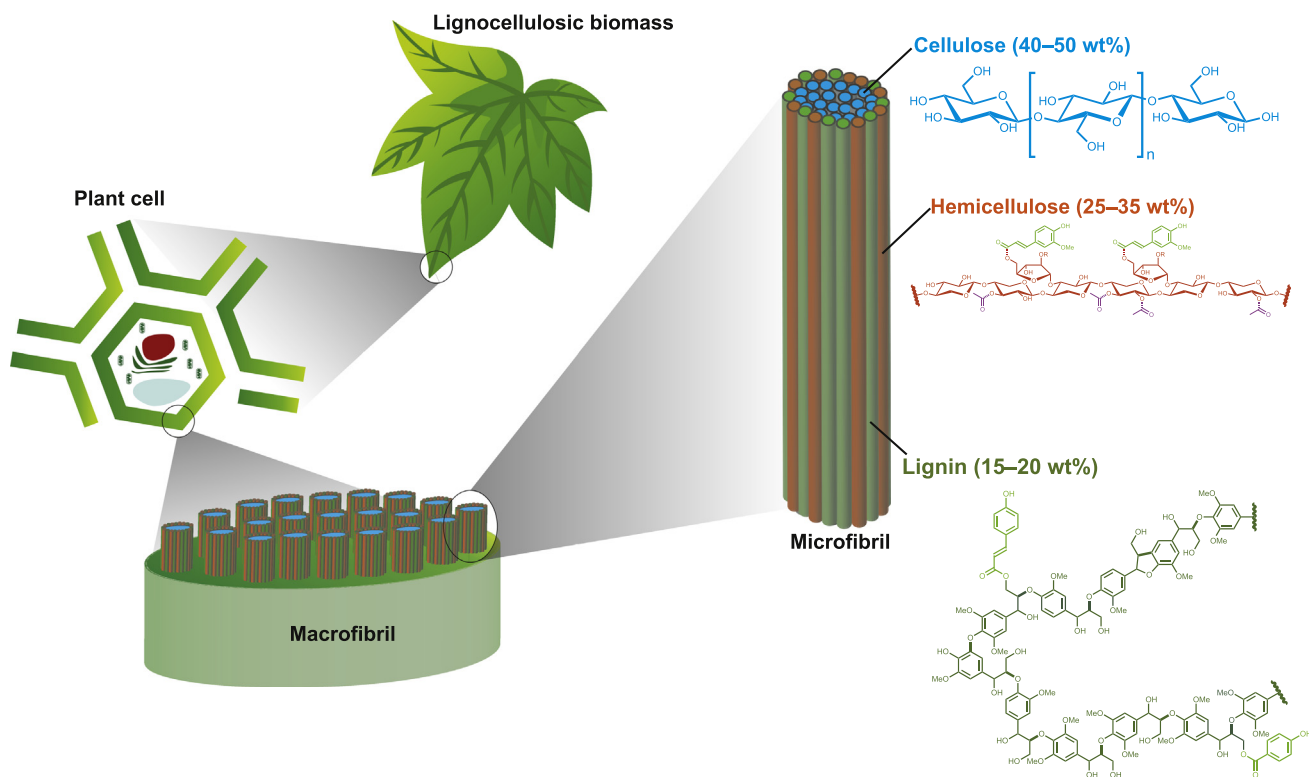
of the various lignin and carbohydrate functionalities, as the overlapping of peaks is completely avoided or largely minimized. The output of this NMR experiment is a bidimensional spectrum where each signal corresponds to a unique C–H bond in the analyzed sample.

Similar to its use for whole-cell-wall characterization, NMR is frequently used to analyze isolated lignin. Despite the absence or reduced signal of carbohydrates, 2D NMR techniques still need to be used to resolve the different functionalities that would otherwise overlap in 1D techniques. Nevertheless, advances have been made to quantify chemical bonds in lignin via spectroscopy.  $^{31}\text{P}$  NMR is a powerful tool that can be used to quantify hydroxyl and phenolic groups, but still requires a functionalization step where the hydroxyl and phenolic groups of lignin are commonly phosphorylated via a reaction with 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholane (TMDP) [29]. Recently, Talebi Amiri and colleagues applied the **HSQC zero (HSQC<sub>0</sub>)** technique, more commonly used on proteins, to quantify chemical bonds present on the lignin backbone and predict the behavior of the polymer under catalytic hydrolytic conditions [30].

Together with NMR methods, functional groups can also commonly be determined by infrared spectroscopy. Although powerful, the two techniques are not always optimized for a complex substrate like lignin and, particularly in whole-cell experiments, are commonly used to provide qualitative rather than quantitative information on the functionalities present in the biopolymer. Specifically, peak ratios can be used to provide some information on the relative ratios of the different functionalities present but not their actual amounts.

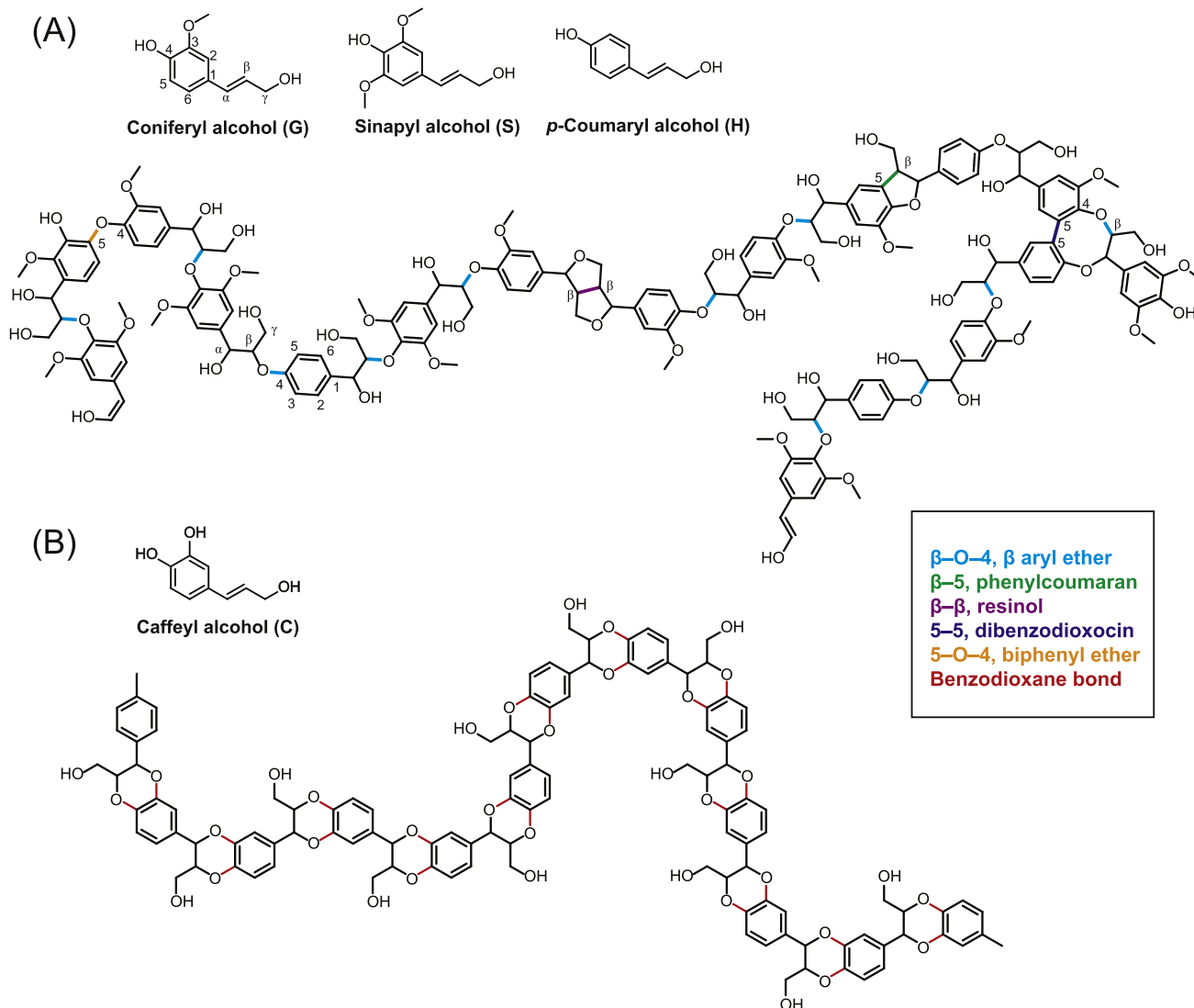
organic solvents instead of a purely aqueous solution.

**Radical biosynthesis of lignin:** in plants, lignin is produced through specific metabolic pathways that involve the formation of radical species. The synthesis starts from the amino acid phenylalanine, which is converted into monolignols, which then polymerize into lignin through an enzyme-initiated radical mechanism.



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**Figure 1. Overview of the Structure of Lignocellulosic Biomass.** Biomass has three main constituents: cellulose, a linear homopolymer of glucose linked through  $\beta$ -1,4-glycosidic bonds that accounts for about 40–50 wt% of the total mass; hemicellulose, a heteropolymer of  $\text{C}_5$  and  $\text{C}_6$  sugars linked through different glycosidic bonds that accounts for about 25–35 wt%; and lignin, an aromatic heteropolymer comprising phenylpropanoid units that forms the remaining 15–20 wt%. Fibrils of cellulose surrounded by hemicellulose and lignin constitute microfibrils. Microfibrils aggregate in macrofibrils, which are the main component of the cell walls of plants.



## Trends In Chemistry

**Figure 2. Model Chemical Structures of Lignin.** The main linkages found in lignin are shown in different colors. The main and most important bond found in hardwood, softwood, and grass lignins is the  $\beta$ -O-4 unit (light blue), which normally constitutes 40–85% of the total linkages depending on the wood species. The other types of bonds present in lignin include the  $\beta$ - $\beta$  (violet), 5-5 (dark purple),  $\beta$ -5 (green), and 5-O-4 (orange) that together account for the remaining 15–60% of interunit linkages (A) [21,22]. Exceptions to these standard linkages can be found in nature. For example, lignin in vanilla seed coats is formed almost exclusively by caffeyl alcohol units held connected together through benzodioxane linkages (red) (B) [23].

Despite the challenges and limitations, several analytical techniques have been applied in the study of the isolated biopolymer. Among the properties of isolated lignin that are commonly reported is molecular weight. Gel permeation chromatography (GPC) is the typical tool for this kind of measurement, although it often requires functionalization to make the polymer soluble for analysis. Moreover, due to variable structures, no calibration standards for lignin exist. Although it is common to use polystyrene as a calibration standard, it cannot be considered to give an accurate measure of the molecular weight as the hydrodynamic volumes for the two polymers differ. In addition to this, an extra source of error can come from the detection systems used for the determination of molecular weights. An example of this was presented recently by

Zinovyev and colleagues [31], who reported that when size exclusion chromatography was combined with multiangle light-scattering detectors (MALSs), molecular weight could be incorrectly estimated due to the autofluorescence of lignin's aromatic structure. Lignin molecule weight has also been investigated by mass spectroscopy, particularly matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS). However, the heterogeneous nature of lignin and the challenge of ionizing all fractions equally severely limit the use of this technique for accurate characterization of lignin [32].

Taken together, the dramatic progress made in the past 15 years, especially with NMR techniques, has allowed the research community to have a much clearer understanding of lignin's structure. This has translated into the ability to better relate lignin's structure to its chemical reactivity and physical properties. This has been at the root of recent progress in the ability to control and tune lignin's behavior for specific applications.

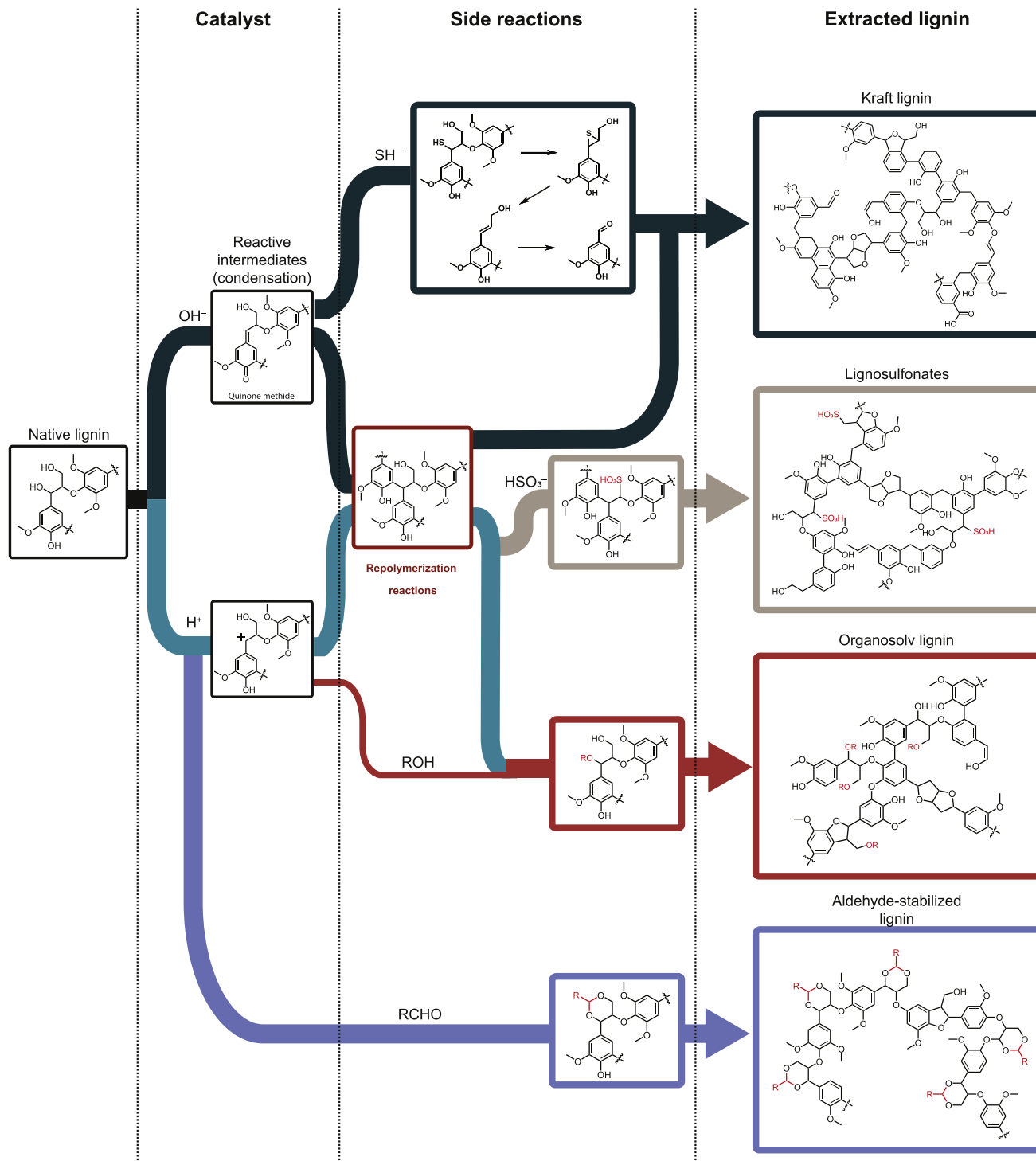
### Lignin Extraction and Its Effects on Structural Features

Before valorizing, modifying, or incorporating lignin into materials, the biopolymer must be isolated [33]. Several processes and methods have been developed over the years to achieve this separation. The pulp and paper industry is the predominant large-scale producer of lignin, where the biopolymer is a byproduct of the isolation and purification of cellulose [34]. The two most common and well-known methods for the industrial extraction of lignin are the Kraft (Figure 3, top pathway) and the sulfite processes (Figure 3, light-blue/gray pathway) [7], which are summarized in Box 1.

These two procedures allow the isolation of lignin at industrial scales using aqueous solutions at different pH, but the severity of the preceding lignin isolation methods invariably leads to a highly condensed and chemically modified biopolymer due to side reactions. In both cases, the harsh conditions of basicity or acidity favor the formation of unstable intermediates on the lignin backbone via the elimination of water molecules (Figure 3). Condensation of these intermediates occurs through intra- or intermolecular reactions with other lignin oligomers, creating new, highly stable C–C linkages. These intermediates can also react with other chemical species present in solution [35,36]. The combination of all of these side reactions, as we discuss later, is one of the key factors that limits the formation of controlled chemical structures and, ultimately, the use of industrial lignins [37,38].

In addition to the industrial methods described earlier, which use aqueous solutions for the extraction of lignin, another class of emerging pulping and lignin valorization procedures use organic solvents at temperatures ranging from 80°C to 250°C to fractionate the biomass. These novel methods are usually referred to as **Organosolv processes**. The resulting Organosolv lignins can be obtained using several solvent mixtures and conditions [39]. Alcohols or dioxane are the most frequently utilized organic solvents for this process and are often combined with water in concentrations generally varying from 40% to 100%. To help the delignification, inorganic acid catalysts (e.g., H<sub>2</sub>SO<sub>4</sub>, HCl) or organic acids (e.g., formic acid) are added at low concentrations (0.1–2%) [40–42]. These acid-catalyzed processes, although with a lesser extent, often lead to condensation and repolymerization reactions similar to those described earlier, hindering lignin's subsequent upgrading or use [43] (Figure 3, red pathway).

Recently, Shuai and colleagues [44] reported that a modified acid-catalyzed Organosolv process with the addition of aldehydes such as formaldehyde could greatly improve the quality and upgradeability of the resulting lignin. Acetal formation is highly favorable and maintains intact a large majority of the ether bonds originally present in the lignin. Because of this functionalization,



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**Figure 3. Common Procedures for Lignin Isolation and the Resulting Chemical Modifications.** Depending on the catalyst used, different reactive intermediates can form on the lignin backbone. The reactive intermediates can then undergo further reactions with other lignin units or with chemicals present in solution. In the Kraft process (top pathway), the quinone methide intermediate can react with hydrogen sulfide to form reactive thiol groups, which at high pH values keep reacting, leading

(Figure legend continued at the bottom of the next page.)

### Box 1. Current Industrial Methods for Lignin Isolation

The two most industrially relevant processes to isolate lignin are the Kraft and sulfite processes [7]. These were developed and optimized mainly by the pulp and paper industry, which isolates pure cellulose from wood for further use in paper, cardboard production, and other applications.

The Kraft process (Figure 3, top pathway) relies on the use of a basic aqueous solution of sodium sulfide at temperatures of 150–180°C. Under these conditions lignin breaks into oligomers that are substantially modified from their native structure but become soluble at pH values above 12, due to the deprotonation of the phenolic functional groups. Hemicellulose, rosin soaps, and inorganic compounds are also solubilized in the same aqueous solution, forming so-called black liquors. The liquors (after being dried) are normally burned in the recovery boiler of the industrial plant to isolate inorganic salts, while the thermal energy that is liberated from the combustion of lignin is then recovered to fulfill the energetic demand of the pulp mills. However, when the production of lignin exceeds the need for energy, the recovery of Kraft lignin can be achieved through a process called Lignoboost that leads to the isolation of a solid lignin after acidification with CO<sub>2</sub> and sulfuric acid and subsequent filtration [101].

In the sulfite process (Figure 3, light-blue/gray pathway), lignin is removed using an aqueous solution of different sulfite or bisulfite salts with pH values ranging from 1 to 5. During the process, lignin is dissolved into the aqueous liquor together with hemicellulose, leaving cellulose behind as a solid. As for Kraft lignin, it is possible to recover lignin from sulfite pulping. In these cases, the 'Magnefite' process is used to recover magnesium lignosulfonates [102], while the Howard process allows the isolation of calcium lignosulfonates by precipitation and filtration with CaO [103].

the lignin obtained can be catalytically depolymerized to monomers at near-theoretical yields (i.e., based on the cleavage of the number of  $\beta$ -O-4 linkages originally present in the lignin), which demonstrated near-complete functionalization [44].

### The Challenges of Using Isolated Lignin as a Raw Material

To produce aromatic chemicals, many recent studies have explored the catalytic depolymerization of lignin to aromatic monomers that could be used as a source of fuels or as building blocks for polymers and functional materials. These approaches are beyond the scope of this review, but several recent articles cover this subject [45–47].

Substituting aromatic materials derived from the synthesis of individual fossil-based building blocks with extracted lignin poses several challenges, most of which come from the fact that most of the briefly reviewed extraction techniques, especially those used at an industrial scale, have little to no control over the lignin's final structure. As characterized during hydrothermal biomass pretreatment, and as described earlier, lignin tends to depolymerize and repolymerize with itself, leading to creation of an elevated number of C–C linkages [48]. The greater presence of these new bonds has the consequence of decreasing the linearity of the oligomers and increasing the average molecular weight of the extracted lignin, which in some cases can lead to reduced solubility. Most importantly, the formation of novel C–C linkages can also reduce the possibilities for further functionalization. This is due to the fact that when condensation and repolymerization occur, the formation of new C–C bonds results either from radical reactions on the aromatic rings or from the disappearance of hydroxyl groups [49]. C–C bonds are also difficult to break selectively, at least not without altering the other interunit linkages [50]. Moreover, when lignin repolymerizes, its oligomers tend to form a wide array of inter- and intramolecular noncovalent bonds (e.g., hydrogen bonds, CH– $\pi$  bonds,  $\pi$ – $\pi$  stacking). These interactions have been hypothesized to hinder the solubility and/or miscibility of lignin with a great variety of solvents and polymers [51,52].

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to the formation of different functional groups such as double bonds, aldehydes, and ketones [35,36]. In the sulfite process (light-blue/gray pathway), new sulfonate groups are created. Organosolv lignin (red pathway) reacts in a path similar to the aforementioned process and also involves a cationic intermediate. However, in some of these processes the alcohols that are present can react with the aforementioned cationic intermediates, forming new ether bonds that can partially avoid the subsequent repolymerization and thus the formation of new C–C linkages. Finally, for aldehyde-stabilized lignin (bottom pathway), the presence of aldehydes in the reaction medium prevents the condensation and repolymerization of lignin by blocking the reactivity of the hydroxyl groups in the  $\alpha$  and  $\gamma$  positions of the monolignols via the formation of a 1,3-dioxane ring (bottom pathway). The proposed final structures of extracted lignins resulting from all of these reaction conditions are shown on the right.

The incorporation of lignin into materials is thus facilitated by it undergoing as limited a number of modifications as possible. This provides most of the original interunit bonds, hydroxyl groups, and aromatic ring positions, which can each be targeted for further chemical modification to meet the target application.

### Strategies for Incorporating Lignin into Novel Materials and Polymers

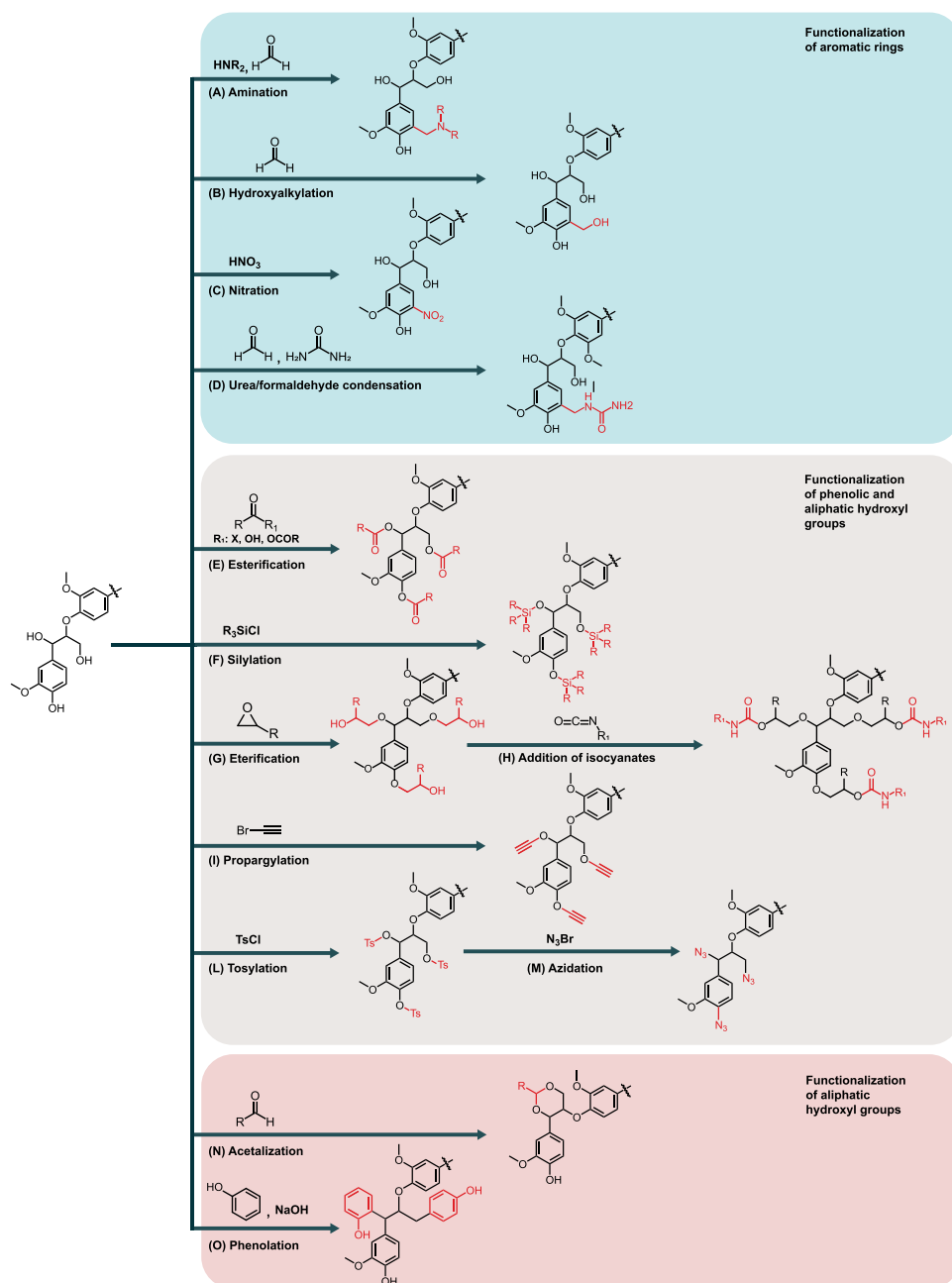
Although the physiochemical properties of lignin do not render it the best candidate for simple blending with other polymers, the simplicity of this concept has led to several attempts to do so for various uses. Lignin has notably been mixed with polyolefins like polyethylene or polypropylene [53] and aromatic polymers such as polystyrene [54]. Other materials that have been explored include blends of lignin with polyethylene terephthalate [55] and poly(butyleneadipate-co-terephthalate) [56] for packaging applications. Lignin has been used as a filler in combination with polysiloxanes to increase the renewable portion of the final polymeric material [57] and with polyacrylonitrile (PAN) for the development of lignin-based carbon fibers [58]. Blending lignin with polylactic acid has been explored for novel 3D-printing materials [59] and with polyamides for the development of flame retardants [60]. Recent work by Romhányi and colleagues has shed some light on the properties, and the consistency of these properties, of lignin–polymer blends [61]. As reported by the authors, there have been many studies of these materials but the results have been inconsistent, as the same types of blends have led to differences in miscibility and physical and mechanical properties. They notably prepared blends of lignosulfonates with several commercial polymers and showed that they could never detect perfect miscibility, but only incorporation of lignin in the form of microdroplets. The size of these microdroplets depended somewhat on the preparation of the blends, but mostly on thermodynamic factors, including intra- and inter-molecular interactions between lignin and the polymers. Finally, the mechanical properties of the blends were quite poor in terms of modulus and tensile strength, and they showed only one case where an application could be met for one of the prepared blends. They suggested that some of these challenges could be overcome by chemical modification of lignin to introduce new functional groups and make the noncovalent interactions more favorable during the blending process. This approach has become increasingly common in past years as our understanding of lignin's structure has improved.

Several functional groups already present in lignin make this biopolymer a good candidate for controlled chemical modification. Functionalization possibilities stem mainly from the reactivity of the aromatic rings of guaiacol and syringol units, as well as in the aliphatic hydroxyl groups present along the lignin backbone. In this review, we touch first on the possibility of functionalization of the aromatic part of the phenylpropanoid units, followed by the combined reactions of phenols and hydroxyls, and finally on functionalization that can be performed at the  $\alpha$  and  $\gamma$  positions of the aliphatic part of the lignin backbone. A comprehensive scheme is provided in [Figure 4](#).

#### Functionalization of the Aromatic Rings

One of the most common reactions that can be performed on the aromatic rings is the hydroxyalkylation of phenolic units using formaldehyde in the presence of a strong base such as NaOH ([Figure 4B](#)). This reaction is analogous to the one that occurs during the formation of phenol formaldehyde resins (the targeted application). The goal is to have lignin perform the same function as phenol and substitute some of this petrol-based and toxic chemical to produce lignin-phenol-formaldehyde (LPF) resins for use as adhesives in the preparation of plywood [62]. Another set of reactions performed on the phenolic units of lignin is amination via the Mannich reaction, which introduces amino groups ([Figure 4A](#)). This approach was performed by Du and colleagues who used Kraft lignin obtained from the Lignoboost process to synthesize and characterize a class of aminated lignin with potential use as polycationic polymers or surfactants





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Figure 4. Possible Chemical Modifications of the Lignin Backbone.

[63]. Nitration can also modify lignin by introducing electron withdrawing nitro groups onto the aromatic ring (Figure 4C) [64].

Finally, lignin is prone to electrophilic aromatic substitution in the presence of formaldehyde and condensation with urea to form so-called lignin-urea-formaldehyde resins (Figure 4D) [65]. All pathways that covalently introduce non-native nitrogen atoms in lignin can allow the synthesis

of novel polyamines and polyamides, but have also been proposed as a way to create a new class of biocompatible and slow releasing fertilizers [66].

#### Reaction of Phenolic and Aliphatic Hydroxyl Groups

In addition to the targeting of lignin's aromatic rings, functionalization possibilities exist for the phenolic and aliphatic OH groups along the oligomer backbone. Esterifications are a category of common reactions for lignin functionalization and involve the reaction of lignin hydroxyl groups with acyl chlorides [67], anhydrides [68], lactones [69], lactides [70], or carboxylic acids [71] (Figure 4E). Reactions with carboxylic acids have notably been used by Larrañeta and colleagues to incorporate up to 40% lignin in a new hydrogel that exhibited antibacterial properties and could be used to deliver hydrophobic drugs such as curcumin. This hydrogel was synthesized from the esterification reaction between lignin's hydroxyl groups and polyethylene glycol with the carboxylic acids present in poly(methylvinyl ether-co-maleic acid) [72]. Esters are also the groups most commonly used to covalently attach lignin to multiple initiators for controlled polymerization, such as atom transfer radical polymerization (ATRP) [73,74] and reversible addition-fragmentation chain transfer (RAFT) polymerization [75,76].

Still within possible applications of esterification functionalizations, acetylations are commonly performed with acetic anhydride and pyridine to decrease the amount of intramolecular hydrogen bonds in lignin to improve its miscibility with other polymers. Zhang and colleagues reported the production of carbon fibers from lignin, where even partial acetylation of the biopolymer increased processability during dry spinning. The remaining unreacted OH groups crosslinked during thermal treatment, leading to final fibers with high tensile strength compared with what had been previously reported in the literature [77]. Acetylation can usually be performed at high yields and selectivity and thus has been used for several applications, including when there is a need to increase the miscibility of lignin with nonpolar materials, to increase lignin solubility in organic solvents [78], or to decrease the glass transition temperature [79]. For this reason, acetylation is still the predominant reaction used to solubilize lignin during sample preparation for gel permeation chromatography. As reported by Buono and colleagues, silylation is a less common alternative reaction that provides similar and sometimes improved yields, thermal properties, and solubility enhancements [80]. Silylation, which is the addition of substituted silyl functionalities to lignin's hydroxyl groups, can be used to quantitatively introduce other functional groups in the lignin backbone (Figure 4F). Li and coworkers notably reported the synthesis of a vinyl-silylated lignin, which was further copolymerized with PAN to produce films. They compared the mechanical behavior of this material with a copolymer of Kraft lignin and PAN and reported that silylation and the introduction of vinyl groups significantly enhanced its properties compared with the unfunctionalized variants [81].

An important set of reactions also includes the etherification of hydroxyl groups to synthesize long-chain polyethers, which can be performed in several ways (Figure 4G). Among these is the oxyalkylation reaction, normally conducted in the presence of epoxides [82] or some of their reactive polymers such as poly(ethylene)-glycol diglycidyl ether (PEGDGE) that allow the linking of a polyether polymer to the lignin [83]. However, epoxides and their derivatives are highly reactive, volatile, and toxic and often require the use of high-pressure reactors [84]. Due to their handling and associated environmental issues, substitute reactions have been proposed including the use of ethylene and propylene carbonates, as reported by Liu [85] and Kühnel [86]. The addition of these long-chain polyols on the lignin substrate has been mainly explored to produce novel lignin-epoxy resins [87] or biobased polyurethanes, due to the possible addition of isocyanates to the hydroxyl groups (Figure 4H) [88,89].

Finally, another strategy for the introduction of various functional groups is to transform lignin's hydroxyls into good leaving groups for the performance of subsequent substitution reactions. This has been accomplished using the tosylation reaction (Figure 4L) [90]. The tosyl group is very versatile, as it allows the introduction of other functional groups such as azides (Figure 4M) that can be either easily reduced to primary amines or further reacted with alkyne groups to form a 1,2,3-triazole through the Huisgen cycloaddition. Panovic and colleagues performed tosylation, azidation, and a final coupling reaction with an alkyne-functionalized fluorophore derived from vanillin, to produce a novel fluorescent lignin functionalized along the whole backbone [91]. Alternatively, alkyne groups can also be introduced on the phenylpropanoid units via the propargylation reaction (Figure 4I) [92]. This strategy was used by Sadeghifar and colleagues to produce a biodegradable film that displayed UV-light-absorbing properties, which was based on cellulose modified with azide groups and subsequently coupled with a propargylated lignin [93].

### Reaction of Aliphatic Hydroxyl Groups

Phenolation reactions on the  $\alpha$  and  $\gamma$  hydroxyl groups can effectively add phenolic groups by grafting them on the lignin side chain, which increases the number of aromatic reactive sites (Figure 4O) [94]. This reaction has often been used to improve the synthesis of LPF resins, as the number of reactive sites in extracted lignin is often drastically lower than in native lignin due to repolymerization during extraction. Additional phenolic groups increase the quantity of reactive positions available on the aromatic rings, which maximizes the number of electrophilic substitution reactions with formaldehyde. This results in increased crosslinking, which allows a higher lignin content in these resins [95].

Importantly, most of the reactions described so far have been performed on lignins that were extracted according to the Kraft, sulfite, or acid-catalyzed Organosolv procedures described earlier. These processes allow the recovery of lignins that have been significantly altered by condensation, repolymerization, and other side reactions. Under these conditions, although a number of chemical functionalities, including the phenolic hydroxyl, remain and can be exploited for further chemical functionalization, the resulting lignin has a high polydispersity and further upgrading stages are required to obtain homogeneous fractions for material applications [35,96]. Therefore, although most of these reactions have been shown to slightly improve the compatibility of lignin with other materials, successful applications remain severely limited.

Improving lignin incorporation into materials could potentially be achieved by maintaining a high number of functional groups in the lignin while avoiding its repolymerization during the extraction process. Functionalizing lignin with aldehydes involves their reaction with the  $\alpha$  and  $\gamma$  hydroxyl groups of the  $\beta$ -O-4 linkage in the presence of an acid catalyst to form acetals (Figure 4N). This reaction avoids loss of functionality by preventing repolymerization reactions, but also leads to extremely efficient functionalization. Analysis by 2D NMR showed that the degree of functionalization could exceed 90% [97]. Although this functionalization was first reported with formaldehyde, it has since been shown that this reaction works efficiently with a large array of aldehydes. It was also notably shown that, by using a variety of multiple aldehydes, the solubility of the resulting lignins could be tuned, making them soluble in vastly different solvents from water to toluene [97–99]. This range of solubility could be further used to tailor lignin incorporation into several polymers.

### Concluding Remarks

In this review, we presented the potential and challenges associated with the direct use of lignin for the replacement of petrol-based polymers and materials. In addition to having a complicated

### Outstanding Questions

Can biomass be efficiently fractionated without degrading or chemically modifying any of these fractions?

How can we analyze the full lignin structure to quantify and characterize the exact sequence of functionalities on native and isolated lignin?

Can condensed lignin and unfavorable native lignin functionalities be selectively broken or transformed to improve lignin's use in materials?

How can we achieve a controlled and quantitative chemical modification on multiple reactive sites on lignin to maximize our control of this biopolymer's properties and its incorporation into materials?

chemical structure that varies across biomass species, lignin has a high reactivity due to the hydroxyl and aromatic functional groups present on its backbone. Most lignin isolation methods do not control this reactivity, which leads to irreversible condensation reactions (see [Outstanding Questions](#)). These reactions tend to increase the molecular weight, branching, functional complexity, and intrinsic tendency to form strong intra- and intermolecular bonds of lignin, making extracted lignin increasingly difficult to incorporate into polymers and materials as such [100]. Therefore, chemical modifications of the lignin backbone are often required to introduce new functionalities that are compatible with the final materials. Aromatic rings, as well as phenolic and aliphatic OH, are the main functional groups that are chemical modification targets in lignin. When these modifications occur, some of the strong intra- and inter-molecular bonds present in the original extracted lignin are broken and thus lignin can be more easily incorporated in blends or covalently bound with other polymers for the development of more renewable or new functional materials. Although lignin has several functional groups that can undergo chemical modifications, their total number is often severely reduced during lignin isolation, limiting the compatibility between lignin and polymers.

However, several recent developments could lead to rapid improvements in lignin use in materials. Improvements in analytical techniques, particularly NMR, have allowed us to gain a much clearer understanding of lignin's functional group distribution. In recent years, techniques have even emerged to quantify these functional groups in isolated lignin. This increased understanding of lignin's functionality has fostered the development of targeted chemical approaches that can both prevent condensation and quantitatively introduce new functionalities on the biopolymer. Together, these techniques could facilitate increased control of lignin's structure to approach the designed functionalities of fossil-based polymers. Such improvements could greatly increase lignin incorporation into everyday materials paving the way towards more sustainable chemicals and products.

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