

Perspective on Lignin Oxidation: Advances, Challenges, and Future Directions

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Abstract

Lignin valorization has gained increasing attention over the past decade. Being the world's largest source of renewable aromatics, its valorization could pave the way towards more profitable and more sustainable lignocellulose biorefineries. Many lignin valorization strategies focus on the disassembly of lignin into aromatic monomers, which can serve as platform molecules for the chemical industry. Within this framework, the oxidative conversion of lignin is of great interest because it enables the formation of highly functionalized, valuable compounds. This work provides a brief overview and critical discussion of lignin oxidation research. In the first part, oxidative conversion of lignin models and isolated lignin streams is reviewed. The second part highlights a number of challenges with respect to the substrate, catalyst, and operating conditions, and proposes some future directions regarding the oxidative conversion of lignin.

Keywords Lignin · Oxidation · Catalysis · Biorefinery · Model compounds

1 Introduction

Lignocellulosic biomass is a promising feedstock for renewable materials, chemicals, and fuels. It is primarily composed of the carbohydrates cellulose and hemicellulose on the one hand, and lignin, a complex phenolic polymer, on the other hand [1]. Lignocellulose processing takes place in a so-called lignocellulose biorefinery, which usually involves biomass fractionation into a carbohydrate- and lignin-derived product stream. While the carbohydrates are used for the production of

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high-value products [2–4], the lignin fraction is primarily burned for energy production. However, lignin constitutes the largest source of bio-aromatics and its conversion into high-value products could significantly augment the viability of lignocellulose biorefineries [1, 5–7]. Therefore, lignin valorization is one of the foremost challenges in current biorefinery research [1, 5–8].

One promising valorization route is the conversion of lignin into chemicals. This involves disassembling of the lignin structure into its phenolic building blocks, which can further be transformed into targeted end products [1]. Lignin is mainly composed of three phenyl propane units, with either a *p*-hydroxyphenyl—(H), guaiacyl—(G), or syringyl—(S) core. These units are connected through various ether and carbon–carbon bonds [1, 6, 8–11]. The β -O-4 ether bond is the most abundant linkage, at least in native lignin (see Fig. 1). Lignin can also contain other building blocks, such as *p*-hydroxybenzoic acid (for instance in poplar), and *p*-coumaric and ferulic acid (in herbaceous crops), which are mainly connected to lignin through ester linkages [1]. While native lignin is highly reactive towards depolymerization, lignin streams isolated from biorefinery processes such kraft, sulphite, or organosolv pulping are much more recalcitrant, which is due to severe structural degradation taking place during the biorefinery process [1, 9]. Structural degradation involves cleavage of labile ether and ester linkages (mainly the β -O-4 ether bond), and formation of stable carbon–carbon linkages through recondensation [1, 8, 12]. Breaking these stable carbon–carbon bonds in a following depolymerization step is very difficult, explaining the low reactivity of degraded lignins. In order to facilitate lignin depolymerization, recently developed biorefinery methods, such as reductive catalytic fractionation (RCF) [13], formaldehyde-assisted fractionation [14], butanosolv pulping [15], or ammonia pretreatment [16, 17], make it possible to minimize lignin condensation during the fractionation stage [12].

Irrespective of the isolation method, various lignin conversion approaches exist, each with their own advantages and limitations. Major strategies include alkaline, acidic, thermal, reductive and oxidative lignin conversion [1, 6, 8, 9]. Oxidative conversion is of great interest, as it can generate highly functionalized, valuable structures such as vanillin [1, 8, 9, 18, 19]. A lot of recent research is devoted to lignin oxidation, which has mainly been performed on either lignin model compounds or real, isolated lignin streams. In this contribution, a brief overview of the available oxidative systems for model compounds and isolated lignins is provided. In a second part, critical remarks, challenges and future directions concerning the oxidation of lignin are addressed.

2 Overview of Lignin Oxidation Research

2.1 Oxidation of Dimeric Model Compounds

This section gives a brief overview of the main catalytic systems available for the oxidation of lignin model compounds. In order to keep it concise, only catalytic systems targeting β -O-4 and β -1 dimeric models (Fig. 1) are included. These models can either be phenolic (with a free hydroxyl group at the 4-position of the A ring)

or non-phenolic (unsubstituted or with an alkoxy group at the 4-position). The catalytic methods are divided into three groups: (1) methods that enable the cleavage of non-oxidized lignin dimeric structures, (2) methods that oxidize side-chain aliphatic alcohol groups without cleaving the inter-unit linkages, thus generating oxidized dimeric structures, and (3) methods that catalyze the cleavage of oxidized dimeric structures. In the latter group, also non-oxidative methods are included. Schematic overviews of the most common catalytic systems are depicted in Figs. 1, 3, and 4.

2.1.1 Oxidative Cleavage of Non-oxidized Dimeric Structures

Oxovanadium complexes are among the most studied catalysts for the oxidation of dimeric lignin model compounds (Fig. 1) [20–28]. Using air or oxygen as oxidant (i.e., aerobic oxidation), a wide range of oxidation products can be obtained and the selectivity can be tuned by changing the substrate or the ligand structure [23]. The most studied oxovanadium complexes are depicted in Fig. 2. Complex 1a catalyzes the redox-neutral cleavage of β -O-4 models (phenolic and non-phenolic), resulting in aryl enones (**2**) [23, 25]. Although no oxidant is required for the reaction, optimal activity was achieved under aerobic conditions [25]. Complex 2a exhibits a remarkably different selectivity. Non-phenolic β -O-4 and β -1 models were oxidized primarily into C_α ketones (**1**), while the phenolic analogues were converted mainly into *p*-quinones (**4**), next to C_α ketones [21, 23]. Complex 3a catalyzed the oxidation of non-phenolic β -O-4 compounds into a mixture of C_α ketones, aryl enones and aromatic acids (**3**) [22], while phenolic β -1 models were converted primarily into C_γ aldehydes (**5**) [21]. In addition to model compounds, also organosolv lignin was subjected to oxidation and depolymerization with complexes 1a, 2a, and 3a. All three catalysts induced a decrease in molecular weight and an increase in side-chain oxidation, but the effects were most pronounced for complex 2a [28].

The catalytic system CuX/L/TEMPO [X: e.g., Cl, OTf; L: e.g., (bi)pyridine, 2,6-lutidine; TEMPO: (2,2,6,6-tetramethylpiperidin-1-yl)oxyl, structure in Fig. 2] is also commonly used for aerobic oxidation of lignin models, and shows a different product selectivity in the conversion of phenolic and non-phenolic lignin dimeric

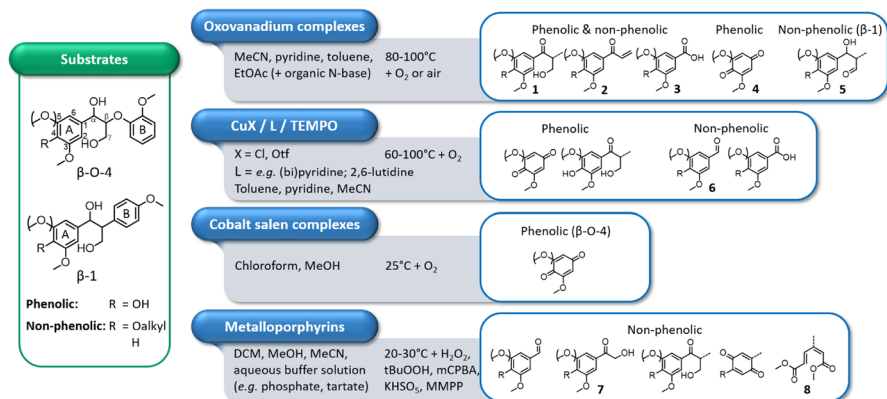


Fig. 1 Overview of catalytic systems used for the oxidation of non-oxidized dimeric lignin models

models. Non-phenolic models were oxidized primarily into aldehydes (**6**), while phenolic compounds were converted into *p*-quinones and C_α ketones [22, 29]. The depolymerization of organosolv lignin was inefficient, which was ascribed to radical coupling reactions [28].

Cobalt salen complexes enable aerobic lignin oxidation at room temperature (representative structure in Fig. 2). Non-phenolic β-*O*-4 models showed low reactivity and generated polymerization products. Phenolic β-*O*-4 models on the other hand were converted into *p*-quinones [30]. Cobalt salen complexes bearing bulky *N*-bases enabled, in addition to S-models, the selective conversion of less reactive G-models into the corresponding *p*-quinones [31]. Direct oxidation of organosolv lignin yielded aldehydes and *p*-quinones in roughly equal proportions, but the absolute monomer yield was low (3.5 wt%) [31].

Synthetic *metalloporphyrins* represent biomimetic systems for lignin peroxidase (LiP) and manganese dependent peroxidase enzymes (MnP) [9, 10, 18, 32], and enable the oxidation of lignin models at room temperature. These catalysts form highly oxidized metallo-oxo complexes upon reaction with the oxidant species. The basic structure of metalloporphyrins is shown in Fig. 2 [18, 32]. Catalyst properties like activity, selectivity, solubility, and stability can be modified by changing the R₁ and R₂ substituents [18, 32]. Also, the reaction medium, which can comprise organic solvents or aqueous buffer solutions, strongly impacts the reaction [33, 34]. Oxidation of dimeric lignin model compounds has mainly been investigated with Fe- and Mn-containing porphyrins, with various oxidants such as H₂O₂, tBuOOH, KHSO₅ and magnesium monoperoxyphthalate (MMPP) [10, 33–36]. In general, Mn complexes performed better than the corresponding Fe complexes in the oxidation of lignin models [32]. Mostly non-phenolic (methylated or ethylated) β-*O*-4 and β-1 model compounds have been studied, which yielded products such as aromatic aldehydes, 2-hydroxyethanone-substituted aromatics (**7**), C_α ketones, quinones and muconic acids (**8**) [33–36]. To address problems such as catalyst loss and degradation, immobilized metalloporphyrins, for instance on silica gels or clays, were examined for lignin oxidation and showed promising results [9, 10, 32, 37].

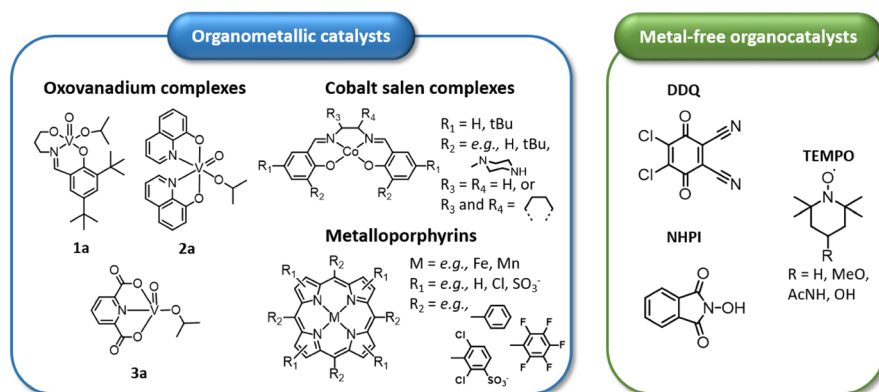


Fig. 2 Main catalysts for the oxidation of dimeric lignin models

In addition to the catalytic systems described above, several other systems have been studied for the oxidative cleavage of dimeric models. Non-phenolic β -*O*-4 models were converted into (1) aromatic aldehydes by persulfates (non-catalytic) [38] and an Fe complex with H₂O₂ or tBuOOH in DMSO [39], (2) aromatic acids by CuCl₂/polybenzoxazine composite catalysts in combination with H₂O₂ [40], (3) a mixture of aromatic aldehydes and acids by Cu- and V-containing hydrotalcites with oxygen [41] and (4) aceto-derivatives by Pd/CeO₂ with oxygen [42]. Non-phenolic β -1 models were transformed into aromatic aldehydes by persulfates [38], Cu-*N*-heterocyclic carbene with oxygen [43] and CuO_x/CeO₂/TiO₂ anatase nanotubes with oxygen under visible light irradiation [44]. While conversion of phenolic β -*O*-4 models was ineffective with persulfates [38], graphene oxide in presence of oxygen could transform these into products such as guaiacol, *p*-quinones, aromatic acids and aldehydes [45]. Methyltrioxorhenium (MeReO₃) in combination with H₂O₂ was able to convert both phenolic and non-phenolic β -*O*-4 models into various oxygenated products (e.g., 2-hydroxyethanone-, 1-hydroxyacetic acid-substituted aromatics and aromatic acids) [46].

2.1.2 Oxidation of Side-Chain Alcohol Groups in Dimeric Structures

Oxidation of the side-chain alcohol groups in β -*O*-4 models constitutes an intriguing strategy to either (1) weaken the β -*O*-4 bond and thus facilitate its cleavage, (2) promote other depolymerization routes (e.g., Baeyer–Villiger oxidation), or (3) add functionality to the lignin polymer. In this section, catalytic systems that enable the selective oxidation of the benzylic alcohol (α -OH) or terminal alcohol (γ -OH), yielding the corresponding C _{α} ketone or C _{γ} aldehyde, respectively, will be discussed. An overview is provided in Fig. 3.

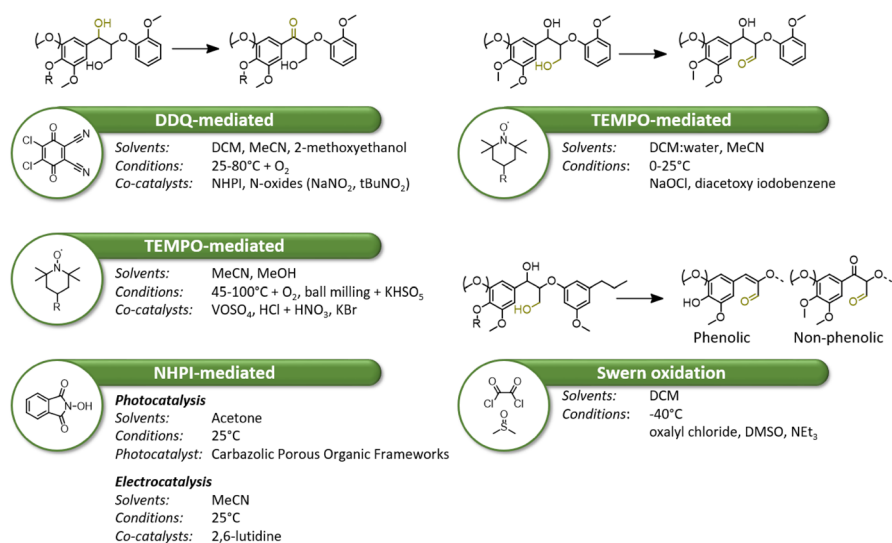


Fig. 3 Selective oxidation of α -OH or γ -OH groups in dimeric lignin models

A variety of catalytic systems has been presented for the selective benzylic oxidation with oxygen. The most common catalytic systems involve the (metal-free) organocatalysts DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) [47, 48], TEMPO [49, 50] and NHPI (*N*-hydroxyphthalimide) [51] (Fig. 2), in combination with nitrogen oxides (e.g., HNO₃, tBuONO) or other co-catalysts (e.g., VOSO₄). NHPI has also been applied in electrocatalytic [52] and photocatalytic [53] oxidation of the benzylic OH group. In addition, metal catalysts, such as Pd/C [54] and certain oxovanadium complexes (vide supra), enable selective benzylic oxidation. Many of these catalytic systems have been successfully subjected to isolated lignin substrates, with HSQC NMR being used to track the formation of C_α ketones [47, 49, 51, 52, 55, 56]. Next to aerobic oxidation, selective benzylic oxidation is possible with other oxidants, such as DDQ and TEMPO [49, 57, 58]. Ball milling with KHSO₅ as oxidant and KBr/HO-TEMPO as catalysts was recently shown to enable a selective oxidation of the benzylic OH group [59]. Furthermore, dehydrogenation of the benzylic alcohol group, with concomitant H₂ production, was demonstrated with an Ir-complex [55].

Only a few studies have reported the selective oxidation of the terminal γ -OH group into the corresponding C _{γ} aldehyde. Different (exotic) systems were tested, often using oxidants other than oxygen. TEMPO was found to catalyze this reaction using NaOCl [49] or (diacetoxyiodo)benzene [60] as oxidant. Swern oxidation (i.e., oxidation with DMSO and oxalyl chloride) enabled the oxidation of the γ -OH group in phenolic β -*O*-4 models, and also dehydrated the benzylic OH group, generating enol-ether compounds [61]. In non-phenolic models on the other hand, both OH groups (α and γ) were oxidized into the corresponding carbonyl groups.

2.1.3 Cleavage of Oxidized Dimeric Structures

The C _{α} ketones and C _{γ} aldehydes generated through oxidation of dimeric models can be converted into a variety of products through oxidative, reductive or redox-neutral processing, as shown in Fig. 4. A first oxidative approach for cleaving C _{α} ketones (of both β -*O*-4 and β -1 models) is Baeyer–Villiger oxidation, which has been performed with H₂O₂ or a peroxy acid and yielded the corresponding esters [48, 62, 63]. These esters could be cleaved through subsequent solvolysis [62]. A second oxidative approach is the Cu-catalyzed aerobic cleavage of the C _{α} –C _{β} bond in C _{α} ketones (β -*O*-4 and β -1), which produced the corresponding acids or esters [50, 64–66]. Reductive approaches focus on cleaving the weakened β -*O*-4 bond in C _{α} ketones. This has been done through photocatalysis (**11**) [53, 67], (transfer) hydrogenolysis (**9**, **10**) [51, 54], or using zinc as selective reductant (**11**) [47, 58]. Redox-neutral cleavage of the β -*O*-4 bond in C _{α} ketones was possible by reaction in aqueous formic acid/formate, which yielded mainly 1,2-propanedione-substituted phenolics (**12**) [68]. C _{γ} aldehydes of β -*O*-4 models on the other hand could be converted into aromatic aldehydes through a base-catalyzed retro-aldol reaction [60].

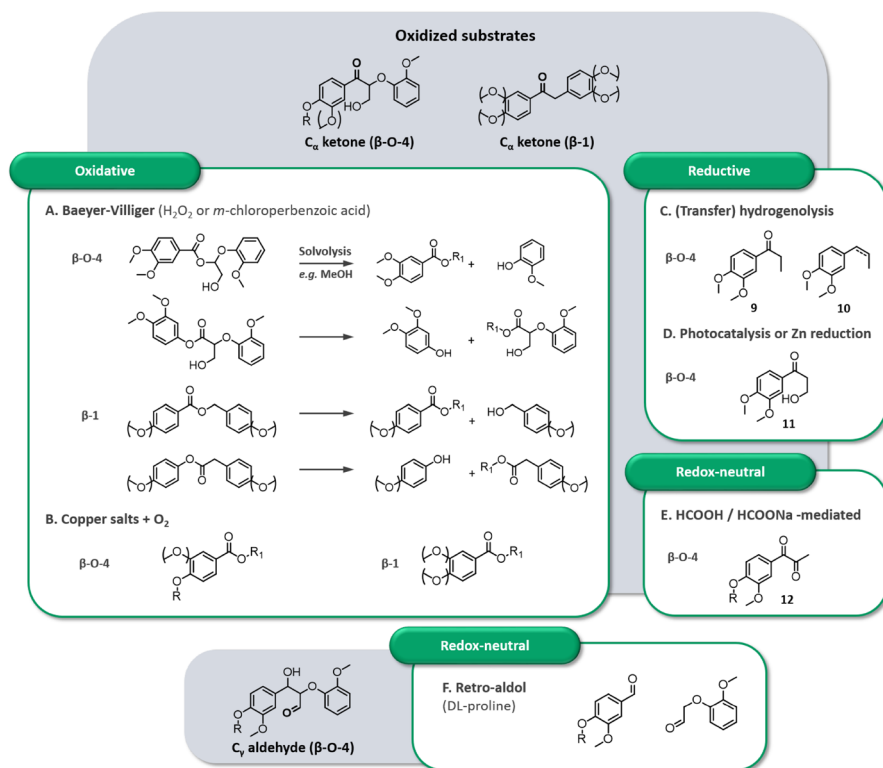


Fig. 4 Cleavage of oxidized dimeric lignin models

2.2 Oxidation of Isolated Lignin Substrates

Next to the conversion of model compounds, extensive research has been devoted to the oxidative depolymerization of isolated lignins. This topic was recently reviewed in detail by our group [1]. The main processes for lignin oxidation are outlined in Fig. 5.

The most common oxidants for lignin conversion are oxygen and hydrogen peroxide, but also nitrobenzene and CuO are frequently used for analytical purposes [69]. When aromatic products are targeted, the oxidation is mainly performed aerobically in aqueous alkaline media (usually NaOH), since this enables the selective production of aromatic aldehydes such as vanillin and syringaldehyde [1, 19, 70, 71]. Also some aromatic acids and acetophenone-like compounds are obtained. The reaction can be performed without a catalyst, although catalysts such as $CuSO_4$ have been shown to enhance the product yields [1, 19, 70, 71]. Aerobic lignin oxidation into aromatics has also been demonstrated in acidic media, either in concentrated acetic acid with a Co–Mn–Zr–Br catalyst system [72] or with diluted aqueous mineral acids such as HCl or $H_3PMo_{12}O$ [40, 73, 74], yielding aromatic aldehydes and acids (or esters). Other studies have examined the oxidation of lignin in ionic liquids (ILs) with oxygen or hydrogen

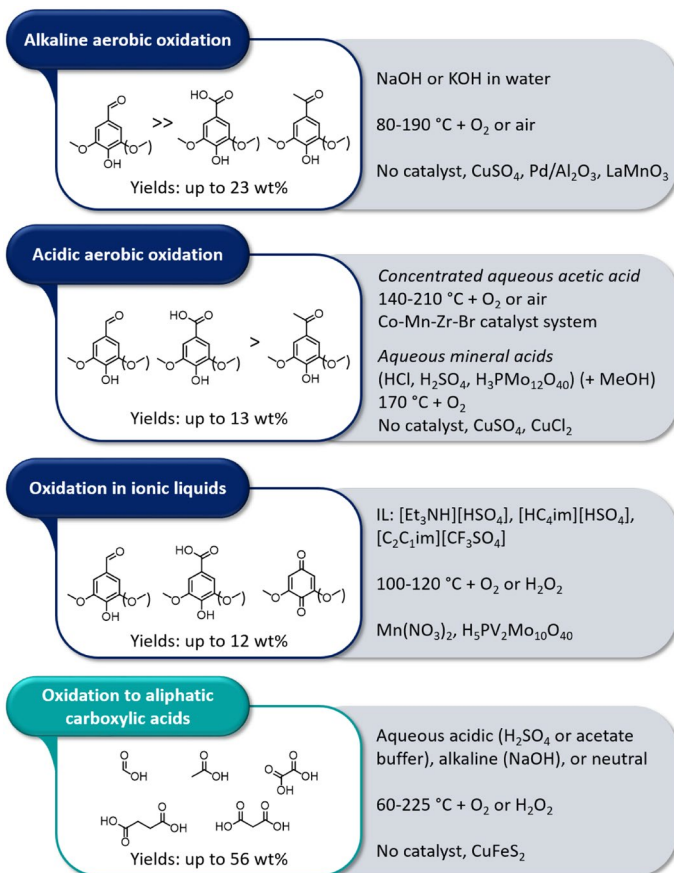


Fig. 5 Overview of main processes for oxidative conversion of real lignin substrates

peroxide [1, 75–77], in an alcohol solvent (methanol) with oxygen [42], and with a peroxy acid (peracetic acid) [78]. In these processes, aromatic aldehydes and acids, quinones and hydroquinones were obtained. Next to aromatic products, lignin oxidation can also be steered towards the generation of small carboxylic acids, such as formic, acetic and oxalic acid [1, 79, 80]. This has been demonstrated under acidic, alkaline and neutral conditions, with oxygen or hydrogen peroxide as oxidant.

3 Challenges in Lignin Oxidation

While lignin oxidation holds great potential for production of chemicals, there are still a lot of difficulties to overcome. Some challenges related to lignin oxidation are discussed here. A distinction is made between (1) substrate- and (2) catalyst/process-related challenges.

3.1 Substrate-Related Challenges

Most studies on lignin oxidation utilize monomeric or dimeric lignin model compounds as substrate. Although many of these substrates closely mimic the structure of real lignin, considerable research is performed with oversimplified model compounds that do not represent the actual lignin structures. For instance, β -*O*-4 model compounds often lack the phenolic OH group, γ -CH₂OH group, and even the α -OH group, while these all significantly influence the reactivity towards oxidation. Especially the influence of the phenolic OH group is frequently overlooked, as most oxidation studies use non-phenolic β -*O*-4 model compounds. The presence or absence of a phenolic OH group usually implies a different reaction mechanism, resulting in a different product selectivity. For instance, phenolic moieties can form phenoxyl radicals and phenolate anions, which enable additional reaction mechanisms or stabilization through electron delocalization. Many oxidative systems can selectively convert non-phenolic β -*O*-4 models, while the conversion of phenolic models is either unselective, proceeds slower, or shows a completely different product selectivity [23, 27, 38, 49, 81].

In order to be applicable to real lignin, an oxidation system should be able to convert phenolic model compounds, because free, non-etherified phenolic units constitute a significant fraction of the aromatic units in lignin (7–13% in native wood lignin [82]). This amount increases upon processing as lignin ether-bonds are cleaved. Furthermore, the question needs to be asked if the non-phenolic model compounds that are used in lignin depolymerization studies adequately represent the reactivity of non-phenolic, etherified units in the lignin polymer. Non-phenolic units in lignin constitute moieties in which the phenolic OH group of the A unit (Fig. 1) is connected to another propylphenol unit, either in the α , β , or 5-position. In the main non-phenolic model compounds, i.e., methylated β -*O*-4 compounds, the phenolic OH group is connected to a methyl group, and this bond is much more persistent than ether bonds in lignin. This is evidenced by a large number of depolymerization studies on methylated β -*O*-4 models, in which the β -*O*-4 ether linkage is cleaved (since the B unit is obtained as a ‘free’ phenolic compound), while the ether linkage between the methyl group and the A unit is retained (since the A unit is obtained as a methylated phenolic compound) [25, 39, 68, 83, 84]. The presence of the methyl group might thus hinder or alter the conversion routes that take place in actual lignin.

Besides examining the conversion of relevant phenolic model compounds, it is important to evaluate the conversion of real lignins, because its complex three-dimensional structure might significantly impact the reaction. Several studies have investigated the conversion of isolated lignins, in addition to model compounds, but the analysis is often limited to assessing the decrease in molecular weight (by GPC) or the introduction of new functional groups (by NMR) [39–41, 46, 55, 61]. However, analyzing the structure (and yield) of the volatile compounds (by GC) is very informative, as this makes it possible to verify if similar products are obtained from real lignin as from the model compounds. Also here, a discrepancy is frequently observed in the product distribution from non-phenolic model compounds and lignin. For instance, Wang et al. obtained a mixture of acetophenone and an

aromatic ester from the oxidation of a non-phenolic β -*O*-4 model compound, while the conversion of real lignin generated mainly aromatic aldehydes [42]. Lu et al. obtained vanillic acid as main product in the oxidation of a non-phenolic model, while real lignin primarily yielded vanillin. In the latter study, conversion of a phenolic model also generated vanillin as main product, which seems to indicate that the real lignin largely follows the same reaction course as the phenolic model compound [81]. Other studies however reported very similar products obtained from the conversion of non-phenolic models and real lignin substrates [47, 68].

3.2 Catalyst- and Process-Related Challenges

Lignin oxidation studies are mainly performed with homogeneous catalysts. These are usually difficult to separate and regenerate, while this is of utmost importance for large-scale processes. Furthermore, many studies use expensive catalyst systems comprising complex structures (e.g., oxovanadium complexes, salen complexes and metalloporphyrins) and multiple cocatalysts (e.g., CuCl/TEMPO/2,6-lutidine [29], NaNO₂/DDQ/NHPI [51], and HCl/HNO₃/AcNH-TEMPO [49]). Also, the complexity of real lignin is out of tune with the high specificity offered by these complex catalyst systems. Thus, applicability to real lignin and recyclability of the catalyst(s) should be primary objectives in lignin research. Catalyst recyclability is generally more practical for heterogeneous catalysts, although it might be difficult to attain a similar catalytic activity and selectivity. A large number of studies however demonstrate the effective oxidation of lignin with heterogeneous catalysts, which is discussed in dedicated reviews [85, 86].

Another challenge is related to the media used for lignin oxidation, which cause certain process and/or down-stream operational problems. Oxidation of lignin, and specifically of lignin model compounds, is frequently performed in organic solvents. These solvents are often not green, hazardous and/or flammable (e.g., pyridine, toluene, acetonitrile, methanol) [87]. The combination of a flammable solvent with oxygen is potentially explosive. Oxidation reactions should be performed outside the flammable region, which depends on the solvent (fuel) and oxygen concentration in the gas phase. Data regarding the flammable regions, however, are scarce and sometimes researchers seem to be operating within the flammable region, as they utilize a flammable solvent at elevated temperature under pressurized pure oxygen [88]. Working with very low oxygen concentrations is usually key to avoid explosions, although low oxygen concentrations also retard the oxidation reactions. Even if there is no explosion danger, solvent loss due to oxidation is usually inevitable. Next to flammable solvents, other reaction media that are often used for lignin oxidation are acidic or highly alkaline solutions, and ionic liquids. Especially alkaline solutions are commonly applied, as lignin oxidation in these media enables the selective production of vanillin (and syringaldehyde) [19]. However, the use of strongly alkaline and acidic media requires expensive reactor equipment, and, particularly for alkaline media, isolation of the reaction products is cumbersome. The conventional route to isolate the reaction products is to acidify the reaction medium and extract the product with an organic solvent, thus requiring large amounts of acid and organic

solvent, and producing large volumes of saline waste water [19, 89]. Advances have been made to avoid the acidification step or the use of organic solvents (e.g., extraction with supercritical CO₂ or adsorption on zeolites or resins), but further research is necessary to enable a more sustainable isolation of the reaction products [19, 89]. Regarding the use of ILs, the IL cost, toxicity, oxidative stability, recuperation, and the ease of product isolation need to be considered.

4 Future Directions

Future research efforts should be directed towards the development of oxidative systems that enable a safe and sustainable conversion of lignin with high product yield and selectivity, straightforward recyclability of catalyst and solvent, minimal solvent loss, and easy isolation of products. In order to demonstrate the feasibility of such systems for lignin oxidation, studies should assess the conversion of relevant lignin model compounds (including phenolic models) and preferably also real lignin substrates. Besides studying the conversion of β -O-4 model compounds, it is important to develop oxidative systems for the conversion of carbon-carbon (C-C)-linked dimeric models (such as β -1 model compounds), as C-C linkages constitute a significant fraction of the inter-unit linkages in lignin. Exciting results on the oxidative cleavage of C-C-linked dimers have been presented in recent years [21, 43, 44]. Next to native C-C bonds in lignin (like β -1 bonds), C-C bonds are also formed during biomass fractionation, which are suggested to comprise linkages between the side-chain α -position and a phenolic ring (for instance in the 5-position). Research on the oxidative cleavage of such C-C-linked dimers might enable the effective depolymerization of condensed lignin substrates such as Kraft lignin.

Additionally, lignin oxidation research can complement new developments in biorefinery research. Recent research efforts have been directed to the creation of lignocellulose fractionation strategies that prevent lignin condensation. Two intriguing developments that have gained recent attention are reductive catalytic fractionation (RCF), in which lignin isolation and reductive depolymerization are combined [13], and formaldehyde-assisted fractionation, in which the β -O-4 bonds are stabilized by formaldehyde during fractionation [14]. Both methods generate a lignin stream with high potential for chemicals production, for instance through oxidative upgrading, but their chemical structure also poses new challenges for upgrading. For instance, the lignin products from RCF usually lack inter-unit ether bonds, α -OH groups and unsaturated side chains [13]. Therefore, oxidative upgrading of these structures requires the oxidation of saturated, non-functionalized benzylic carbon atoms. In formaldehyde-stabilized lignins, the β -O-4 bonds are almost completely preserved as acetal structures [14], which should enable a rather mild oxidative depolymerization, although recuperation of the formaldehyde might be challenging.

In line with RCF, lignin isolation might also be combined with oxidative depolymerization. This involves the direct oxidation of native lignin, and has been successfully performed by alkaline aerobic oxidation, which provided high yields of aromatic aldehydes from native wood lignin [90]. However, while RCF effectively retains the carbohydrates in a solid pulp (and thus effectively fractionates the lignin

and carbohydrates), the applied conditions during alkaline aerobic oxidation inevitably solubilize and convert a substantial part of the carbohydrate fraction [91]. Other oxidative depolymerization strategies, as described above (e.g., acidic aerobic oxidation, oxidation in ionic liquids), are expected to better preserve the carbohydrates, and might possibly enable an efficient ‘oxidative fractionation’.

Finally, the application potential of the oxidation products requires further exploration. Lignin oxidation can yield a variety of products, such as aromatic acids and aldehydes, *p*-quinones and aliphatic (di)carboxylic acids, but also novel structures are frequently obtained. Aromatic acids and aldehydes are regarded as promising polymer building blocks, and vanillin is an important flavor and fragrance component [70]. Lignin-derived quinones might be used in the production of hydrogen peroxide and could be applied as energy carrier in batteries [18, 92]. Aromatic aldehydes, acids and *p*-quinones might also be used as precursor for pharmaceuticals or other fine chemicals [6]. Aliphatic (di)carboxylic acids already have various applications in food, polymer and pharmaceutical industries [18]. New structures with highly functionalized side-chains, such as 1,2-propanedione-(**12**) [68] and 3-hydroxy-1-propanone-(**11**) substituted phenolics [47], might constitute platform compounds for a myriad of new chemicals. For the latter structures, various possible transformation routes were recently assessed by Westwood et al. [47]. Expanding the application window of both conventional and new oxidation products will strengthen the role of lignin oxidation in future biorefineries.

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