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ARTICLE

Toward the Oxidative Deconstruction of Lignin: Oxidation of β-1 and β-5 Linkages

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There have been numerous reports on methods for the oxidative cleavage of β-O-4 linkages in lignin model compounds, but relatively few reports of how those methods affect other linkages that are present in lignin. We have investigated the effect of several of these oxidation methods on the β-1 and the β-5 lignin linkages, using four β-1 and β-5 model compounds. We observed that direct oxidative cleavage of C-C bonds occurs in metal-catalyzed TEMPO oxidation systems and with iron porphyrin oxidations, neither of which had we observed in similar oxidations on β-O-4 models. The β-5 linkage proved to be largely resistant to all of these oxidative systems, but the dihydrofuran ring in the β-5 model **3** was opened when treated with $KMnO_4$ at elevated temperature. Most promising was the oxidation of **2** with DDQ, which produced the benzylic ketone in high yield (84%), as it does in reactions with β-O-4 models. This reaction exhibits selectivity for the benzylic position as well as compatibility with phenols, characteristics that are highly desirable for a two-step, benzylic oxidation/Baeyer-Villiger route to cleavage of lignin.

Introduction

Biomass, and the products that may be derived from it, are considered as one of the most promising substitutes for fossil fuels.[1] Lignin, which is the second most abundant biopolymer on earth, contributes 15-30% by weight and 40% by energy to ligno-cellulosic biomass.[2] The main byproduct of paper and pulp industry, an estimated 50 million tons of extracted lignin was isolated[3] in 2010 but only 2% was used, primarily in low-value applications such as low-grade fuel for heat or for power generation.[4] Unfortunately, these uses do not take advantage of the full potential of lignin to produce high-value products, and it is this potential that stimulates the desire not only to isolate lignin from biomass but also to increase the commercial value of lignin-based products. Since lignin behaves as a resin that fills the spaces between hemicellulose and cellulose (which are both polymers of C5 and C6 sugars[5]) to supply the rigidity to the overall plant structure, separation of the lignin from the sugars should make the hemicellulose and cellulose fractions more accessible to biological and chemical digestion.[5]

Lignin is an amorphous polymer produced by enzyme-mediated phenol radical coupling polymerization of three different lignol monomers, resulting in a complex crosslinked-structure.[3, 6] β-O-4 linkages (Fig. 1) are the most common linkages between monolignols, comprising almost half of the linkages in lignin[7] (~46% in softwood lignin and ~60% in hardwood lignin)[8]. Cleavage of β-O-4 linkages has drawn a great deal of attention as a way to disassemble lignin because of their frequency and fragility. It has been suggested that most β-ethers are destroyed during lignin processing and/or isolation - for example the β-O-4 content is very low after the kraft process.[9]

In practice, breaking β-O-4 linkages does not liberate large quantities of monomers, indicating that conditions optimized for cleaving this specific linkage do not cleave all other linkages. These other types of linkages, such as β-1 and β-5 linkages, should be of interest since they constitute significant portions of lignin biomass. These two linkages contribute 7-9% and 9-12% in lignin, respectively, depending on processing methods and lignin sources.[2] Rather than involving an ether linkage, in β-1 and β-5 linkages the two aromatic units are linked via a two-carbon bridge (see Fig. 1).

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†Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}CNMR spectra of products. HRMS of products **15**, **21**, **22**, **26** and **28**. See DOI: 10.1039/x0xx00000x

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These three linkages (β-O-4, β-1 and β-5) can behave differently under the same oxidative conditions. For example, catalytic vanadium oxidative cleavage methods are highly efficient for β-O-4 linkages but ineffective for cleavage of β-1 linkages.[10] Sedai[11] reported copper and vanadium-catalyzed aerobic oxidations of a 1:1 mixture of β-1 and β-O-4 models and determined that vanadium-catalyzed oxidation of the β-O-4 model was slightly faster than oxidation of the β-1 model while with the copper catalyst, oxidation of β-1 model was faster than oxidation of the β-O-4 model.

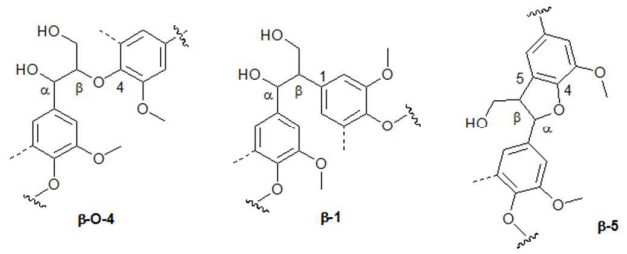


Fig. 1 Structures of β-O-4, β-1 and β-5 linkages

Therefore, in this study we examined the effect of established β-O-4 oxidation strategies on the more robust β-1 and β-5 linkages, in an effort to understand how these structures respond under oxidative conditions proposed for lignin deconstruction based on their effect on β-O-4 linkages. We investigated the yields and selectivities of these oxidation methods on β-1 and β-5 linkages, using both stoichiometric and catalytic systems that have been previously applied to other linkages. Thus, we performed oxidations under conditions used previously so that the relative reactivity of the different linkages can be compared. Accordingly, product yields are not fully optimized for β-1 and β-5 linkages but the results shed light on what may happen to these linkages in lignin under conditions optimized for reaction of the more common β-O-4 linkages.

To study the oxidation chemistry of these linkages we prepared four model compounds, including β-1 models (1,2-diaryl-1,3-propanediols) **1** and **2** and β-5 models (phenylcoumarans) **3** and **4** (see Fig. 2). Hydroxyl groups are introduced in α and γ positions in β-1 model compounds **1** and **2** to compare the compatibility and selectivity with various oxidation conditions, wherein electron-donating methoxy groups on the aromatic rings can enhance the probability of oxidations. In addition, the free phenolic hydroxyl groups (abundant in real lignin) in **2** and **4** can test the compatibility with diverse oxidants and other reagents.

Results and Discussion

Preparation of lignin model compounds

Preparation of β-1 model compounds **1** and **2** followed the methods reported by Cho.[12] Aldol condensation of ester **5** with aldehyde **6** produced ester **7**, which was reduced with $LiAlH_4$ to give **1** (R_2=OCH_3) and **2** (R_2=OH) (see Scheme 1).

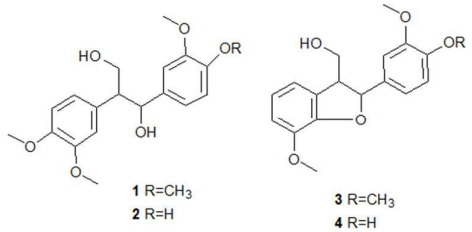
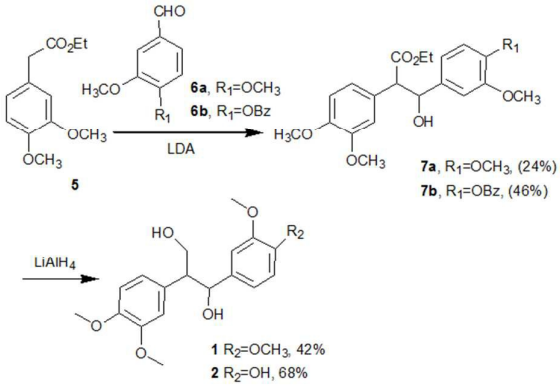


Fig. 2 Structures of β-1 and β-5 model compounds



Scheme 1 Preparation of **1** and **2**

Following the method of Brunow,[13] compounds **3** and **4**, models for the β-5 linkage, were prepared by aldol condensation between o-vanillin and acetophenone **8** to produce chalcone **9**. After protection of the phenolic hydroxyl, epoxide **10** was formed by treatment with H_2O_2 in a phase-transfer system. 1,3-propanediol **11** was obtained by rearrangement of epoxide **10** with boron trifluoride diethyl etherate and subsequent $NaBH_4$ reduction. Palladium-catalyzed debenzylation with H_2 and acid-catalyzed ring closure produced **3** and **4** (see Scheme 2).

Stoichiometric oxidations of 1-4

With models **1-4** in hand we examined the oxidation of these compounds under conventional stoichiometric oxidation conditions. We began with oxidation using $KMnO_4$, as this reagent has been used for oxidative degradation and analysis of different lignins.[14] In these

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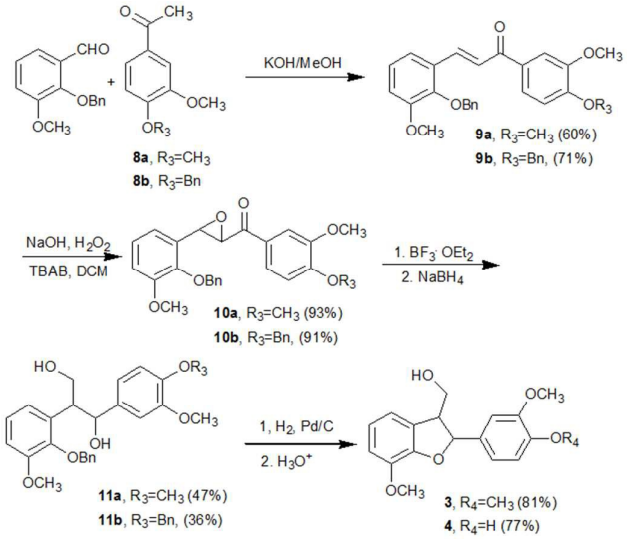
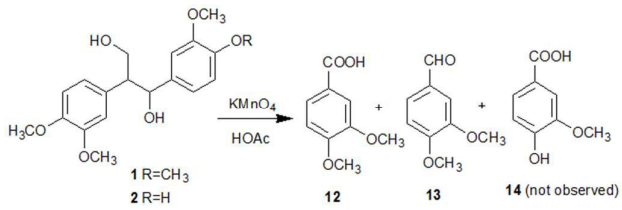
analyses, monomeric benzoic acids are produced, providing the ratio of monolignols in the lignin. When **1** was treated with $KMnO_4$ under acidic conditions, the expected benzoic acid **12** was the major product (85%). Oxidation of **2** produced benzoic acid **12** (15 %) and benzaldehyde **13** (12%) as well as material that was not chromatographically mobile, which we suspect is the result of phenolic oxidative coupling.[15] We did not detect vanillic acid (**14**) after running at 120 °C for 19h, consistent with oxidative polymerization of the unprotected phenol in **2** and in products derived from the phenolic ring of **2** (see Scheme 3).



Scheme 2 Preparation of **3** and **4**

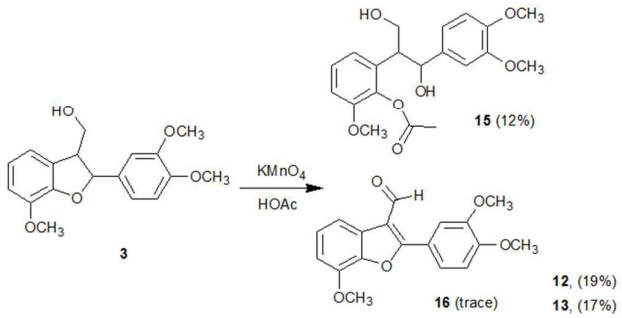


Scheme 3 $KMnO_4$ oxidation of **1** and **2**

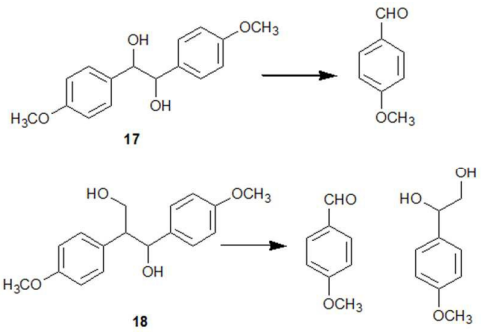
When carried out on β-5 model **3**, $KMnO_4$ oxidation produced acid **12** (19%) and aldehyde **13** (17%), as well as **15** (12%), a β-1 structure that has been acetylated at an undetermined hydroxyl. A trace amount of aldehyde **16** was also isolated (see Scheme 4).

As with the oxidation of **2**, $KMnO_4$ oxidation of **4** (which bears an unprotected phenolic hydroxyl) resulted in the formation of chromatographically immobile material, which we believe to be the polymeric products of phenolic oxidative coupling. No small molecule products were observed.

Stoichiometric and catalytic oxidation of β-1 and β-O-4 lignin model compounds with $Co(OAc)_3$ have been reported by DiCosimo.[16] Oxidation of dihydroanisoin **17** and of 1,2-bis(4-methoxyphenyl) propane-1,3-diol **18** with stoichiometric amounts of Co(III) acetate produced anisaldehyde by cleavage of the C_α-C_β bond (Scheme 5) via a single electron transfer oxidation progress, but only acid-catalyzed dehydration occurred under catalytic conditions.



Scheme 4 $KMnO_4$ oxidation of **3**



Scheme 5 Examples of oxidations of β-1 models using stoichiometric amounts (2 eq.) of Co(III), reported by Cosimo[16]

Co(III)-based homogeneous oxidation catalysts are often synthesized by *in situ* oxidation of commercially available Co(II) compounds.[17] In our hands, oxidation of **1** with stoichiometric amounts of $Co(OAc)_2$ under one atmosphere of O_2 produced aldehyde **13** in 82% yield. Oxidation of **2** was more complicated, as stilbene **19** (9%) and diacetate **20** (2%) were isolated, in addition to acetates **21** (28%) and **22** (7%) (see Scheme 6). The β-5 models **3** and **4** proved largely resistant to oxidation under

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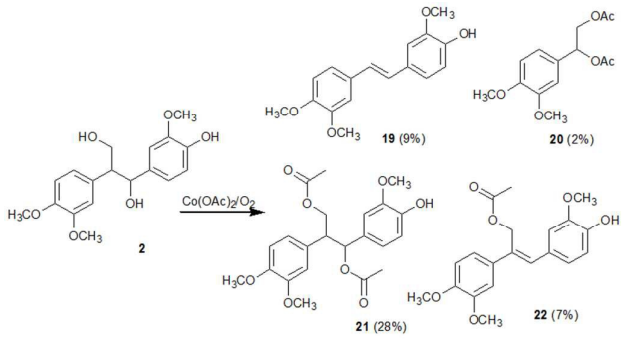
these conditions, simply producing the γ-acetates **23** from **3** (88%) and **24** from **4** (70%), with no apparent oxidation in either case (see Fig. 3).



Scheme 6 $Co(OAc)_2/O_2$ oxidation of **2**

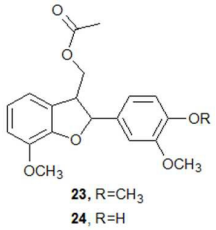


Fig. 3 Structures of γ-acetates **23** and **24**

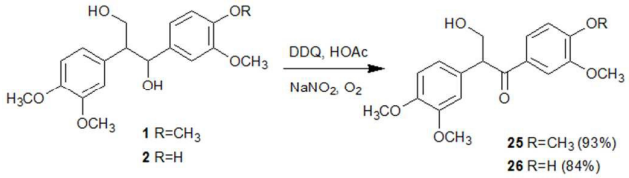
Catalytic oxidations of 1-4

Utilization of waste lignin as a source of value-added materials, such as fuels and feedstock chemicals, requires very inexpensive treatment methods. Consumption of reagents in stoichiometric oxidations is unlikely to be cost-effective, so the development of catalytic methods that rely on O_2 as the only consumed oxidant is essential.

DDQ oxidation of 1-4

DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) is known to be an efficient oxidant.[18, 19] The oxidation of alcohols using catalytic amounts of DDQ (0.2 eq.) with $Mn(OAc)_3$ as co-oxidant was reported by Cosner,[20] but large amounts of byproducts were also produced due to the large amount of $Mn(OAc)_3$ used. Shen[21] and coworkers reported a DDQ/tert-butyl nitrite catalyst system that can effectively oxidize alcohols to the corresponding ketones at 80 °C in DCE under 0.2 MPa O_2. Zhang[22] reported that oxidative dehydrogenation of 9,10-dihydro-anthracene to anthracene can be achieved by applying a catalytic metal-free DDQ/$NaNO_2$ system in the presence of O_2, using $NaNO_2$ as a shuttle between O_2 and reduced DDQ. Wang[23] reported that alcohols to can be oxidized to corresponding ketones at room temperature, with yields up to 97%, by use of a catalytic amount of DDQ in the presence of AcOH with $NaNO_2$ as a co-catalyst and O_2 as the ultimate oxidant. AcOH catalyses the decomposition[24] of $NaNO_2$ to NO and therefore is crucial to the catalytic cycle. Recently, investigation of reactivity of β-O-4, β-β and Hibbert's ketones in birch lignin under both stoichiometric and catalytic DDQ oxidation systems has been reported,[25] and results from HSQC NMR spectra suggested that as increasing amounts of DDQ were used a significant number of the benzylic hydroxyl groups of the β-O-4 linkages were oxidized.

In earlier work, we found that under the DDQ/$NaNO_2$/AcOH system, oxidations of β-O-4 models proceeded in low yields in 19 hours and in all cases, the bulk of the starting materials were recovered unchanged.[26] In contrast, the benzylic hydroxyl groups in β-1 model compounds **1** and **2** were selectively oxidized to the corresponding ketones in high yields in the same 19 hour reaction time, and it is particularly notable that clean oxidation of compound **2** was achieved in 84% yield (see Scheme 7). The presence of the unprotected phenolic hydroxyl in **2** is problematic in the TEMPO-based oxidations (see below). Chromatographically immobile material was not observed in DDQ-catalyzed reactions, suggesting that polymerization did not occur with this oxidation system.



Scheme 7 DDQ oxidation of **1** and **2**

Not surprisingly, benzofuran derivatives were produced from oxidations of compounds **3** and **4** with DDQ-based oxidations. In DDQ oxidations of compound **3** we found that further oxidation of the γ-hydroxyl also occurs; producing aldehyde **16** in 56% yield along with benzofuran alcohol **27** in only 18% yield. The gamma hydroxyl group in compound **4** remained unaffected under these oxidation conditions, and 43% of starting material **4** was recovered (see Scheme 8).

Compatibility with unprotected phenols is a highly desirable characteristic of the DDQ oxidation of **2**, which produced ketone **26** in high yield without any phenolic oxidative coupling products, suggesting that the oxidation proceeded without generation of a phenolic radical.

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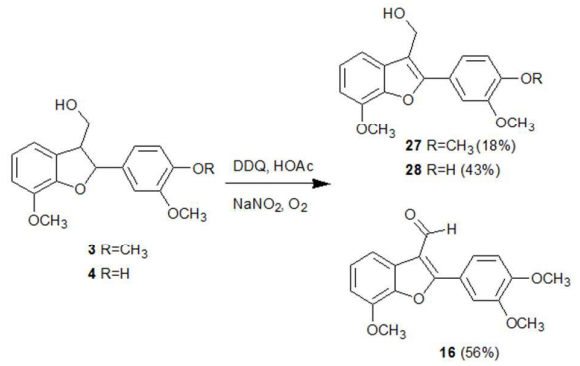
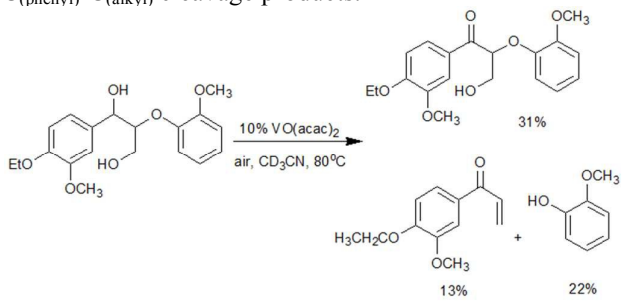


Scheme 8 DDQ oxidation of **3** and **4**

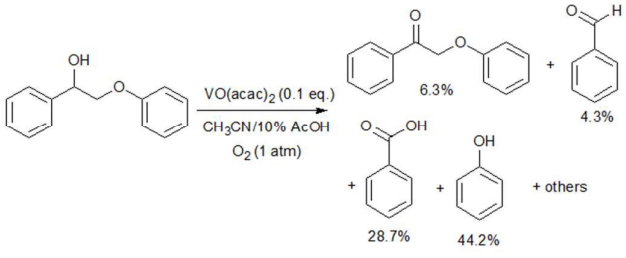
Vanadium-catalyzed oxidation of 1-4

Aerobic oxidations of benzylic alcohols,[27, 28] phenols[29] and diols[30] by vanadium complexes have been reported. Son,[31] Hanson[32] and Chan[33] reported vanadium-catalyzed oxidation of β-O-4 lignin models, in which elimination products, as well as benzylic alcohol oxidation products, were observed (see Scheme 9). Oxidation of phenolic β-O-4 lignin models with a combination of 0.1 eq of NEt_3 and vanadium complexes at 80 °C afforded unexpected $C_{(phenyl)}$-$C_{(alkyl)}$ cleavage products.[32]



Scheme 9 C-O Bond cleavage and benzylic alcohol oxidation using catalytic $VO(acac)_2$ reported by Son[31]

Ma[34] has reported an acetic acid promoted oxidative C-C bond cleavage of a β-O-4 model catalyzed by commercial available $VO(acac)_2$ using molecular oxygen as ultimate oxidant (Scheme 10).



Scheme 10 Acid-promoted oxidation of a β-O-4 model with catalytic $VO(acac)_2$ reported by Ma[34]

Application of the $VO(acac)_2/O_2$ oxidation system to the oxidation of nonphenolic β-1 model **1** gave C_α-C_β bond cleavage products **12** (19%) and **13** (31%), along with diketone **29** (4%) (see Fig. 4), and 56% recovered **1**. Prolonging the reaction time did not increase the yield of C-C cleavage products.

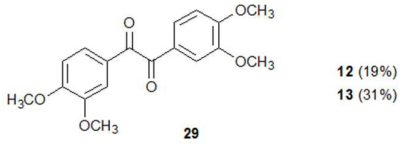


Fig. 4 Vanadium oxidation products from **1**

Chromatographically immobile materials were the major products formed from $VO(acac)_2/O_2$ oxidation of phenolic model **2**, along with small amounts of acid **12** (trace), aldehyde **13** (4%), vanillin (5.4%), and 25% recovered starting material. Little evidence of reaction was observed when nonphenolic β-5 model **3** was treated under same conditions, even when the mixture was stirred at 100 °C for 48h.

Interestingly, when **4** (which, like **2**, has an unprotected phenol) was treated with $VO(acac)_2/O_2$, no chromatography immobile products were observed. Other than recovered starting material, the only identifiable products resulted from acetylation of the phenolic hydroxyl group (3%) and trace amount of aromatization of **4** to produce 2, 3-dihydrobenzofuran derivative **28**.

TEMPO-based oxidation of 1-4

TEMPO (2,2,6,6-tetra-methyl-piperidin-1-oxy) is a stable nitroxyl radical that has been employed as a co-catalyst in aerobic oxidations[35-37] of alcohols because such reactions take place under mild conditions and can show good selectivity.[38] Recently, Wang[39] introduced hydrochloric acid into the $NaNO_2$/TEMPO system, and alcohol oxidations were achieved with high conversion, yield, and selectivity at room temperature under one atmosphere of O_2. Aerobic oxidation of lignin β-O-4 model compounds with a Cu(I)-TEMPO system have been reported by number of groups[38, 40-45] and these reactions resulted in C-O and C-C bond cleavage products. A $Fe(NO_3)_3$/TEMPO system[46] was used to catalyze aerobic oxidation of alcohols to aldehydes/ketones and benzylic alcohol oxidation was obtained in 78% yield in β-O-4 lignin models.[38] Sedai[11] also reported aerobic oxidation of phenolic and non-phenolic β-1 lignin models with a CuOTf/TEMPO catalytic system, wherein C-C cleavage products were observed. These results are particularly significant, because in our hands,[26] oxidation of lignin models with unprotected phenolic hydroxyl groups produced

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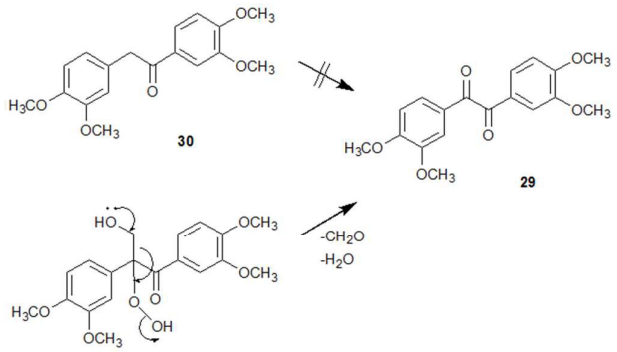
significant amounts of chromatographically immobile products.

A variety of different TEMPO-based oxidation systems have been developed, in which different co-catalysts are employed. To enable a direct comparison between these different systems, we compared the yields of oxidation products at a standard reaction time of 19 hours.

The benzylic hydroxyl group in **1** was selectively oxidized to ketone **25** under $NaNO_2$/HCl/TEMPO system and we again isolated the unexpected 1,2-diketone product **29** in 12% yield. A small amount of 1,2-diketone **29** (see Fig. 4) was isolated when **1** was treated with $VO(acac)_2/O_2$ as well. Diketone **29** could result from one of several pathways, including benzylic oxidation of **30** (see Scheme 11), which is the *retro*-Aldol condensation product of **25**. An authentic sample of **30** was prepared by acylation of veratrole with dimethoxyphenyl acetic acid, and then subjected to TEMPO/O_2/HCl/$NaNO_2$ oxidation and to $VO(acac)_2/O_2$ oxidation, but neither of these reactions produced **29**. Accordingly, we suspect that **29** results from autoxidation of the benzylic C-H in **25**, followed by the loss of CH_2O and water (see Scheme 11). This hypothesis was supported by the observation that exposing **25** to the $NaNO_2$/HCl/TEMPO oxidation system resulted in formation of **29**.

Oxidation of **1** afforded acid **12** (27%), aldehyde **13** (75%) and diketone **29** (19%) when treated with a CuCl/TEMPO/O_2 system, while ketone **25** (46%) and aldehyde **13** (31%) were the only products observed when **1** was treated with the $Fe(NO_3)_3$/TEMPO/O_2 system (see Table 1).



Scheme 11 Possible routes to produce **29** from the autoxidation product of **25**

Table 1 TEMPO-based oxidation of **1**

	12	**13**	**25**	**29**
TEMPO, O_2, HCl/$NaNO_2$	0%	0%	46%	12%
TEMPO, O_2/$Fe(NO_3)_3$	0%	31%	46%	0%
TEMPO, O_2/CuCl	27%	75%	0%	19%

All TEMPO-based oxidations of β-5 model **3** produced benzofuran carboxaldehyde **16**, with few other minor side products. Of the three methods we examined, the TEMPO/O_2/$NaNO_2$/HCl method was the most efficient, producing a 50% yield of **16** after the standard reaction time. The other methods did not produce above a 16% yield of **16** after the same reaction time.

We find that TEMPO-based oxidations are generally not compatible with unprotected phenolic hydroxyls. In all TEMPO-based oxidations of **4**, we only obtained chromatographically immobile material, again presumably polymer. In reactions of **2**, we obtained immobile material in most cases, although small amounts of acid **12,** aldehyde **13** and ketone **26** were observed (see Table 2). It is notable that C-C bond cleavage products acid **12** and aldehyde **13** were produced by the CuCl/TEMPO/O_2 system than by the other two systems, suggesting that Cu(I)/O_2 is an active oxidant of **2** and does more than just re-oxidize TEMPO.

Table 2 TEMPO oxidation of **2**

Conditions	**12**	**13**	**26**
TEMPO, O_2, HCl/$NaNO_2$	0%	0%	0%
TEMPO, O_2/$Fe(NO_3)_3$	0%	trace	16%
TEMPO, O_2/CuCl	19%	11%	19%

TPPFeCl/t-BuOOH Oxidation of 1 - 4

We previous found that the benzylic OH in the β-O-4 model **31** was oxidized to corresponding ketone **32** with a porphyrin/t-BuOOH oxidation system[47] but under same conditions we find that C-C bond cleavage dominated in the oxidation of the nonphenolic β-1 model **1**. The primary products of this reaction were 3,4-dimethoxybenzoic acid **12** (15%) and 3,4-dimethoxybenzaldehyde **13** (50%). Only 8% of the corresponding ketone **25** was formed, and 11% of starting material was recovered. The same porphyrin-based oxidation of the nonphenolic β-5 model **3** generated a 22% yield of aromatized aldehyde **16**, a 3% yield of alcohol **27**, and surprisingly a 16% yield of 3,4-dimethoxy benzaldehyde **13** was obtained, resulting from opening of the dihydrofuran ring. Starting material **3** (28%) was also recovered (Scheme 12).

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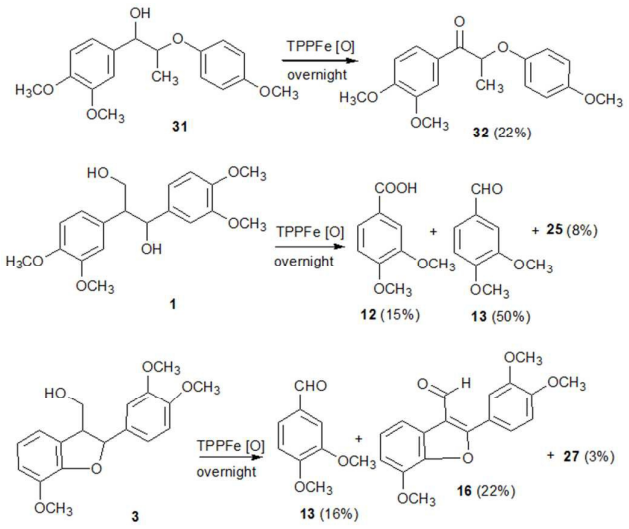

Scheme 12 Porphyrin oxidations of β-O-4, β-1 and β-5 models

Conclusions:

We have prepared several compounds as models for the β-1 and β-5 linkages in the biopolymer lignin, and we investigated the chemistry of these compounds under conditions that have been applied to the common β-O-4 linkage. We observed that in many cases benzylic hydroxyl groups can be selectively oxidized by several different oxidants. However, direct oxidative cleavage of C-C bonds in β-1 models was observed in metal-catalyzed TEMPO oxidation systems and with stoichiometric strong oxidants (i.e. $KMnO_4$ and Co(III) acetate), unlike the result of these reactions when applied to β-O-4 models. Interestingly, different TEMPO-based oxidation systems produced different arrays of products, suggesting that the reagents used to reoxidize TEMPO ($NaNO_2/O_2$, $Fe(NO_3)_3/O_2$, and $CuCl/O_2$) are not completely innocent - they play roles as oxidants beyond just the reoxidation of TEMPO.[11] Benzylic oxidation dominated in metal-free catalyzed TEMPO oxidation of both non-phenolic β-O-4 and β-1 compounds, while C-C bond cleavage was observed in copper or iron catalyzed TEMPO oxidation of non-phenolic β-1 models. Oxidative cleavage of β-O-4 model compounds does not occur in a significant extent under the same conditions.[38] In all cases, chromatographically immobile products (presumed to be polymers) were formed when phenolic β-O-4, β-1 and β-5 models were treated under the same conditions. In addition, aromatization of the dihydrofuran ring in compound **3** took place in all TEMPO-based oxidations.

It is not surprising that the β-5 linkage proved to be more difficult to cleave than the β-1 linkage. Oxidation most often resulted in simple aromatization of the dihydrofuran. Reactions that opened the dihydrofuran ring in the β-5 model **3** were only observed when **3** were treated with $KMnO_4$ at elevated temperature.

Oxidative approaches to lignin depolymerization always risk the formation of intractable material by oxidative coupling of phenolic monomers that are liberated in the course of depolymerization. In most cases, here and elsewhere,[48, 49] the presence of unprotected phenols tends to lead to formation of insoluble and chromatographically immobile materials, presumably oxidative coupling products. We found that while some reagents produce immobile materials from oxidation of unprotected phenols **2** and **4**, several proved to be somewhat compatible with phenols. Oxidation of **2** with $KMnO_4$ and with $VO(acac)_2$ both produced mononuclear aromatic products though cleavage of the C_α-C_β bond, but most of the material from the phenol-bearing ring was lost. Most promising was the oxidation of **2** with DDQ, which produced benzylic ketone **26** in high yield. This reaction exhibits selectivity for the benzylic position as well as compatibility with phenols, characteristics that are highly desirable for a two-step, benzylic oxidation/Baeyer-Villiger route to cleavage of lignin.

When subjected to TPPFeCl/tBuOOH oxidation, β-1 models react quite differently from β-O-4 models. The β-1 model **1** undergoes C-C bond cleavage, whereas the β-O-4 models studied earlier[47] produce benzylic ketones. This difference highlights the need to understand how different lignin linkages behave under oxidizing conditions. An effective approach to oxidative deconstruction of lignin will need to consider the effect of oxidation on each of the diverse array of linkages present in lignin.

Experimental section

Column chromatography was performed using silica gel-60 (Supelco) and preparative TLC was carried out with 1 mm plates (Merck). ^1H and ^{13}CNMR spectra were obtained at room temperature on a Varian INOVA 400 MHz spectrometer, with chemical shifts (δ) referenced to the residual solvent signal.

Following the method of Cho,[12] compounds **1** and **2** were prepared by the following procedure:

Preparation of 1

A solution of 1.3 mL 2.5M n-BuLi (3.28 mmol) was added to a stirred solution of diisopropylamine (0.46 mL, 3.28 mmol) in 3 mL dry THF at -78 °C under N_2 atmosphere. After 30 mins ethyl 3,4-dimethoxyphenyl acetate **5** (0.74 g, 3.28 mmol) was added dropwise and then the resulting solution was stirred for 1 h followed by

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addition of veratrylaldehyde **6a** (0.45 g, 2.73 mmol). After 3 h additional stirring at the same temperature, the mixture was diluted with 10 mL H_2O and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and evaporated in *vacuo*. Purification by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give **7a** as a yellow oil (0.25 g, 0.64 mmol, 24%).

$LiAlH_4$ (0.043 g, 1.126 mmol) was added into as a solution of ester **7a** (0.22 g, 0.563 mmol) in 10 mL THF in ice bath. The mixture was stirred for 30 mins at 0 ^oC and then for 3 h at room temperature. The solution was diluted with 5 mL H_2O and acidified with 5 mL 1 M HCl solution then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and evaporated in *vacuo*. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to produce **1** as a yellow oil (0.08 g, 0.23 mmol, 42%).

Preparation of 2

Ethyl 3,4-dimethoxyphenyl acetate **5** (0.74 g, 3.28 mmol,) was added dropwise in solution of THF containing 2.5 M LDA (2.4 mL, 6.0 mmol) in 10 mL dry THF at -78 ^oC under N_2 atmosphere and stirred for 1h. The resulting solution was stirred for 1 h followed by addition of aldehyde **6b** (0.7 g, 2.73 mmol). After 3 h additional stirring at the same temperature, the mixture was diluted with 10 mL H_2O and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and evaporated in *vacuo* to produce a crude brown oil (1.4 g). Purification by column chromatography on silica gel (hexane/ethyl acetate = 2:1) to yield **7b** as a yellow oil (0.6 g, 1.25 mmol, 46%).

$LiAlH_4$ (0.1 g, 2.5 mmol) was added into as a solution of ester **7b** (0.6 g, 1.25 mmol) in 10 mL THF in ice bath. The mixture was stirred for 30 mins at 0 ^oC then for 3 h at room temperature. The solution was diluted with 5 mL H_2O and acidified with 5 mL 1M HCl solution then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated in *vacuo*. The crude was purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1) to produce **2** as a yellow oil (0.21 g, 0.628 mmol, 68%).

Following the method of Brunow,[13] compounds **3** and **4** were prepared by the following procedure:

Preparation of 3

A solution of 12 g KOH in 20 mL methanol was added dropwise to a stirred solution of 3,4-dimethoxy-acetophenone **8a** (1.09 g, 6 mmol) and 2-(benzyloxy)-3-methoxybenzaldehyde (1.45 g, 6 mmol) in 20 mL methanol. After stirring for 24 h, the solution was neutralized by adding 4 M HCl. The yellow precipitate formed was isolated by vacuum filtration, and the filter cake was washed with methanol, then with water. The solid was dried and recrystallized from methanol to produce chalcone **9a** as a yellow oil (0.92 g, 2.35 mmol, 60%).

A solution of 5 mL 30% hydrogen peroxide and 6 mL 4% (w/v) aqueous NaOH was added dropwise to chilled solution of chalcone **9a** (0.818 g, 2 mmol) in DCM (10 mL, precooled to 0 ^oC in an ice bath). Phase transfer catalyst TBAB (0.1g, 0.31mmol) was added and then the mixture was stirred at ice bath for 30 mins and overnight at room temperature. Saturated aqueous $Na_2S_2O_3$ (10 mL) was added to quench the reaction. The solution was extracted with dichloromethane (3 x 20 mL) and the combined organic layers were dried with Na_2SO_4. Evaporation of the solvent gave **10a** as a yellow oil (0.78 g, 1.86 mmol, 93%).

Fresh BF_3-diethyl etherate (1.8 g, 13 mmol) was added dropwise into as solution of **10a** (0.55 g, 1.3 mmol) in 20 mL dry diethyl ether. The mixture was stirred at room temperature for 2.5 h and then quenched by adding water (20 mL). The organic layer was separated and extracted the aqueous layer with ethyl acetate (3 x 20 mL). All organic layers were combined and dried with Na_2SO_4. Evaporation of solvent gave a dark brown product that was used in the next step without purification.

The crude product was dissolved in 20 mL dioxane-H_2O (v/v=1:1), then $NaBH_4$ (0.4 g, 7.14 mmol) was added to the solution. The mixture was stirred for 24 h then acidified with 1M HCl to pH=7, and extracted with dichloromethane (3 x 20 mL). The combined organic layers were washed with saturated aqueous NaCl, dried with Na_2SO_4 and evaporation of solvent gave orange oil. Purification by column chromatography on silica gel (hexane/ethyl acetate = 3:1) gave **11a** as a yellow oil (1.3 g, 3.07 mmol, 47%).

A suspension of benzyl ether **11a** (0.2 g, 0.47 mmol) and 20 mg 10% Pd/C in 10 mL methanol was stirred under 1 atm H_2 (balloon). The hydrogenation consumption ceased after 3 h. The catalyst was filtered off and evaporation of solvent gave the 1,3-diol as a yellow oil (0.15 g, 0.45 mmol, 92%), wherein (80 mg, 0.24 mmol) of the resulting 1,3-diol was then dissolved in 5 mL dioxane-H_2O (v/v=1:1) and was treated with 1.0 mL 0.2 M HCl at 50 ^oC for 7 h. The solution was cooled, then neutralized with 1 M aqueous NaOH to pH=7 and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried with Na_2SO_4. Evaporation of solvent gave **3** as a yellow oil (66 mg, 0.209 mmol, 88%).

Preparation of 4

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A solution of 5.6 g KOH in 20 mL methanol was added dropwise to a stirred solution of 1-(4-(benzyloxy)-3-methoxyphenyl)ethanone **8b** (2.7 g, 10.5 mmol) and 2-(benzyloxy)-3-methoxybenzaldehyde (2.5 g, 10.5 mmol) in 40 mL methanol. After stirring for 24 h, the solution was neutralized by adding 4 M HCl. The yellow precipitate formed was isolated by vacuum filtration, and the filter cake was washed with methanol, then with water. The solid was dried and recrystallized from methanol to produce chalcone **9b** (3.6 g, 7.5 mmol, 71%) as yellow plates which were used in the following step.

A solution of 7.8 mL 30% hydrogen peroxide and 11 mL 4% (w/v) aqueous NaOH was added dropwise to chilled solution of chalcone **9b** (3.5 g, 7.26 mmol) in DCM (20 mL, precooled to 0 ^{o}C in an ice bath). Phase transfer catalyst TBAB (0.35g, 1.08 mmol) was added and then the mixture was stirred at ice bath for 30 mins and overnight at room temperature. Saturated aqueous $Na_2S_2O_3$ (10 mL) was added to quench the reaction. The solution was extracted with dichloromethane (3 x 20 mL) and the combined organic layers were dried with Na_2SO_4. Evaporation of the solvent gave **10b** as a yellow oil (3.6 g, 7.25 mmol, 99%).

Fresh BF_3-diethyl etherate (10.26 g, 72 mmol) was added dropwise into as solution of **10b** (3.6 g, 7.2 mmol) in 50 mL dry diethyl ether. The mixture was stirred at room temperature for 2.5 h and then quenched by adding water (100 mL). The organic layer was separated and extracted the aqueous layer with ethyl acetate (3 x 20 mL). All organic layers were combined and dried with Na_2SO_4. Evaporation of solvent gave a dark brown product that was used in the next step without purification.

The crude product was dissolved in 50 mL dioxane-H_2O (v/v=1:1), then $NaBH_4$ (2.6 g, 46.4 mmol) was added to the solution. The mixture was stirred for 24 h then acidified with 1M HCl to pH=7, and extracted with dichloromethane (3 x 20 mL). The combined organic layers were washed with saturated aqueous NaCl, dried with Na_2SO_4 and evaporation of solvent gave orange oil. Purification by column chromatography on silica gel (CH_2Cl_2/ethyl acetate = 4:1) gave **11b** as a yellow oil (1.3 g, 2.6 mmol, 36%).

A suspension of benzyl ether **11b** (1.3 g, 2.6 mmol) and 0.1g 10% Pd/C in 30 mL methanol was stirred under 1 atm H_2 (balloon). The hydrogenation consumption ceased after 3 h. The catalyst was filtered off and evaporation of solvent gave the 1,3-diol as a yellow oil (0.76 g, 2.37 mmol, 92%) which was then dissolved in 30 mL dioxane-H_2O (v/v=1:1) and was treated with 10 mL 0.2 M HCl at 50 ^{o}C for 7 h. The solution was cooled, then neutralized with 1 M aqueous NaOH to pH=7 and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were dried with Na_2SO_4. Evaporation of solvent gave **4** as a yellow oil (0.6 g, 1.98 mmol, 84%).

General Procedure for the $KMnO_4$-Catalyzed Oxidation of 1-4

A mixture of lignin model (1 eq.) and $KMnO_4$ (2 eq.) in AcOH (4 mL/mmol) was stirred at 120 ^{o}C for 19 h. The mixture was then cooled, diluted with water and extracted with ethyl acetate. The combined organic layers were washed with aqueous KOH, aqueous HCl, and water, then dried over Na_2SO_4 and concentrated under vacuum. The products were purified by column chromatography on silica gel.

$KMnO_4$ oxidation of 1. A mixture of **1** (90 mg, 0.26 mmol) and $KMnO_4$ (164 mg, 0.52mmol) in AcOH (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give acid **12** (40 mg, 0.22 mmol, 85%) as white solid.

$KMnO_4$ oxidation of 2. A mixture of **2** (36 mg, 0.11 mmol) and $KMnO_4$ (34 mg, 0.22mmol) in AcOH (1 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give acid **12** (3 mg, 0.016 mmol, 15%) and aldehyde **13** (2 mg, 0.013 mmol, 12%) as white solids. Chromatographically immobile was also observed.

$KMnO_4$ oxidation of 3. A mixture of **3** (76 mg, 0.24 mmol) and $KMnO_4$ (76 mg, 0.48mmol) in AcOH (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1) to give acid **12** (11 mg, 0.06 mmol, 19%), aldehyde **13** (9 mg, 0.05 mmol, 17%), and **15** (14mg, 0.04 mmol, 12%) as yellow oils. A trace amount of aldehyde **16** was also isolated. NMR spectra of **12** and **13** are identical to literature reports.[50, 51]

15:(2-(1-(3,4-dimethoxyphenyl)-1,3-dihydroxypropan-2-yl)-6-methoxyphenyl acetate): ^{1}HNMR (400 MHz, $CDCl_3$): 6.94 (2 H, d, J = 9.2 Hz), 6.89 (1 H, dd, J = 9.0 Hz, 5.9 Hz), 6.86 - 6.80 (3 H, m), 5.47 (1 H, d, J = 7.4 Hz), 4.43 (1 H, dd, J 11.1, 5.6), 4.32 (1 H, dd, J = 11.1 Hz, 7.4 Hz), 3.90 (3 H, d, J = 1.4 Hz), 3.87 (3 H, s), 3.85 (3 H, s), 3.84 - 3.77 (1 H, m), 2.02 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 170.8, 149.2, 149.1, 148.0, 144.5, 133.0, 127.4, 121.5, 118.8, 116.6, 112.2, 111.0, 109.3, 88.2, 65.5, 56.0, 55.9, 55.9, 50.4, 20.8. HRMS (ESI) *m/z* $[M + NH_4 - H_2O]^+$ calcd for $C_{20}H_{26}NO_6$ 376.1760, found 376.1754.

$KMnO_4$ oxidation of 4. A mixture of **4** (240 mg, 0.80 mmol) and $KMnO_4$ (251 mg, 1.59 mmol) in 8 mL AcOH was used. An insoluble product (138 mg) was isolated, along with 86 mg of ethyl acetate-soluble and chromatography mobile (100% MeOH) material was also

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isolated but could only be identified as a complex mixture of products.

General Procedure for the Co(III) Catalyzed Oxidation of 1-4:

A mixture of lignin model (1 eq.), $Co(OAc)_2 \cdot 4H_2O$ (2 eq.) and AcOH (2 mL/mmol) were stirred under an O_2 atmosphere (balloon) at 120 °C for 19h. The mixture was extracted with DCM and the organic layer was washed with chilled water. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude products were purified by column chromatography on silica gel.

Co(III) oxidation of 1. Products afforded from a mixture of **1** (90 mg, 0.26 mmol) and $Co(OAc)_2 \cdot 4H_2O$ (129 mg, 0.52 mmol) were purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1) to give aldehyde **13** (35 mg, 0.21 mmol, 81.5%).

Co(III) oxidation of 2. Products afforded from a mixture of **2** (90 mg, 0.27 mmol) and $Co(OAc)_2 \cdot 4H_2O$ (134 mg, 0.54 mmol) were purified column chromatography on silica gel (hexane/ethyl acetate = 1:1) (hexane/ethyl acetate = 3:1) to give a yellow solid stilbene (**19**) (7 mg, 0.024 mmol, 9.1%), a yellow oil diester (**20**) (1.8 mg, 0.006 mmol, 2.4%), a yellow oil isomeric diester (**21**) (31.5 mg, 0.075 mmol, 27.9%) and a yellow oil isomeric ester (**22**) (8.5 mg, 0.02 mmol, 7.5%).

19:**(E)-4-(3,4-dimethoxystyryl)-2-methoxyphenol**
^{1}HNMR (400 MHz, $CDCl_3$): 7.04 (1 H, d, J = 1.9 Hz), 7.02 (2 H, dd, J = 4.9 Hz, 3.1 Hz), 7.00 - 6.98 (1 H, m), 6.91 - 6.87 (3 H, m), 6.84 (1 H, d, J = 8.2 Hz), 5.62 (1 H, s), 3.94 (3 H, s), 3.93 (3 H, s), 3.89 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 149.1, 148.6, 146.7, 145.3, 130.7, 130.2, 126.8, 126.3, 120.1, 119.5, 114.5, 111.3, 108.6, 108.0, 55.9, 55.9, 55.8.

Diester 20: **(1-(3,4-dimethoxyphenyl)-1,2-ethanediol-1, 2-diacetate**). ^{1}HNMR (400 MHz, $CDCl_3$): 6.94 (1 H, ddd, J = 8.2 Hz, 2.0 Hz, 0.4 Hz), 6.90 (1 H, d, J = 2.0 Hz), 6.85 (1 H, d, J = 8.3 Hz), 5.97 (1 H, dd, J = 6.7 Hz, 5.4 Hz), 4.31 (1 H, s), 4.30 (1 H, s), 3.89 (3 H, s), 3.85 (3 H, s), 2.10 (3 H, s), 2.05 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 170.4, 169.8, 149.2, 149.0, 128.9, 119.2, 111.1, 110.0, 73.0, 65.9, 55.8, 55.7, 20.9, 20.6.

Diester (**21**): ^{1}HNMR (400 MHz, $CDCl_3$, mixture of diastereomers): 6.83 – 6.77 (1 H, m), 6.77 - 6.73 (2 H, m), 6.72 (1 H, d, J = 2.5 Hz), 6.70 - 6.67 (1 H, m), 6.65 (2 H, dd, J = 7.8 Hz, 1.9 Hz), 6.61 (1 H, d, J = 1.9 Hz), 6.55 (1 H, dd, J = 8.2 Hz, 2.0 Hz), 6.45 (1 H, d, J = 2.0 Hz), 6.00 (1 H, d, J = 7.6 Hz), 5.90 (1 H, d, J = 8.7 Hz), 5.61 (1 H, s), 5.53 (1 H, s), 4.47 (1 H, dd, J = 11.1 Hz, 7.2 Hz), 4.32 (1 H, dd, J = 11.1 Hz, 5.3 Hz), 4.25 (1 H, dd, J = 11.2 Hz, 6.2 Hz), 4.08 (1 H, dd, J 11.2 Hz, 6.9 Hz), 3.84 (3 H, s), 3.80 (3 H, s), 3.79 (2 H, s), 3.77 (3 H, s), 3.72 (2 H, s), 3.69 (2 H, s), 3.41 – 3.35 (1 H, m), 3.32 (1 H, q, J = 6.9 Hz), 2.06 (2 H, s), 1.99 (2 H, s), 1.93 (3 H, s), 1.90 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$, mixture of diastereomers): 170.9, 170.7, 169.9, 169.7, 148.5, 148.4, 148.1, 148.0, 146.2, 145.9, 145.6, 145.2, 130.2, 130.2, 130.1, 130.1, 121.1, 121.0, 120.2, 120.1, 114.2, 114.0, 112.1, 112.0, 110.8, 110.8, 110.1, 109.7, 76.3, 75.5, 64.6, 55.8, 55.8, 55.8, 55.8, 55.8, 55.7, 49.8, 49.5, 21.2, 21.0, 20.9, 20.8. HRMS (ESI, NH_4Cl buffer) m/z $[M + NH_4]^+$ calcd for $C_{22}H_{30}NO_8$ 436.1971, found 436.1965.

Ester 22 (mixture of diastereomers): ^{1}HNMR (400 MHz, $CDCl_3$,): 7.08 - 7.02 (2 H, m), 6.99 (1 H, s), 6.93 (1 H, d, J = 8.1 Hz), 6.91 - 6.88 (2 H, m), 6.88 - 6.84 (2 H, m), 6.82 (1 H, dd, J = 8.2 Hz, 1.8 Hz), 6.77 (1 H, d, J = 1.8 Hz), 6.72 (1 H, d, J = 8.2 Hz), 6.64 (1 H, dd, J = 8.2 Hz, 2.0 Hz), 6.58 (1 H, s), 6.49 (1 H, d, J = 1.9 Hz), 5.66 (1 H, s), 5.53 - 5.51 (1 H, m), 5.15 (2 H, s), 4.87 (2 H, d, J = 1.2 Hz), 3.93 (3 H, s), 3.91 (3 H, s), 3.90 (3 H, s), 3.89 (3 H, s), 3.76 (3 H, s), 3.54 (3 H, s), 2.06 (3 H, s), 2.06 (2 H, s). ^{13}CNMR (100 MHz, $CDCl_3$, mixture of diastereomers): 171.0, 170.7, 149.1, 148.8, 148.8, 148.4, 146.3, 145.7, 145.3, 144.9, 134.2, 133.9, 133.2, 132.4, 131.0, 129.4, 129.0, 128.4, 123.3, 122.4, 121.1, 118.7, 114.4, 113.9, 112.2, 111.4, 111.3, 111.2, 111.1, 109.6, 69.6, 62.2, 55.9, 55.9, 55.9, 55.9, 55.8, 55.4, 29.7, 21.0. HRMS (ESI) m/z $[M\text{-}CH_3COO]^+$ calcd for $C_{18}H_{19}O_4$ 299.1283, found 299.1279.

Co(III) oxidation of 3. Products afforded from a mixture of **3** (90 mg, 0.28 mmol) and $Co(OAc)_2 \cdot 4H_2O$ (142 mg, 0.57 mmol) were purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1), gave the γ-acetate from **3** as a brown oil (90 mg, 0.25 mmol, 88%).

23:**((2-(3,4-dimethoxyphenyl)-7-methoxy-2,3-dihydro-benzofuran-3-yl)methyl acetate**): ^{1}HNMR (400 MHz, $CDCl_3$): 6.95 - 6.79 (6 H, m), 5.45 (1 H, d, J = 7.5 Hz), 4.42 (1 H, dd, J = 11.2 Hz, 5.6 Hz), 4.30 (1 H, dd, J = 11.1 Hz, 7.4 Hz), 3.87 (3 H, s), 3.84 (6 H, d, J = 4.7 Hz), 3.82 - 3.76 (1 H, m), 2.00 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 170.8, 149.1, 149.1, 148.0, 144.5, 133.0, 127.4, 121.5, 118.8, 116.6, 112.1, 110.9, 109.2, 88.2, 65.5, 56.0, 55.9, 55.9, 50.4, 20.8.

Co(III) oxidation of 4. Products afforded from a mixture of 4 (63 mg, 0.21 mmol) and $Co(OAc)_2 \cdot 4H_2O$ (0.41 mg, 0.41 mmol) were purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1) to give a phenyl acetate from 4 as a brown oil (49 mg, 0.13 mmol, 70%). Chromatography immobile products were also observed.

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24: 4-(3-(hydroxymethyl)-7-methoxy-2,3-dihydrobenzofuran-2-yl)-2-methoxyphenyl acetate: ^{1}HNMR (400 MHz, $CDCl_3$): 6.91 (1 H, d, J = 4.5 Hz), 6.88 (3 H, m), 6.85 - 6.82 (2 H, m), 5.67 (1 H, s), 5.45 (1 H, d, J = 7.5 Hz), 4.44 (1 H, dd, J = 11.1 Hz, 5.6 Hz), 4.32 (1 H, dd, J = 11.1 Hz, 7.5 Hz), 3.89 (3 H, s), 3.86 (3 H, s), 3.80 (1 H, dd, J = 10.9 Hz, 5.2 Hz), 2.02 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 170.6, 147.7, 146.4, 145.5, 144.3, 132.2, 127.2, 121.3, 119.32, 116.3, 114.0, 111.9, 108.4, 88.1, 65.2, 55.7, 55.7, 50.2, 20.5.

General DDQ oxidation of 1-4

A mixture of substrate (1 eq.), DDQ (0.1 eq.), $NaNO_2$ (0.1 eq.), CH_2Cl_2 (20 mL/mmol) and acetic acid (2 mL/mmol) was stirred under an O_2 atmosphere (balloon) at room temperature for 22 h. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated aqueous NaCl, dried over Na_2SO_4 and then concentrated under vacuum. The products were purified column chromatography on silica gel.

DDQ oxidation of 1. A mixture of **1** (50 mg, 0.14 mmol), DDQ (3.3 mg, 0.014 mmol), $NaNO_2$ (0.93 mg, 0.014 mmol), CH_2Cl_2 (2 mL) and acetic acid (0.2 mL) was used. The products were purified column chromatography on silica gel (hexane/ethyl acetate = 1:1) to produce ketone **25** as a yellow oil (46 mg, 0.13 mmol, 93%).

25: (**1,2-bis(3,4-dimethoxyphenyl)-3-hydroxypropan-1-one**). ^{1}HNMR (400 MHz, $CDCl_3$): 7.54 (1 H, dd, J = 8.4 Hz, 2.0 Hz), 7.51 (1 H, d, J = 2.0 Hz), 6.82 – 6.75 (3 H, m), 6.74 (1 H, d, J = 1.7 Hz), 4.66 (1 H, dd, J = 8.3 Hz, 4.9 Hz), 4.22 (1 H, dd, J = 11.3 Hz, 8.3 Hz), 3.86 (3 H, s), 3.85 (3 H, s), 3.83 (1 H, m), 3.81 (3 H, s), 3.80 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 198.4, 153.3, 149.3, 148.8, 148.4, 129.4, 129.2, 123.7, 120.7, 111.6, 111.0, 110.8, 110.0, 65.1, 55.9, 55.9, 55.8, 55.4.

DDQ oxidation of 2. A mixture of **2** (93 mg, 0.28 mmol), DDQ (6.6 mg, 0.028 mmol), $NaNO_2$ (1.86 mg, 0.028 mmol), CH_2Cl_2 (6 mL) and acetic acid (0.4 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 1:1) to produce ketone **26** as an orange oil (78 mg, 0.23 mmol, 84%).

26: (**2-(3,4-dimethoxyphenyl)-3-hydroxy-1-(4-hydroxy 3-methoxyphenyl)propan-1-one**): ^{1}HNMR (400 MHz, $CDCl_3$): 7.56 - 7.50 (2 H, m), 6.86 - 6.83 (1 H, m), 6.82 - 6.79 (2 H, m), 6.76 (1 H, d, J =1.6 Hz), 6.07 (1 H, s), 4.67 (1 H, dd, J =8.3 Hz, 5.0 Hz), 4.24 (1 H, dd, J = 11.2 Hz, 8.4 Hz), 3.90 (3 H, s), 3.89 - 3.85 (1 H, m), 3.84 (3 H, s), 3.83 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 198.5, 150.5, 149.4, 148.5, 146.5, 129.1, 129.1, 124.4, 120.7, 113.8, 111.7, 111.0, 110.5, 65.3, 55.9, 55.9, 55.8, 55.4. HRMS (ESI) m/z [M - H]$^+$ calcd for $C_{18}H_{19}O_6$ 331.1182, found 331.1172.

DDQ oxidation of 3. A mixture of **3** (140 mg, 0.44 mmol), DDQ (10 mg, 0.044 mmol), $NaNO_2$ (3 mg, 0.044 mmol), CH_2Cl_2 (8 mL) and acetic acid (0.6 mL) was used. The products were purified by column chromatography (hexane/ethyl acetate = 3:1) to produce aldehyde **16** as a yellow solid (36 mg, 0.11 mmol, 56%) and benzofuran alcohol **27** as a yellow oil (12 mg, 0.038 mmol, 18%). Starting material **3** (35mg, 25%) was also recovered.

16: (2-(3,4-dimethoxyphenyl)-7-methoxybenzofuran-3-carbaldehyde). ^{1}HNMR (400 MHz, $CDCl_3$): 10.29 (1 H, s), 7.79 (1 H, d, J = 7.9 Hz), 7.42 (1 H, d, J = 8.3 Hz), 7.30 - 7.21 (1 H, m), 6.98 (1 H, d, J = 8.3 Hz), 6.87 (1 H, d, J = 8.1 Hz), 4.01 (3 H, s), 3.96 (3 H, s), 3.94 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 186.6, 165.5, 151.7, 149.3, 144.9, 143.0, 127.3, 125.6, 123.0, 121.0, 116.9, 114.4, 111.5, 111.2, 107.9, 56.2, 56.1, 56.0

27: (**(2-(3,4-dimethoxyphenyl)-7-methoxybenzofuran-3-yl)methanol**): ^{1}HNMR (400 MHz, $CDCl_3$): 7.47 - 7.41 (2 H, m), 7.26 - 7.24 (1 H, m), 7.18 (1 H, t, J = 7.8 Hz), 6.95 (1 H, d, J = 8.9 Hz), 6.81 (1 H, dd, J = 7.9 Hz, 1.2 Hz), 4.91 (2 H, s), 4.02 (3 H, s), 3.96 (3 H, s), 3.92 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 154.1, 149.8, 149.1, 145.2, 142.9, 131.1, 123.6, 122.9, 120.6, 113.9, 111.5, 111.1, 110.5, 106.7, 56.1, 56.0, 56.0, 55.6.

DDQ oxidation of 4. A mixture of **4** (93 mg, 0.31 mmol), DDQ (7.3 mg, 0.031 mmol), $NaNO_2$ (2 mg, 0.031 mmol), CH_2Cl_2 (3 mL) and acetic acid (0.44 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to produce a yellow oil **28** (40 mg, 0.13 mmol, 43%) and starting material **4** (40 mg, 43%) was recovered as well.

28: (**(2-(3,4-dimethoxyphenyl)-7-methoxybenzofuran-3-yl)methanol**): ^{1}HNMR (400 MHz, $CDCl_3$): 7.44 (1 H, d, J = 1.9 Hz), 7.41 (1 H, dd, J = 8.3 Hz, 2.0 Hz), 7.29 - 7.26 (1 H, m), 7.20 (1 H, t, J = 7.8 Hz), 7.02 (1 H, d, J = 8.3 Hz), 6.83 (1 H, dd, J = 7.8 Hz, 1.1 Hz), 5.83 (1 H, s), 4.93 (2 H, s), 4.04 (3 H, s), 3.99 (3 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 154.3, 146.7, 146.6, 145.3, 142.9, 131.1, 123.7, 122.4, 121.3, 114.7, 113.7, 111.5, 110.0, 106.7, 56.2, 56.1, 55.7. HRMS (ESI) m/z [M - H]$^+$ calcd for $C_{17}H_{15}O_5$ 299.0919, found 299.0914.

General VO(acac)$_2$ oxidation of 1-4

A mixture of lignin model (1 eq.), VO(acac)$_2$ (0.3 eq.), MeCN (30 mL/mmol) and 10% aqueous AcOH (0.3 mL) were stirred under an O_2 atmosphere (balloon) at 100 ^{o}C for 48h. The mixture was extracted with EA and the organic layer was washed with chilled water. The

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combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The product mixtures were purified by column chromatography on silica gel.

$VO(acac)_2$ oxidation of 1. A mixture of **1** (100 mg, 0.287 mmol), $VO(acac)_2$ (24.1 mg, 0.086 mmol) were used. The mixture products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give acid **12** (10 mg, 0.055 mmol, 19%), aldehyde **13** (15 mg, 0.09 mmol, 31.4%), a yellow solid diketone **29** (3.5mg, 0.01 mmol, 3.7%). Starting material **1** was also recovered (56 mg, 52.8%).

29: (**1,2-bis(3,4-dimethoxyphenyl)ethane-1,2-dione**). ^{1}HNMR (400 MHz, $CDCl_3$): 7.59 (1 H, s), 7.47 (1 H, d, *J* = 8.3 Hz), 6.88 (1 H, d, *J* = 8.5 Hz), 3.95 (6 H, s). ^{13}CNMR (100 MHz, $CDCl_3$): 193.4, 154.8, 149.5, 126.4, 126.3, 110.3, 56.2, 56.1.

$VO(acac)_2$ oxidation of 2. A mixture of **2** (122 mg, 0.365 mmol), $VO(acac)_2$ (30.68 mg, 0.11 mmol) were used. The product mixture was purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give acid **12** (trace), aldehyde **13** (3 mg, 0.018 mmol, 5%), vanillin (3 mg, 0.0197 mmol, 5.4%). Starting material **2** was recovered (30 mg, 24.6%) as well. Chromatographically immobile material was also observed.

$VO(acac)_2$ oxidation of 4. A mixture of **4** (82 mg, 0.27 mmol), $VO(acac)_2$ (22.8 mg, 0.08 mmol) were used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give the phenyl acetate and a yellow oil **28** (trace). Starting material was also recovered (50 mg, 60.9%).

General TEMPO/$NaNO_2$/NaCl/HCl oxidation of 1-4.

A mixture of lignin model (1 eq.), TEMPO (0.15 eq.), $NaNO_2$ (0.25 eq.), 36% aqueous HCl (0.5 eq.), NaCl (0.5 eq.) and CH_2Cl_2 (20 mL/mmol) stirred under an O_2 atmosphere (balloon) at room temperature for 23 h. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, then with water. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The product mixtures were purified by column chromatography on silica gel.

Oxidation of 1. A mixture of **1** (50 mg, 0.145 mmol), TEMPO (3.4 mg, 0.021 mmol), $NaNO_2$ (2.5 mg, 0.0359 mmol), 36% aqueous HCl (6 µL, 0.0717 mmol), NaCl (4.2 mg, 0.0717 mmol) and DCM (2 mL) was used. The mixture products were purified by column chromatography on silica gel (hexane/ethyl acetate = 2:1) to give a yellow oil ketone **25** (23 mg, 0.06 mmol 46%) and diketone **29** (6 mg, 0.018 mmol, 12%).

Oxidation of 2. A mixture of **2** (34 mg, 0.1 mmol), TEMPO (2.4 mg, 0.075 mmol), $NaNO_2$ (1.7 mg, 0.025 mmol), 36% aqueous HCl (4.3 µL, 0.05 mmol), NaCl (2.9 mg, 0.05 mmol) and CH_2Cl_2 (2 mL) was used. The product was chromatographically immobile.

Oxidation of 3. A mixture of **3** (136 mg, 0.43 mmol), TEMPO (10 mg, 0.0645 mmol), $NaNO_2$ (7.5 mg, 0.1 mmol), 36% aqueous HCl (17 µL, 0.2 mmol), NaCl (12.6 mg, 0.2 mmol) and CH_2Cl_2 (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give aldehyde **16** as a yellow solid (40 mg, 0.13 mmol, 50%).

Oxidation of 4. A mixture of **4** (95 mg, 0.314 mmol), TEMPO (7.6 mg, 0.047 mmol), $NaNO_2$ (5.4 mg, 0.078 mmol), 36% aqueous HCl (13 µL, 0.157 mmol), NaCl (9.1 mg, 0.157 mmol) and CH_2Cl_2 (2 mL) was used. The products were chromatographically immobile.

General $Fe(NO_3)_3$ /TEMPO oxidation of 1-4

A mixture of substrate (1 eq.), TEMPO (0.1 eq.), $Fe(NO_3)_3{\cdot}9H_2O$ (0.05 eq.), NaCl (0.1 eq.) and DCE (10 mL/mmol) stirred under an O_2 atmosphere (balloon) at room temperature for 19h. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, then with water. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The products were purified by column chromatography on silica.

$Fe(NO_3)_3$ /TEMPO oxidation of 1. A mixture of 1 (80 mg, 0.23 mmol), TEMPO (3.6 mg, 0.023 mmol), $Fe(NO_3)_3{\cdot}9H_2O$ (4.6 mg, 0.0115 mmol), NaCl (1.3 mg, 0.023 mmol) and DCE (2 mL) was used. The mixture products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give aldehyde **13** (12 mg, 0.072 mmol, 31%) and ketone **25** (37 mg, 0.106 mmol, 46%).

$Fe(NO_3)_3$ /TEMPO oxidation of 2. A mixture of 2 (37mg, 0.11 mmol), TEMPO (1.9 mg, 0.011 mmol), $Fe(NO_3)_3{\cdot}9H_2O$ (2.2 mg, 0.005 mmol), NaCl (0.6 mg, 0.011 mmol) and DCE (2 mL) was used. The mixture products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give aldehyde **13** (trace), and a yellow oil **26** (6mg, 0.018mmol, 16%). Chromatographically immobile material was also observed.

$Fe(NO_3)_3$ /TEMPO oxidation of 3. A mixture of 3 (73 mg, 0.23 mmol), TEMPO (3.9 mg, 0.023 mmol), $Fe(NO_3)_3{\cdot}9H_2O$ (4 mg, 0.01 mmol), NaCl (1.3 mg, 0.023 mmol) and DCE (2 mL) was used. The mixture products were purified by column chromatography on silica gel

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(hexane/ethyl acetate = 3:1) to give aldehyde **16** (11 mg, 0.035 mmol, 15.2%). Starting material **3** was also recovered (53 mg, 73%).

$Fe(NO_3)_3$ /TEMPO oxidation of 4. A mixture of 4 (100 mg, 0.33 mmol), TEMPO (5.1 mg, 0.033 mmol), $Fe(NO_3)_3 \cdot 9H_2O$ (6.6 mg, 0.0165 mmol), NaCl (2 mg, 0.033 mmol) and DCE (3 mL) was used. The reaction products were chromatographically immobile.

General CuCl /TEMPO oxidation of 1-4.

A mixture of substrate (1 eq.), TEMPO (0.3 eq.), CuCl (0.2 eq.) and pyridine (10 mL/mmol) stirred under an O_2 atmosphere (balloon) at 100 ^oC for 19h. The mixture was extracted with ethyl acetate and the organic layer was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHSO_4$, then with water. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The product mixtures were purified by column chromatography on silica gel.

CuCl /TEMPO oxidation of 1. A mixture of **1** (100 mg, 0.287 mmol), TEMPO (13.4 mg, 0.086 mmol), CuCl (5.7 mg, 0.057 mmol) and pyridine (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give acid **12** (36 mg, 0.198 mmol, 75.4%), aldehyde **13** (14 mg, 0.084 mmol, 27%) and diketone **29** (18 mg, 0.054 mmol, 19%).

CuCl /TEMPO oxidation of 2. A mixture of **2** (122 mg, 0.365 mmol), TEMPO (17.1 mg, 0.11 mmol), CuCl (7.2 mg, 0.073 mmol) and pyridine (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give a yellow oil acid **12** (12.6 mg, 0.069 mmol, 19%) and aldehyde **13** (6.8 mg, 0.041 mmol, 11%). Chromatographically immobile material also observed.

CuCl /TEMPO oxidation of 3. A mixture of **3** (75 mg, 0.24 mmol), TEMPO (11.2 mg, 0.072 mmol), CuCl (4.7 mg, 0.047 mmol) and pyridine (2 mL) was used. The products were purified by column chromatography on silica gel (hexane/ethyl acetate = 3:1) to give aldehyde **16** (10 mg, 0.032 mmol, 13%). Starting material **3** was also recovered (47 mg, 63%).

CuCl /TEMPO oxidation of 4. A mixture of 4 (90 mg, 0.30 mmol), TEMPO (14 mg, 0.09 mmol), CuCl (5.9 mg, 0.06 mmol) and pyridine (3 mL) was used. The product mixture was chromatography immobile.

Conflicts of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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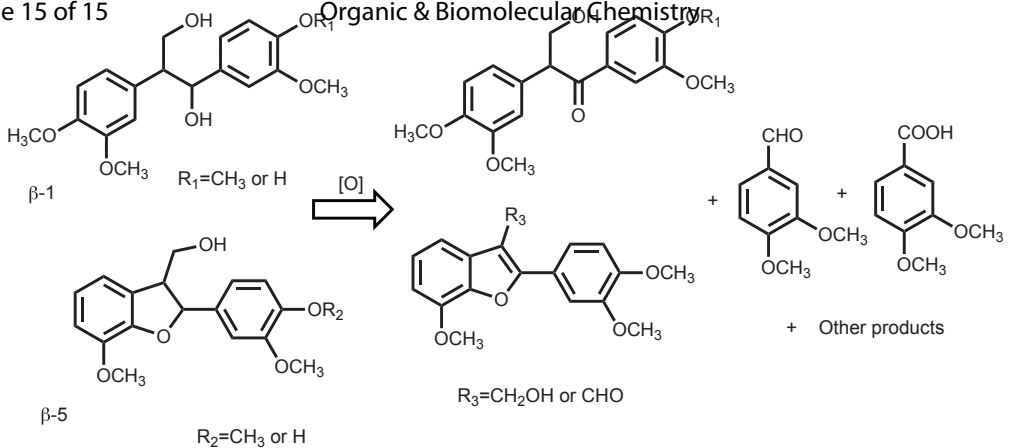

Production of monomers and other products from the oxidation of β-1 and β-5 lignin models