Light-Driven Depolymerization of Native Lignin Enabled by Proton-Coupled Electron Transfer

Suong Nguyen, Phillip Murray, Robert Knowles

Submitted date: 22/08/2019 • Posted date: 23/08/2019
Licence: CC BY-NC-ND 4.0

Citation information: Nguyen, Suong; Murray, Phillip; Knowles, Robert (2019): Light-Driven Depolymerization of Native Lignin Enabled by Proton-Coupled Electron Transfer. ChemRxiv. Preprint.

Here we report a catalytic, light-driven method for the redox-neutral depolymerization of native lignin biomass at ambient temperature. This transformation proceeds via a proton-coupled electron-transfer (PCET) activation of an alcohol O–H bond to generate a key alkoxy radical intermediate, which then drives the β-scission of a vicinal C–C bond. Notably, this depolymerization is driven solely by visible light irradiation, requiring no stoichiometric chemical reagents and producing no stoichiometric waste. This method exhibits good efficiency and excellent selectivity for the activation and fragmentation of β-O-4 linkages in the polymer backbone, even in the presence of numerous other PCET-active functional groups. DFT analysis suggests that the key C–C bond cleavage reactions produce non-equilibrium product distributions, driven by excited-state redox events. These results provide further evidence that visible-light photocatalysis can serve as a viable method for the direct conversion of lignin biomass into valuable arene feedstocks.
Light-Driven Depolymerization of Native Lignin Enabled by Proton-Coupled Electron Transfer

Suong T. Nguyen, Philip R. D. Murray and Robert R. Knowles*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544, United States

Supporting Information Placeholder

ABSTRACT: Here we report a catalytic, light-driven method for the redox-neutral depolymerization of native lignin biomass at ambient temperature. This transformation proceeds via a proton-coupled electron-transfer (PCET) activation of an alcohol O–H bond to generate a key alkoxy radical intermediate, which then drives the β-scission of a vicinal C–C bond. Notably, this depolymerization is driven solely by visible light irradiation, requiring no stoichiometric chemical reagents and producing no stoichiometric waste. This method exhibits good efficiency and excellent selectivity for the activation and fragmentation of β-O-4 linkages in the polymer backbone, even in the presence of numerous other PCET-active functional groups. DFT analysis suggests that the key C–C bond cleavage reactions produce non-equilibrium product distributions, driven by excited-state redox events. These results provide further evidence that visible-light photocatalysis can serve as a viable method for the direct conversion of lignin biomass into valuable arene feedstocks.

Figure 1. (a) Stephenson’s photocatalytic lignin depolymerization. (b) C–C bond cleavage of a model lignin dimer via O–H PCET. (c) Photocatalytic depolymerization of native lignin via O–H PCET.

Lignin accounts for nearly 30% of the organic carbon on Earth, and is often proposed as a renewable alternative to petroleum for the production of aromatic feedstock chemicals.1 However, the selective conversion of polymeric lignin into useful monomeric products is challenging due to its robust and complex structure, which is comprised of three structurally distinct cinnamyl alcohol subunits linked through strong C–O and C–C bonds.2,3 Accordingly, traditional lignin valorization methods require harsh reaction conditions and high temperatures or pressures, as well as produce stoichiometric chemical waste streams.1,4–3 As a consequence, these processes can suffer from poor product selectivity, product repolymerization, and challenges associated with product separation and purification. Hence, much current research is focused on the development of new chemical strategies for depolymerization that are highly selective and operate under mild conditions, allowing for the generation of well-defined product distributions.4

In this context, photocatalytic approaches to lignin valorization have begun to garner significant interest.5 These reactions typically occur under milder conditions than conventional thermal reactions, and excited-state mechanisms can afford alternative cleavage products. A number of groups have recently developed novel strategies for lignin cleavage using both homogenous and heterogenous photocatalysts, including leading reports by Stephenson,6 Soo,7 Mariano8 and Wang.9 Despite this growing interest, many of these reports focus on the cleavage of model systems and small-molecule lignin fragments, and few have been adapted for use in the depolymerization of plant-derived polymeric lignin material. In a notable exception, Stephenson and co-workers recently developed a highly selective two-step depolymerization protocol for native lignin that operates at ambient temperature through rupture of the central C–O bond of the β-O-4 linkage, providing up to 2.4 wt% of monomeric arene products (Figure 1a).10 To the best of our knowledge, no complementary methods for photocatalytic C–C bond cleavage have been reported for use in the valorization of unfunctionalized native lignin.

Our group has recently developed a number of photocatalytic methods for C–C bond functionalization based on the proton-coupled electron transfer (PCET) activation of the O–H bonds in simple aliphatic alcohols.10 In these reactions, an excited-state oxidant and a weak Brønsted base jointly mediate the PCET oxidation of an alcohol substrate to furnish a reactive alkoxy radical intermediate that undergoes subsequent β-scission to cleave a vicinal C–C bond. We previously demonstrated that this method can be used to effect the efficient fragmentation of a model lignin dimer 1 to furnish aldehyde 1a and alkoxyarene 1b in good yields (Figure 1b).10b Here, we extend these results and demonstrate that this PCET protocol can also mediate the depolymerization of native lignin (Figure
These reactions are mediated by three distinct molecular catalysts—an Ir(III) chromophore, a dialkyl phosphate base, and an aryl thiol H-atom donor—that function together to selectively cleave the C–C bond of the lignin β-O-4 linkage in a redox-neutral fashion. Notably, this process occurs near room temperature, requires no stoichiometric reagents, produces no stoichiometric waste, and consumes only photons. In addition, computational analysis suggests that visible-light irradiation is able to drive these reactions in opposition to a thermodynamic bias, producing an out-of-equilibrium product distribution wherein the products resulting from C–C cleavage are higher in free energy than their corresponding alcohol precursors. The development, optimization, and experimental implementation of the process are described herein.

**Table 1.** Catalytic C–C bond cleavage reactions of model lignin dimers

| Entry | Dimer | Conditions | 1a/2a (%) | 1b (%) |
|-------|-------|------------|-----------|--------|
| 1     | 1     | PBr2OP(O)(OMe), TRIP thiol, toluene | 89 | 65 |
| 2     | 2     | PBr2OP(O)(OMe), TRIP thiol, toluene | 47 | 36 |
| 3     | 3     | 3,4-diﬂuorothiophenol, dioxane | 65 | 58 |
| 4     | 1     | PBr2OP(O)(OMe), toluene | 84 | 68 |

*All reactions were performed on 0.2 mmol scale. Yields were determined by 1H-NMR analysis of the crude reaction mixtures relative to an internal standard.

In our previous report on the catalytic β-scission of aliphatic alcohols, we observed that model lignin dimer 1 underwent selective C–C bond cleavage at the β-O-4 linkage with high efficiency under the action of [Ir(dF(CF3)ppy)2(5,5'-d(CF3)ppy)]PF6 (Ir), 2,4,6-trisopropylbenzene thiol (TRIP thiol), and tetrabutylyphosphonium dimethylphosphate upon blue light irradiation to provide 3,4-dimethoxybenzaldehyde (1a) and (2-hydroxyethyl)guaiaacol (1b) in 89% and 65% isolated yield, respectively (Table 1, entry 1). We expected that analogous reactivity in native lignin may prove more challenging due to the presence of endogenous phenols, which are excellent substrates for PCET activation themselves. Given the large bond strength difference between phenol and aliphatic alcohol O–H bonds (BDFEs ~ 89 and 105 kcal/mol, respectively), we were concerned that phenol activation may occur preferentially and thus serve to poison the desired C–C bond cleavage reactivity. We were thus pleased to find that subjection of phenolic model compound 2 to the established cleavage conditions provided vanillin (2a) and 1b in 47% and 36% yields, respectively (entry 2). Additional optimization with 2 revealed that a catalyst set comprised of Ir, tetrabutylphosphonium di tert-butylphosphate, and 3,4-diﬂuorothiophenol in dioxane solvent improved the yields of 2a and 1b to 65% and 58% yield, respectively (entry 3). When applied to methoxy dimer 1, these new conditions gave comparable results to those previously reported (entry 4).

Encouraged by these results, we next investigated the catalytic depolymerization of native lignin material derived from grand fir, which was extracted from the corresponding sawdust using a previously reported acidolysis procedure (See SI for details). This lignin sample was determined to contain 100% guaiacyl (G) subunits based on two-dimensional HSQC analysis (see SI for details), consistent with literature reports on the structure of pine family lignins. Upon blue light irradiation of 48 mg of lignin in dioxane with the optimal catalysts at ambient temperature for 48 h, an average of 51% of the sample was converted to an EtOAc-soluble fraction, while the rest of the original mass (an average of 44 wt%) was collected as an insoluble solid (Figure 2). HSQC analysis of the soluble fraction supports successful depolymerization via rupture of the β-O-4 linkage, as the characteristic signals attributed to C–C–H and C–C–H as compared to the initial lignin were substantially diminished (Figure 2a). Additionally, HSQC signals for aldehyde products were also observed, consistent with the hypothesized C–C bond scission mechanism (Figure 2a). Furthermore, gel permeation chromatography (GPC) measurements revealed a notable decrease in the molecular weight of the fragmented lignin as compared to the original polymer, as well as the appearance of lower-MW oligomeric and polymeric material (Figure 2b). MS analysis of the post-reaction mixture also suggested an increase in low-MW products following depolymerization compared with the original lignin sample (See SI).

The major monomeric products from the depolymerization reaction described above were identified through HPLC analysis by comparison with authentic standards. Overall, vanillin (M3) and 4-(2-hydroxyethoxy)-3-methoxybenzaldehyde (M1) were determined to be the major monomers, formed in 2.1 and 1.3 wt%, respectively (Table 2, entry 1). In addition, 3,4-dimethoxybenzaldehyde (M4) was observed as a minor product (~0.1 wt%). The structures of M2 and M4 suggest that these products were formed via the C–C bond scission of consecutive β-O-4 linkages. Control experiments revealed a complete loss of reactivity in the absence of either iridium photocatalyst or visible light irradiation (entries 6, 7). With no phosphate base or thiol, only trace quantities of M2 (0.2 and 0.7 wt% respectively) were observed (entries 8, 9). In the reactions without phosphate, it is possible that arene radical cation-based fragmentation pathways may be operative, in line with previous studies by Mariano. In the reactions without thiol, the phenolic O–H bonds present in lignin itself may serve as H-atom donors.
We next sought to establish the stability of the monomeric products under the reaction conditions. After 24 h of irradiation of the pure monomeric products under the optimized conditions, we recovered 92%, 89% and 92% of M1, M2 and M3, respectively. Interestingly, no conversion of M3 to M1 through further β-scission of the primary alcohol was observed in these stability studies, highlighting the high selectivity of this protocol for cleavage of the central C–C bond of the β-O-4 linkage.

The depolymerization of lignin material derived from other plant species was also examined (Table 2, entries 2–4). Lignin samples obtained from ponderosa, cedar and larch sawdust were subjected to blue LED irradiation under the optimal catalytic conditions, resulting in depolymerization reactivity comparable to that of grand fir lignin. The amount of insoluble material following the reaction varied by species, with cedar providing 33 wt% relative to the original weight of lignin samples, while ponderosa lignin produced 50 wt%. Moreover, cedar and larch lignin produced higher total yields of monomeric products (up to 4.8 and 5.1 wt%, respectively) compared to the fir and ponderosa (3.4 and 3.7 wt%, respectively).

We next demonstrated the feasibility of this depolymerization protocol on a preparative scale (Figure 3). Upon subjecting 480 mg of ponderosa lignin to the optimized reaction conditions, we were pleased to find that monomers M1 and M2 were formed in 2.4 and 1.6 wt% respectively, in close agreement to the yields obtained in the 48 mg scale reactions (Table 2, entry 2). Monomer M2 was also isolated directly from the reaction mixture by silica gel chromatography (11.6 mg, 2.4 wt%).

A previous computational analysis of these light-driven β-scission reactions suggested that they often provide non-equilibrium product distributions, wherein the products resulting from C–C bond cleavage are higher in energy than the corresponding starting materials. While the exact thermochemistry associated with depolymerization of a structurally complex macromolecule is challenging to determine computationally, DFT analysis of the cleavage of the β-O-4 model systems 1 and 2 suggests that the redox-neutral scission events here may also proceed in a contra-thermodynamic fashion (Figure 4). As such, these processes represent an intriguing example of achieving out-of-equilibrium fragmentation chemistry through the use of excited-state redox events.

Table 2. Identification and quantification of monomeric products from lignin depolymerization.*

| Entry | Biomass       | EtOH-insoluble fraction (wt%) | M1 (wt%) | M2 (wt%) | M3 (wt%) | M2+M3 (wt%) |
|-------|---------------|-----------------------------|----------|----------|----------|-------------|
| 1     | Grand fir     | 44                          | <0.1     | 2.1      | 1.3      | 3.4         |
| 2     | Ponderosa     | 50                          | <0.1     | 2.3      | 1.4      | 3.7         |
| 3     | Cedar         | 33                          | <0.1     | 3.0      | 1.8      | 4.8         |
| 4     | Larch         | 39                          | <0.1     | 1.9      | 3.2      | 5.1         |

| Entry | Change from conditions 1 | M1 (wt%) | M2 (wt%) | M3 (wt%) |
|-------|--------------------------|----------|----------|----------|
| 5     | none                     | <0.1     | 2.1      | 1.3      |
| 6     | no Ir photocatalyst      | 0        | 0        | 0        |
| 7     | no light                 | 0        | 0        | 0        |
| 8     | no phosphate base        | 0        | 0.2      | 0        |
| 9     | no thiol HAT catalyst    | 0        | 0.7      | 0.3      |

*All reactions were performed with 48 mg of native lignin. Yields were determined by HPLC analysis of the crude reaction mixtures relative to an internal standard. Yield reported in parentheses is for isolated and purified material.

In conclusion, we have developed a mild, one-step, light-driven protocol for the redox-neutral depolymerization of native lignins. Despite the presence of numerous chemically distinct hydroxyl groups in the polymer, this PCET-driven approach exhibits selectivity for cleavage of the central C–C bond of the β-O-4 linkage, providing a well-defined and isolable set of monomeric arene products. We are hopeful that these results will prompt further interest in both utilizing PCET methods to achieve selective lignin depolymerization, and applications in the depolymerization of other classes of macromolecules.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, computational data, and characterization data (PDF)

AUTHOR INFORMATION

Corresponding Author
*rganes@princeton.edu

ORCID
Suong T. Nguyen: 0000-0002-5745-9096
Philip R. D. Murray: 0000-0001-7873-5232
Robert R. Knowles: 0000-0003-1044-4900

Notes
No competing financial interests have been declared.
ACKNOWLEDGMENT

This work was funded by the Bioinspired Light-Escalated Chemistry Energy Frontier Research Center, which is funded by the U.S. Department of Energy, Office of Science, Office of Basic Energy Sciences, under Award DE-SC0019370. We thank Rick Register and Sravya Jangareddy for assistance with GPC measurements, and Bradley Carrow for helpful discussions.

REFERENCES

(1) (a) Zakzeski, J.; Bruijnincx, P. C. A.; Jongerius, A. L.; Weckhuysen, B. M. The CATALYTIC Valorization of Lignin for the Production of Renewable Chemicals. Chem. Rev. 2010, 110, 3552–3599; (b) Alonso, D. M.; Bond, J. Q.; Dumesic, J. A. Catalytic conversion of biomass to biofuels. Green Chem. 2010, 12, 1493–1513.

(2) Sun, Z.; Frèdich, B.; de Santi, A.; Elangovan, S.; Barta, K. Bright Side of Lignin Depolymerization: Toward New Platform Chemicals. Chem. Rev. 2018, 118, 614–678.

(3) (a) Pandey, M. P.; Kim, C. S. Lignin Depolymerization and Conversion: A Review of Thermochemical Methods. Chem. Eng. Technol. 2011, 34, 29–41; (b) Wang, H.; Tucker, M.; Ji, Y. Recent Development in Chemical Depolymerization of Lignin: A Review. J. Appl. Polym. Sci. 2013, 138645; (c) Beiling, R.; Valange, S.; Chatel, G. Heterogeneous catalytic oxidation for lignin valorization into valuable chemicals: what results? What next? Green Chem. 2016, 18, 1839–1854.

(4) (a) Gao, F.; Webb, J. D.; Sorek, H.; Wemmer, D. E.; Hartwig, J. F. Fragmentation of Lignin Samples with Commercial Pd/C under Ambient Pressure of Hydrogen. ACS Catal. 2016, 6, 7385–7392; (f) Feghali, E.; Carrot, G.; Thùery, P.; Genre, C.; Cantat, T. Convergent reductive depolymerization of wood lignin to isolated phenol derivatives by metal-free catalytic hydrosilylation. Energ. Environ. Sci. 2015, 8, 2734–2743; (c) Staik, K.; Taccardi, N.; Bösman, A.; Wasserscheid, P. Oxidative Depolymerization of Lignin in Ionic Liquids. ChemSusChem 2010, 3, 719–723; (d) Yamamoto, K.; Hosoya, T.; Yoshikoa, K.; Miyayui, H.; Ohno, H.; Yamada, T. Tetra-t-butylammonium Hydroxide 30-Hydrate as Novel Reaction Medium for Lignin Conversion. ACS Sustain. Chem. Eng. 2017, 5, 10111–10115; (e) de Vries, J. G.; Westwood, N. J.; Barta, K. Phenolic acetals from lignins of varying compositions via iron(II) triflate catalysed depolymerisation. Green Chem. 2017, 19, 2774–2782; (f) Rahimi, A.; Ulbrich, A.; Coon, J. J.; Stahl, S. S. Formic-acid-induced depolymerization of oxidized lignin to aromatics. Nature 2014, 515, 249; (g) Lancefield, C. S.; Ojo, O. S.; Tran, F.; Westwood, N. J. Isolation of Functionalized Phenolic Monomers through Selective Oxidation and C–O Bond Cleavage of the b–O–4 Linkages in Lignin. Angew. Chem., Int. Ed. 2015, 54, 258–262; (h) Bouque, I.; da Costa Sousa, L.; Balan, V.; Bhalla, A.; da Costa Sousa, L.; Balan, V.; Dumusc, J. A.; Hegg, E. L.; Dale, B. E.; Ralph, J.; Coon, J. J.; Stahl, S. S. Lignin Conversion to Low-Molecular-Weight Aromatics via an Aerobic Oxidation-Hydrosilylation Sequence: Comparison of Different Lignin Sources. ACS Sustain. Chem. Eng. 2018, 6, 3367–3374.

(5) The ratios between catalyst loadings used in the reaction of native lignin are equivalent to those in the reaction of model dimers.

(6) Lim, S. H.; Nahm, K.; Ra, C. S.; Cho, D. W.; Yoon, U. C.; Latham, J. A.; Dunaway-Mariano, D.; Mariano, P. S. Effects of Alkoxo Groups on Aromatic Rings of Lignin b–O–4 Model Compounds on the Efficiencies of Single Electron Transfer–Promoted Photochemical and Enzymatic C–C Bond Cleavage Reactions. J. Org. Chem. 2013, 78, 9431–9443; (b) Cho, D. W.; Latham, J. A.; Park, H. J.; Yoon, U. C.; Langan, P.; Dunaway-Mariano, D.; Mariano, P. S. Regioselectivity of Enzyme-Catalyzed Photochemical Single Electron Transfer Promoted Carbon–Carbon Bond Fragmentation Reactions of Tetrameric Lignin Model Compounds. J. Org. Chem. 2011, 76, 2840–2852.

(7) Gazi, S.; Hung Ng, W. K.; Ganguly, R.; Putra Moeljadi, A. M.; Hirao, H.; Sso, H. S. Selective photocatalytic C–C bond cleavage under ambient conditions with earth abundant vanadium complexes. Chem. Sci. 2015, 6, 7130–7142.

(8) Cho, D. W.; Parthasarathi, R.; Pimentel, A. S.; Maestas, G. D.; Park, H. J.; Yoon, U. C.; Dunaway-Mariano, D.; Gnanakaran, S.; Langan, P.; Mariano, P. S. Nature and Kinetic Analysis of Carbon–Carbon Bond Fragmentation Reactions of Carion Radicals Derived from SET-Oxidation of Lignin Model Compounds. J. Org. Chem. 2010, 75, 6549–6562.

(9) Liu, H.; Li, H.; Lu, J.; Zeng, S.; Wang, M.; Luo, N.; Xu, S.; Wang, F. Photocatalytic Cleavage of C–C Bond in Lignin Models under Visible Light on Mesoporous Graphitic Carbon Nitride through π–π Stacking Interaction. ACS Catal. 2018, 8, 4761–4771.

(10) (a) Ayala, H. G.; Wang, H.; Tarantino, K. T.; Orbe, H. S.; Knowles, R. R. Catalytic Ring-Opening of Cyclic Alcohols Enabled by PCET Activation of Strong O–H Bonds. J. Am. Chem. Soc. 2016, 138, 10794–10797; (b) Ota, E.; Wang, H.; Frye, N. L.; Knowles, R. R. A Redox Strategy for Light-Driven, Out-of-Equilibrium Isomerizations and Application to Catalytic C–C Bond Cleavage Reactions. J. Am. Chem. Soc. 2019, 141, 1457–1462; (c) Zhao, K.; Yamashita, K.; Carpenter, J. E.; Sherwood, T. C.; Ewing, W. R.; Cheng, P. T. W.; Knowles, R. R. Catalytic Ring Expansions of Cyclic Alcohols Enabled by Proton-Coupled Electron Transfer. J. Am. Chem. Soc. 2019, 141, 8752–8757.

(11) (a) Mayer, J. M.; Hrovat, D. A.; Thomas, J. L.; Borden, W. T. Proton-Coupled Electron Transfer versus Hydrogen Atom Transfer in Benzy1/Toluen, Methoxy1/Methanol, and Phenox1/Phenol Self-Exchange Reactions. J. Am. Chem. Soc. 2002, 124, 11142–11147; (b) Biczók, L.; Gupta, N.; Linschitz, H. Coupled Electron-Proton Transfer in Interactions of Triplet C60 with Hydrogen-Bonded Phenois: Effects of Solvation, Deuteration, and Redox Potentials. J. Am. Chem. Soc. 1997, 119, 12601–12609.

(12) Warren, J. J.; Tronic, T. A.; Mayer, J. M. Thermochromism of Proton-Coupled Electron Transfer Reagents and its Implications. Chem. Rev. 2010, 110, 6961–7001.

(13) Das, A.; Rahimi, A.; Ulbrich, A.; Alhreich, M.; Motagamwala, A. H.; Bhalla, A.; da Costa Sousa, L.; Balan, V.; Dumesic, J. A.; Hegg, E. L.; Dale, B. E.; Ralph, J.; Coon, J. J.; Stahl, S. S. Lignin Conversion to Low-Molecular-Weight Aromatics via an Aerobic Oxidation-Hydrosilylation Sequence: Comparison of Different Lignin Sources. ACS Sustain. Chem. Eng. 2018, 6, 3367–3374.

(14) The ratios between catalyst loadings used in the reaction of native lignin are equivalent to those in the reaction of model dimers.

(15) (a) Lim, S. H.; Nahm, K.; Ra, C. S.; Cho, D. W.; Yoon, U. C.; Latham, J. A.; Dunaway-Mariano, D.; Mariano, P. S. Effects of Alkoxo Groups on Aromatic Rings of Lignin b–O–4 Model Compounds on the Efficiencies of Single Electron Transfer–Promoted Photochemical and Enzymatic C–C Bond Cleavage Reactions. J. Org. Chem. 2013, 78, 9431–9443; (b) Cho, D. W.; Latham, J. A.; Park, H. J.; Yoon, U. C.; Langan, P.; Dunaway-Mariano, D.; Mariano, P. S.Regioselectivity of Enzyme-Catalyzed Photochemical Single Electron Transfer Promoted Carbon–Carbon Bond Fragmentation Reactions of Tetrameric Lignin Model Compounds. J. Org. Chem. 2011, 76, 2840–2852.

(16) Kim, S.; Chmely, S. C.; Nimlos, M. R.; Bomble, Y. J.; Foust, T. D.; Paton, R. S.; Beckham, G. T. Computational Study of Bond Dissociation Enthalpies for a Large Range of Native and Modified Lignins. J. Phys. Chem. Lett. 2011, 2, 2846–2852.
* one-step  
* redox-neutral  
* room temperature  
* no stoichiometric reagents
Supporting Information

Light-Driven Depolymerization of Native Lignin Enabled by Proton-Coupled Electron Transfer

Suong T. Nguyen, Philip R. D. Murray, and Robert R. Knowles*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544, United States

Correspondence to: rknowles@princeton.edu

Table of Contents

| Section                                                                 | Pages |
|-------------------------------------------------------------------------|-------|
| General Information                                                     | S2    |
| Synthesis of Lignin Model Dimers and Monomeric Products                 | S3    |
| General Procedure for Catalytic Reactions on Model Lignin Dimers         | S4    |
| Native Lignin Extraction and Purification                               | S5    |
| General Procedure for Depolymerization Reactions of Dioxosolv-Lignin    | S6    |
| Identification and Quantification of Monomeric Products from Lignin Depolymerization | S7–9  |
| NMR Spectra for Native and Depolymerized Lignin                         | S10–21|
| NMR Spectra for Isolated Vanillin from Lignin Depolymerization Reaction | S22   |
| Overlay GPC for Native and Depolymerized Lignin                         | S23–24|
| HRMS Analysis for Original and Depolymerized Grand Fir Lignin Sample    | S25   |
| DFT computational details and results                                   | S2–27 |
| Optimized Geometries                                                   | S28–23|
| References                                                              | S34   |
**General Information**

Sawdust samples (ground finings) were ordered from a seller (WildThingsForestry) in Heron, MT via Etsy (www.etsy.com). Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego. All solvents were purified according to the method of Grubbs. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished by flash chromatography on Silicycle F60 silica gel according to the method of Still. All reactions were carried out in well ventilated fume hoods. Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. Visualization of the developed chromatogram was performed by irradiation with UV light. Yields refer to purified compounds unless otherwise noted.

$^1$H and $^{13}$C NMR spectra were recorded on a Bruker 500 (500 and 126 MHz for $^1$H and $^{13}$C respectively), and are internally referenced to residual solvent signals, CDCl$_3$ referenced at $\delta$ 7.26 and 77.16 ppm, and DMSO-$d_6$ referenced at $\delta$ 2.50 and 39.52 ppm. Data for $^1$H is reported as follows: chemical shift ($\delta$ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = quintet, h = sextet, m = multiplet), broad peaks (br), coupling constant (Hz) and assignment. Data for $^{13}$C NMR is reported in terms of chemical shift and no special nomenclature is used for equivalent carbons. Heteronuclear single quantum coherence spectroscopy (HSQC) was recorded on a Bruker 500 spectrometer.

Gel permeation chromatography (GPC) was conducted at 35 °C using two 30 cm Polymer Laboratories PLgel Mixed-C columns, a Wyatt Optilab T-rEX refractive index detector ($\lambda$ = 658 nm, 25 °C), and a UV diode array detector. THF was used as the mobile phase, and the systems were calibrated with narrow-distribution polystyrene standards.
Synthesis of Lignin Model Dimers and Monomeric Products

(1S*,2S*)-1-(3,4-dimethoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (1)

The titled compound was synthesized according to a literature report. Spectra are consistent with reported literature.⁴

(1S*,2S*)-1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)propane-1,3-diol (2)

The titled compound was synthesized according to a literature report. Spectra are consistent with reported literature.⁵

4-(2-Hydroxyethoxy)-3-methoxybenzaldehyde (M3)

The titled compound was synthesized according to a literature report. Spectra are consistent with reported literature.⁶

Monomeric products M1 (3,4-dimethoxybenzaldehyde) and M2 (vanillic aldehyde) are commercially available.
General Procedure for Catalytic Reactions on Model Lignin Dimers

General Information and Setup

Reactions were run in 2-dram borosilicate vials equipped with screwcaps and teflon septa under inert atmosphere. Reactions were irradiated with commercially available 34 W Kessil KSH150B Blue LED lamps with fans positioned such that the vials were kept at room temperature throughout irradiation and stirring. As a caution, the light from the lamps is very bright and appropriate safety precautions should be taken.

General Procedure for Catalytic C–C Bond Cleavage of Lignin Model Dimers 1 and 2

To a screw cap 2-dram vial was charged with a magnetic stir bar, substrate (0.2 mmol, 1.0 equiv.), and [Ir(dF(CF₃)ppy)₂(5,5’-d(CF₃)-bpy)](PF₆) (3 mol%, 6.0 μmol, 6.8 mg). The vial was brought into a glove box where the appropriate base (0.05 mmol, 25 mol%) was added. The vial was sealed with a Teflon septum and removed from the glove box. The vial was then put under positive pressure of Ar. Solvent (4 mL, 0.05 M) was added, followed by the appropriate thiophenol (0.05 mmol, 25 mol%). The reaction was irradiated with one blue LED Kessil lamp and stirred at ambient temperature for 48 h. The reaction mixture was concentrated under reduced pressure. The yields were determined by ¹H-NMR analysis with biphenyl as an internal standard.

General Procedure for Product Stability Tests (M1, M2 and M3)

To a screw cap 2-dram vial was charged with a magnetic stir bar, monomer (0.1 mmol, 1.0 equiv.), and [Ir(dF(CF₃)ppy)₂(5,5’-d(CF₃)-bpy)](PF₆) (3.4 mg, 3.0 μmol, 3 mol%). The vial was brought into a glove box where tetrabutylphosphonium di-tert-butyl phosphate (12.0 mg, 0.025 mmol, 25 mol%) was added. The vial was sealed with a Teflon septum and removed from the glove box. The vial was then put under positive pressure of Ar. Dioxane (2 mL, 0.05 M) was added, followed by 3,4-difluorothiophenol (5.6 μL, 0.05 mmol, 50 mol%). The reaction was irradiated with one blue LED Kessil lamp and stirred at ambient temperature for 24 h. The reaction mixture was concentrated under reduced pressure. The yields were determined by ¹H-NMR analysis with biphenyl as an internal standard.
Native Lignin Extraction and Purification

All four lignin samples (grand fir, ponderosa, cedar, and larch) were extracted using a modified protocol that was previously reported by Stahl.\textsuperscript{7}

The dried and ground sawdust (10 g) was suspended in 120 mL of a dioxane/water mixture (9/1 v/v) containing 0.2 M HCl. The mixture was stirred at reflux (setpoint temperature of 100 °C) under an Ar atmosphere for 30 min. After being cooled to room temperature, the mixture was vacuum-filtered through a Buchner funnel. The filter cake was washed with ca. 100 mL of dioxane/water mixture (9/1 v/v). The combined filtrate was then neutralized with saturated aqueous NaHCO\textsubscript{3} solution until the pH approached to 5–7. Next, the solution was concentrated by rotary-evaporation (45 °C) until the point of precipitation (ca. 50 mL volume remaining). Then, a minimal amount of acetone/water mixture (9/1 v/v) was added if necessary to dissolve any lignin precipitated (<5 mL). This solution was then added dropwise into ca. 400 mL of iced water. The mixture was left in the freezer (−20 °C) for 4 hours, and the precipitate was collected by vacuum filtration to give crude dioxosolv-lignin.

This crude dioxosolv-lignin was dissolved in a minimal amount of acetone/methanol mixture (9/1 v/v) (1 volume). This dark red solution was added dropwise to rapidly stirring diethyl ether (10 volumes). The precipitate lignin was collected via suction filtration and dried under reduced pressure. This purification process was then repeated once more. Purified lignin was then dried overnight under high vacuum at room temperature before usage. The extraction yields for lignin samples and the 2D HSQC NMR spectra of the isolated lignin samples are shown below.

\textbf{Table S1.} Lignin extraction yields for different samples of biomass.

| Biomass  | Mass of biomass | Mass of extracted lignin | wt\% Extracted lignin |
|----------|-----------------|--------------------------|------------------------|
| Grand Fir| 50 g            | 1.34 g                   | 2.7 wt\%               |
| Ponderosa| 25 g            | 0.69 g                   | 2.8 wt\%               |
| Cedar    | 25 g            | 0.78 g                   | 3.1 wt\%               |
| Larch    | 10 g            | 0.22 g                   | 2.2 wt\%               |
General Procedure for Catalytic Depolymerization Reaction of Dioxosolv-Lignin

Note: For the calculation of reaction stoichiometry and catalyst loading, guaiacyl moiety was selected as a monomeric unit (MW = 166.176 g/mol). The loadings of Ir photocatalyst, phosphate base and thiol were reported as molar concentration for convenience.

To a screw cap 2 dram vial was charged a magnetic stir bar, dioxosolv-lignin (48 mg) and [Ir(dF(CF₃)ppy)₂(5,5’-d(CF₃)-bpy)](PF₆) (1.5 mM, 3.0 μmol, 3.4 mg). The vial was brought into a glove box where tetrabutylphosphonium di-tert-butyl phosphate (12.5 mM, 0.025 mmol, 12.0 mg) was added. The vial was sealed with a Teflon septum and removed from the glove box. The vial was then put under positive pressure of Argon. Dioxane (2 mL, 0.05 M) was added, followed by 3,4-difluorothiophenol (25 mM, 0.05 mmol, 5.6 μL). The reaction was irradiated with two blue LED Kessil lamps, kept at ambient temperature by using 3 fans, and stirred for 48 h. After the reaction, internal standard (3-acetamidoacetophenone) was added to the reaction mixture, which was then concentrated under reduced pressure. Ethyl acetate was then added. The non-soluble fraction was separated and dried under high vacuum overnight before the weight was determined. The soluble-fraction containing monomeric, lower-MW polymeric and oligomeric products was passed through a silica plug. This organic solution was concentrated under reduced pressure, dissolved in EtOH/Hexanes mixture (1/4 v/v), and filtered through a syringe filter. This solution was then submitted to HPLC analysis.

Procedure for Catalytic Depolymerization Reaction of Dioxosolv-Lignin on a Preparative Scale

To a screw cap 60-mL vial was charged a magnetic stir bar, dioxosolv ponderosa lignin (480 mg) and [Ir(dF(CF₃)ppy)₂(5,5’-d(CF₃)-bpy)](PF₆) (1.5 mM, 30.0 μmol, 34 mg). The vial was brought into a glove box where tetrabutylphosphonium di-tert-butyl phosphate (12.5 mM, 0.25 mmol, 120 mg) was added. The vial was sealed with a Teflon septum and removed from the glove box. The vial was then put under positive pressure of Argon. Dioxane (20 mL, 0.05 M) was added, followed by 3,4-difluorothiophenol (25 mM, 0.50 mmol, 56 μL). The reaction was irradiated with four blue LED Kessil lamps, kept at ambient temperature by using 5 fans, and stirred for 72 h. After the reaction, internal standard (3-acetamidoacetophenone) was added to the reaction mixture, which was then concentrated under reduced pressure. Ethyl acetate was then added, and the soluble fraction was separated from the insoluble solid. An aliquot of the soluble-fraction was passed through a silica plug. This organic solution was concentrated under reduced pressure, redissolved in EtOH/Hexanes mixture (1/4 v/v), and filtered through a syringe filter. This solution was then submitted to HPLC analysis. The crude organic-soluble extract was dissolved in dichloromethane, and passed through a 2 x 1 inch plug of silica, eluting with ethyl acetate, to remove highly polar material. The plug was rinsed with ca. 200 mL of ethyl acetate. Solvents were removed, and the residue was purified by flash column chromatography on silica (10 g, 10–100% ethyl acetate/hexanes). The fractions containing vanillin (M2) (eluting early in the procedure) were combined to afford 18.2 mg of ca. 70% pure monomer. The fractions containing 4-(2-hydroxyethoxy)-3-methoxybenzaldehyde (M3) (eluting late in the procedure) were combined to afford 17.7 mg of ca. 40% pure monomer. The M2 monomer was further purified by preparative TLC (25% ethyl acetate/hexanes) to afford 11.6 mg of >95% pure M2 monomer. The M3 monomer was further purified by first trituration with diethyl ether and syringe filtration, before preparative TLC (70% ethyl acetate/hexanes) to afford 10.1 mg of ca. 70% pure M3 monomer. The remainder appears to consist of oligomeric and polymeric material.
Identification and Quantification of Monomeric Products from Lignin Depolymerization

Products were identified and confirmed by exact mass detected via GC/MS analysis and HPLC retention times to authentic standards that were either purchased or synthesized (Table S2).

Quantification of monomeric products from lignin depolymerization was performed an Agilent 1260 Infinity Series LC using a commercial Agilent column (4.6 mm × 250 mm × 5 μm particle size), followed by integration of UV absorption traces at specified wavelength (230 nm). Mobile phase A was hexanes and B was ethanol. The flow rate was 1.0 mg/mL at room temperature, and the gradient program was 5% B for 25 min. The UV detector acquired spectra from 191–950 nm. Filter bandwidth was set at 4 nm, the wavelength step was set to 1 nm. Of each solution 1 μL was injected onto the column for analysis. 3-acetamidoacetophenone was used as an internal standard; and all compounds quantified by UV absorption were normalized to the standard signal.

Table S2. Retention times of monomeric products and internal standard.

| Compound            | Retention time (min) |
|---------------------|----------------------|
| M1                  | 6.12 – 6.29          |
| M2                  | 8.90 – 9.16          |
| M3                  | 20.97 – 22.0         |
| Internal standard   | 18.29 – 18.71        |

Figure S1. An example of HPLC traces of the reaction mixture after depolymerization reaction of lignin.
Figure S2. HPLC traces of commercial internal standard.

Figure S3. HPLC traces of commercial authentic M1.

Figure S4. HPLC traces of commercial authentic M2.
Figure S5. HPLC traces of independently synthesized M3.
NMR Spectra for Native and Depolymerized Lignin

Figure S6. Original HSQC for native grand fir lignin (in DMSO-d$_6$).

Figure S7. Assigned HSQC for native grand fir lignin (in DMSO-d$_6$).
Figure S8. Original HSQC for depolymerized grand fir lignin (in DMSO-d$_6$).

Figure S9. Assigned HSQC for depolymerized grand fir lignin (in DMSO-d$_6$). Signals attributed to C$\alpha$–H and C$_\beta$–H and of the $\beta$-O-4 linkage in the original lignin were substantially diminished.
**Figure S10.** Original HSQC for initial grand fir lignin (in DMSO-d$_6$). Insignificant aldehyde signal was observed, which was assigned to the drawn aldehyde-containing subunit.

**Figure S11.** Original HSQC for depolymerized grand fir lignin (in DMSO-d$_6$). Mixture of different aldehyde-containing products was observed following depolymerization.
Figure S12. Original HSQC for native ponderosa lignin (in DMSO-d$_6$).

Figure S13. Original HSQC for native ponderosa lignin (in DMSO-d$_6$).
Figure S14. Original HSQC for depolymerized ponderosa lignin (in DMSO-d$_6$).

Figure S15. Assigned HSQC for depolymerized ponderosa lignin (in DMSO-d$_6$). Signals attributed to $\text{C}_\alpha$–H and $\text{C}_\beta$–H and of the $\beta$-O-4 linkage in the original lignin were substantially diminished.
Figure S16. Original HSQC for initial ponderosa lignin (in DMSO-\textit{d}_6). Insignificant aldehyde signal was observed, which was assigned to the drawn aldehyde-containing subunit.

Figure S17. Original HSQC for depolymerized ponderosa lignin (in DMSO-\textit{d}_6). Mixture of different aldehyde-containing products was observed following depolymerization.
Figure S18. Original HSQC for native cedar lignin (in DMSO-d$_6$).

Figure S19. Assigned HSQC for native cedar lignin (in DMSO-d$_6$).
Figure S20. Original HSQC for depolymerized cedar lignin (in DMSO-d$_6$).

Figure S21. Assigned HSQC for depolymerized cedar lignin (in DMSO-d$_6$). Signals attributed to C$_\alpha$–H and C$_\beta$–H and of the $\beta$-O-4 linkage in the original lignin were substantially diminished.
**Figure S22.** Original HSQC for initial cedar lignin (in DMSO-d$_6$). Insignificant aldehyde signal was observed, which was assigned to the drawn aldehyde-containing subunit.

**Figure S23.** Original HSQC for depolymerized cedar lignin (in DMSO-d$_6$). Mixture of different aldehyde-containing products was observed following depolymerization.
Figure S24. Original HSQC for native larch lignin (in DMSO-d$_6$).

Figure S25. Assigned HSQC for native larch lignin (in DMSO-d$_6$).
Figure S26. Original HSQC for depolymerized larch lignin (in DMSO-d$_6$).

Figure S27. Assigned HSQC for depolymerized larch lignin (in DMSO-d$_6$). Signals attributed to C$_\alpha$–H and C$_\beta$–H and of the $\beta$-O-4 linkage in the original lignin were substantially diminished.
Figure S28. Original HSQC for initial larch lignin (in DMSO-d$_6$). Insignificant aldehyde signal was observed, which was assigned to the drawn aldehyde-containing subunit.

Figure S29. Original HSQC for depolymerized larch lignin (in DMSO-d$_6$). Mixture of different aldehyde-containing products was observed following depolymerization.
NMR Spectra for Isolated Vanillin from Preparative Scale Lignin Depolymerization Reaction (M2)

Figure S30. $^1$H-NMR for purified vanillin (M2) in CDCl$_3$.

Figure S31. $^{13}$C-NMR for purified vanillin (M2) in CDCl$_3$. 
Overlay GPC for Native and Depolymerized Lignin

Figure S32. GPC analysis of dioxosolv grand fir lignin before (blue, $M_w = 2371$, $M_n = 1568$) and after reaction (yellow, $M_w = 1621$, $M_n = 1374$).

Figure S33. GPC analysis of dioxosolv larch lignin before (blue, $M_w = 1951$, $M_n = 1512$) and after reaction (yellow, $M_w = 1361$, $M_n = 1133$).
Figure S34. GPC analysis of dioxosolv cedar lignin before (blue, $M_w = 2250$, $M_n = 1652$) and after reaction (yellow, $M_w = 1267$, $M_n = 1130$).

Figure S35. GPC analysis of dioxosolv ponderosa lignin before (blue, $M_w = 2639$, $M_n = 1888$) and after reaction (yellow, $M_w = 1667$, $M_n = 1168$).
HRMS Analysis for Original and Depolymerized Grand Fir Lignin Sample

Figure S36. HRMS analysis of original grand fir lignin sample.

Figure S37. HRMS analysis of depolymerized grand fir lignin following depolymerization. An increase in low-MW products was observed compared to the original lignin sample.
DFT computational details and results

All calculations used DFT methodology as implemented in the Gaussian 16 series of computer programs. All complexes underwent geometry optimization, and stationary points were subjected to normal mode analysis. All calculations were performed in the gas phase at 25 °C and 1 atm pressure.

For the calculation of Gibbs Free Energies for the C–C bond cleavage reactions of lignin dimers, we employed the same functional and basis sets as previously reported in the computational study of bond dissociation enthalpies for lignin dimers. M06-2X functional with basis set 6-31G(d) was employed for the geometry optimization and vibrational frequency calculation. The M06-2X functional with basis set 6-311++G(d,p) was used for single-point energy calculation.

Figure S38. Fragmentation of non-phenolic lignin dimer 1.

Table S3. Thermodynamic parameters for calculating $\Delta G^\circ$ of the fragmentation of non-phenolic lignin dimer 1. Energies are given in hartree and entropy is provided in entropy units.

| Entry | Job name                        | E+ZPE       | G            | H            | S          |
|-------|---------------------------------|-------------|--------------|--------------|------------|
| 1     | Lignin dimer 1                  | -1149.922769| -1149.977089 | -1149.898222 | 165.991    |
| 2     | 3,4-Dimethoxybenzaldehyde (1a)  | -574.194037 | -574.397110  | -574.347864  | 103.646    |
| 3     | (2-Hydroxyethyl)guaiacol (1b)   | -575.540037 | -575.578046  | -575.527578  | 106.218    |

$\Delta G^\circ = (-575.578046 - 574.397110 + 1149.977089) \times 627.509 = +1.21 \text{ (kcal/mol)}$
Figure S39. Fragmentation of phenolic lignin dimer 2.

Table S4. Thermodynamic parameters for calculating $\Delta G^\circ$ of the fragmentation of phenolic lignin dimer 2. Energies are given in hartree and entropy is provided in entropy units.

| Entry | Job name                     | E+ZPE       | G           | H           | S       |
|-------|------------------------------|-------------|-------------|-------------|---------|
| 1     | Lignin dimer 2               | -1110.664578 | -1110.716735 | -1110.641513 | 158.318 |
| 2     | Vanillic aldehyde (2a)       | -535.100465  | -535.135637  | -535.089659  | 96.769  |
| 3     | (2-Hydroxyethyl)guaiacol (1b)| -575.540037  | -575.578046  | -575.527578  | 106.218 |

$\Delta G^\circ = (-575.578046 - 535.135637 + 1110.716735) \times 627.509 = +1.92 \text{ (kcal/mol)}$
Optimized Geometries

Optimized geometries in Cartesian coordinates (Å) and energies (hartree) for stationary points.

1. **Lignin dimer 1:**

E(M06-2X/6-31G(d)) = -1149.9624970
Zero-point correction= 0.384067 (Hartree/Particle)
Thermal correction to Energy= 0.407670
Thermal correction to Enthalpy= 0.408614
Thermal correction to Gibbs Free Energy= 0.329747
Sum of electronic and zero-point Energies= -1149.578430
Sum of electronic and thermal Energies= -1149.554827
Sum of electronic and thermal Enthalpies= -1149.553883
Sum of electronic and thermal Free Energies= -1149.632751

E(M06-2X/6-311++G(d,p)) = -1150.306836 a.u.

Calculation Type = FREQ
Calculation Method = RM06-2X
Basis Set = 6-31G(d)
Charge = 0
Spin = Singlet
RMS Gradient Norm = 0.000003 a.u.
Imaginary Freq = 0
Dipole Moment = 2.058515 Debye
Point Group = C1

| Symbol | X     | Y     | Z     |
|--------|-------|-------|-------|
| C      | 3.49833600 | -1.60878700 | -0.52778700 |
| C      | 2.19956800 | -1.66258900 | -1.03308100 |
| C      | 1.37388900 | -0.53900700 | -0.97615800 |
| C      | 1.86338700 | 0.63861100  | -0.40833700 |
| C      | 3.15319500 | 0.69726300  | 0.10281400  |
| C      | 3.98485500 | -0.43451900 | 0.03584300  |
| H      | 4.16090200 | -2.46706300 | -0.57211800 |
| H      | 1.83220200 | -2.58100000 | -1.48409800 |
| H      | 1.23793200 | 1.52426500  | -0.36462600 |
| C      | -0.06399500 | -0.60495400 | -1.43150400 |
| H      | -0.18564100 | -1.46778600 | -2.10917000 |
| C      | -1.01792900 | -0.84083900 | -0.25436300 |
| H      | -1.03407800 | 0.05952400  | 0.37407000  |
| O      | -0.39901100 | 0.59709100  | -2.08106500 |
| H      | -1.36570400 | 0.68517500  | -2.01813500 |
| O      | -2.30398100 | -1.03695000 | -0.87217300 |
| C      | -3.38258000 | -0.59471000 | -0.15007000 |
| C      | -4.23643000 | -1.48757900 | 0.47598400  |
| C      | -3.65172900 | 0.78608100  | -0.10541500 |
| C      | -5.35669300 | -1.02175600 | 1.16773200  |
| H      | -4.01293600 | -2.54721000 | 0.40261400  |
2. 3,4-Dimethoxybenzaldehyde (1a)

E(M06-2X/6-31G(d)) = -574.372413
Zero-point correction= 0.178376 (Hartree/Particle)
Thermal correction to Energy= 0.189588
Thermal correction to Enthalpy= 0.190532
Thermal correction to Gibbs Free Energy= 0.141286
Sum of electronic and zero-point Energies= -574.194037
Sum of electronic and thermal Energies= -574.182825
Sum of electronic and thermal Enthalpies= -574.181881
Sum of electronic and thermal Free Energies= -574.231127

E(M06-2X/6-311++G(d,p)) = -574.538396 a.u.

Calculation Type = FREQ
Calculation Method = RM06-2X
Basis Set = 6-31G(d)
Charge = 0
Spin = Singlet
RMS Gradient Norm = 0.000019 a.u.
Imaginary Freq = 0
Dipole Moment = 3.294809 Debye
Point Group = C1

| Symbol | X       | Y       | Z       |
|--------|---------|---------|---------|
| C      | 0.15338300 | -1.63784900 | -0.00001200 |
| C      | -1.21769800 | -1.38930200 | 0.00013800   |
| C      | -0.78141500 | 0.99216000  | -0.00007100  |
| C      | 0.58284800  | 0.75807000  | -0.00007700  |
| C      | 1.05741600  | -0.57849200 | -0.00022700  |
| C      | 0.51361600  | -2.65956400 | 0.00007500   |
| H      | -1.93536700 | -2.20310000 | 0.00027800   |
| H      | -1.16862500 | 2.00650200  | -0.00023600  |
| O      | 2.40048700  | -0.70857700 | -0.00044100  |
| O      | 1.54436900  | 1.71220100  | -0.00009100  |
| C      | 1.11293900  | 3.05429000  | 0.00023300   |
3. (2-Hydroxyethyl)guaiacol (1b):

$$E(M06-2X/6-31G(d)) = -575.565822$$
Zero-point correction= 0.202533 (Hartree/Particle)
Thermal correction to Energy= 0.214048
Thermal correction to Entropy= 0.214992
Thermal correction to Gibbs Free Energy= 0.164524
Sum of electronic and zero-point Energies= -575.363288
Sum of electronic and thermal Energies= -575.351774
Sum of electronic and thermal Enthalpies= -575.350830
Sum of electronic and thermal Free Energies= -575.401297

$$E(M06-2X/6-311++G(d,p)) = -575.742570 \text{ a.u.}$$

Calculation Type = FREQ
Calculation Method = RM06-2X
Basis Set = 6-31G(d)
Charge = 0
Spin = Singlet
RMS Gradient Norm = 0.000019 a.u.
Imaginary Freq = 0
Dipole Moment = 3.367003 Debye
Point Group = C1

| Symbol | X         | Y         | Z         |
|--------|-----------|-----------|-----------|
| O      | 1.18145900| -0.22236700| -1.26098600|
| C      | -0.00473200| -0.50563500| -0.64792300|
| C      | -0.38853500| -1.83973000| -0.57639800|
| C      | -0.87028500| 0.49043300| -0.15223700|
| C      | -1.61097200| -2.20698900| -0.01327000|
| H      | 0.29199500| -2.57783100| -0.99139800|
| C      | -2.08223200| 0.11998600| 0.42492500|
| C      | -2.45059800| -1.22554600| 0.49140900|
| H      | -1.89446600| -3.25306000| 0.03040900|
| H      | -2.75285300| 0.87585000| 0.81644700|
| H      | -3.40209400| -1.49261800| 0.93924300|
4. **Lignin dimer 2:**

E(M06-2X/6-31G(d)) = -1110.678377
Zero-point correction= 0.355186 (Hartree/Particle)
Thermal correction to Energy= 0.377307
Thermal correction to Enthalpy= 0.378251
Thermal correction to Gibbs Free Energy= 0.303029
Sum of electronic and zero-point Energies= -1110.323191
Sum of electronic and thermal Energies= -1110.301070
Sum of electronic and thermal Enthalpies= -1110.300126
Sum of electronic and thermal Free Energies= -1110.375348

E(M06-2X/6-31++G(d,p)) = -1111.019764 a.u.

Calculation Type = FREQ
Calculation Method = RM06-2X
Basis Set = 6-31G(d)
Charge = 0
Spin = Singlet
RMS Gradient Norm = 0.000006 a.u.
Imaginary Freq = 0
Dipole Moment = 1.657778 Debye
Point Group = C1

| Symbol | X      | Y      | Z      |
|--------|--------|--------|--------|
| C      | 2.26389800 | 0.29841800 | 0.88116700 |
| H      | 3.08014300 | 0.89794800 | 1.29595500 |
| H      | 1.34480400 | 0.57925300 | 1.41620800 |
| O      | 2.59654200 | -1.05375400 | 1.09808100 |
| H      | 1.84357200 | -1.58385300 | 0.79631900 |
| O      | -0.43450400 | 1.77371300 | -0.27709500 |
| C      | -1.27942200 | 2.79590300 | 0.20491800 |
| H      | -1.45273100 | 2.69430700 | 1.28305500 |
| H      | -0.76165000 | 3.73407000 | 0.00685900 |
| H      | -2.24265400 | 2.79302100 | -0.31856600 |
| C      | 2.13079000 | 0.61991300 | -0.59763700 |
| H      | 1.87692900 | 1.67360900 | -0.74211400 |
| H      | 3.07404100 | 0.39805700 | -1.10214100 |
|  | X | Y | Z |
|---|---|---|---|
| C | 0.23311900 | -0.59623600 | -1.43993000 |
| H | 0.12409800 | -1.47239200 | -2.10276500 |
| C | -0.70640600 | -0.83392900 | -0.25175300 |
| H | -0.73553700 | 0.07407800 | 0.36512900 |
| O | -0.13271600 | 0.58795100 | -2.10276500 |
| H | -1.10051000 | 0.65632600 | -2.03663300 |
| O | -1.99405000 | 0.07407800 | 0.36512900 |
| C | -3.07439100 | -0.63326600 | -0.12833600 |
| C | -3.90488600 | -1.53313900 | 0.51862400 |
| C | -3.36979100 | 0.74268700 | -0.10086300 |
| C | -5.02761400 | -1.07897100 | 1.21422000 |
| H | -3.66164100 | -2.58926200 | 0.45839800 |
| C | -4.48187600 | 1.19716400 | 0.59864100 |
| C | -5.30585700 | 0.27946300 | 1.25610200 |
| H | -5.67408800 | -1.78807400 | 1.71983700 |
| H | -4.71916900 | 2.25440900 | 0.62940200 |
| H | -6.17346600 | 0.64260600 | 1.79734100 |
| C | -0.34484300 | -2.02413400 | 0.63715300 |
| H | -1.23688500 | 2.30007400 | 1.20757800 |
| H | -0.07561900 | -2.88743600 | 0.00749200 |
| O | 0.65170400 | -1.72063800 | 1.58465100 |
| H | 1.48526900 | -1.59054800 | 1.10852800 |
| O | 3.87247200 | 1.98735600 | 0.56714500 |
| C | 4.07981000 | 1.97736900 | 1.97427700 |
| H | 4.38141900 | 2.98980500 | 2.24536500 |
| H | 3.15034400 | 1.71979100 | 2.49616000 |

5. Vanillic aldehyde (2a):

\[ E(\text{M06-2X/6-31G(d)}) = -535.087472 \]
Zero-point correction= 0.149214 (Hartree/Particle)
Thermal correction to Energy= 0.159076
Thermal correction to Enthalpy= 0.160020
Thermal correction to Gibbs Free Energy= 0.114042
Sum of electronic and zero-point Energies= -534.938258
Sum of electronic and thermal Energies= -534.928396
Sum of electronic and thermal Enthalpies= -534.927452
Sum of electronic and thermal Free Energies= -534.973430

\[ E(\text{M06-2X/6-311++G(d,p)}) = -535.249679 \text{ a.u.} \]

Calculation Type = FREQ
Calculation Method = RM06-2X
Basis Set = 6-31G(d)
Charge = 0
Spin = Singlet
RMS Gradient Norm = 0.000009 a.u.
Imaginary Freq = 0  
Dipole Moment = 2.764070 Debye  
Point Group = C1

| Symbol | X       | Y       | Z       |
|--------|---------|---------|---------|
| C      | -0.19227500 | 1.89281400 | 0.00003100 |
| C      | -1.40234900 | 1.20818800 | -0.00003700 |
| C      | -0.19210200 | -0.89121000 | -0.00014300 |
| C      | 1.01832300  | -0.21519400 | -0.00005700 |
| C      | 1.01282200  | 1.19772300  | 0.00002500  |
| H      | -0.17299100 | 2.98029700  | 0.00010200  |
| H      | -2.35104800 | 1.73439400  | -0.00002200 |
| H      | -0.21745500 | -1.97671500 | -0.00023300 |
| O      | 2.24458300  | -0.79015600 | -0.00092000 |
| C      | 2.28956600  | -2.19941200 | 0.00050800  |
| H      | 3.34556200  | -2.46737900 | 0.00088200  |
| H      | 1.80717000  | -2.61265100 | 0.89491500  |
| H      | 1.80763500  | -2.61341400 | 0.89379900  |
| C      | -2.67980400 | -0.92247800 | -0.00020300 |
| O      | -3.77222500 | -0.40319700 | -0.00021500 |
| H      | -2.57846300 | -2.02933300 | -0.00029400 |
| C      | -1.40216000 | -0.18195400 | -0.00012400 |
| O      | 2.22209300  | 1.80462500  | 0.00008800  |
| H      | 2.09185600  | 2.76375900  | 0.00020100  |
References

(1) Perrin, D. D.; Armarego, W. L. F., Purification of Laboratory Chemicals. 4th ed.; Butterworth-Heinemann: Oxford, 1997.
(2) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. Safe and Convenient Procedure for Solvent Purification. Organometallics 1996, 15, 1518–1520.
(3) Still, W. C.; Kahn, M.; Mitra, A. Rapid chromatographic technique for preparative separations with moderate resolution. J. Org. Chem. 1978, 43, 2923–2925.
(4) Ota, E.; Wang, H.; Frye, N. L.; Knowles, R. R. A Redox Strategy for Light-Driven, Out-of-Equilibrium Isomerizations and Application to Catalytic C–C Bond Cleavage Reactions. J. Am. Chem. Soc. 2019, 141, 1457–1462.
(5) Lancefield, C. S.; Teunissen, L. W.; Weckhuysen, B. M.; Bruininx, P. C. A. Iridium-catalysed primary alcohol oxidation and hydrogen shuttling for the depolymerisation of lignin. Green Chem. 2018, 20, 3214–3221.
(6) Lee, I.; Yang, J.; Lee, J. H.; Choe, Y. S. Synthesis and evaluation of 1-(4-[18F]fluoroethyl)-7-(4'-methyl)curcumin with improved brain permeability for β-amyloid plaque imaging. Bioorg. Med. Chem. Lett. 2011, 21, 5765–5769.
(7) Das, A.; Rahimi, A.; Ulbrich, A.; Alherech, M.; Motaganwala, A. H.; Bhalla, A.; da Costa Sousa, L.; Balan, V.; Dumesic, J. A.; Hegg, E. L.; Dale, B. E.; Ralph, J.; Coon, J. J.; Stahl, S. S. Lignin Conversion to Low-Molecular-Weight Aromatics via an Aerobic Oxidation-Hydrolysis Sequence: Comparison of Different Lignin Sources. ACS Sustain. Chem. Eng. 2018, 6, 3367–3374.
(8) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian 16 Rev. B.01, Wallingford, CT, 2016.
(9) Kim, S.; Chmely, S. C.; Nimlos, M. R.; Bomble, Y. J.; Foust, T. D.; Paton, R. S.; Beckham, G. T. Computational Study of Bond Dissociation Enthalpies for a Large Range of Native and Modified Lignins. J. Phys. Chem. Lett. 2011, 2, 2846–2852.
