HETEROGENEOUS BASE METAL CATALYZED OXIDATIVE DEPOLYMERIZATION OF LIGNIN AND LIGNIN MODEL COMPOUNDS

John Adam Jennings
University of Kentucky, johnadam.jennings@gmail.com
Author ORCID Identifier: https://orcid.org/0000-0003-4502-5415
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John Adam Jennings, Student

Dr. Mark Crocker, Major Professor

Dr. Mark Lovell, Director of Graduate Studies
HETEROGENEOUS BASE METAL CATALYZED OXIDATIVE DEPOLYMERIZATION OF LIGNIN AND LIGNIN MODEL COMPOUNDS

DISSERTATION

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the College of Arts and Sciences at the University of Kentucky

By
John Adam Jennings
Lexington, Kentucky

Director: Dr. Mark Crocker, Professor of Chemistry
Lexington, Kentucky
2017

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ABSTRACT OF DISSERTATION

HETEROGENEOUS BASE METAL CATALYZED OXIDATIVE DEPOLYMERIZATION OF LIGNIN AND LIGNIN MODEL COMPOUNDS

With the dwindling availability of petroleum, focus has shifted to renewable energy sources such as lignocellulosic biomass. Lignocellulosic biomass is composed of three main constituents, lignin, cellulose and hemicellulose. Due to the low value of cellulosic ethanol, utilization of the lignin component is necessary for the realization of an economically sustainable biorefinery model. Once depolymerized, lignin has the potential to replace petroleum-derived molecules used as bulk and specialty aromatic chemicals. Numerous lignin depolymerization strategies focus on cleavage of $\beta$-aryl ether linkages, usually at high temperatures and under reductive conditions.

Alternatively, selective benzylic oxidation strategies have recently been explored for lignin and lignin models. In this work, heterogeneous catalytic methods using supported base metals and layered-double hydroxides were evaluated for the oxidation of lignin models both before and after benzylic oxidation. Additionally, by studying putative reaction intermediates, insights were gained into the mechanisms of oxidative fragmentation of the model compounds.

Generally, it was found that after benzylic oxidation models were more susceptible to oxidative fragmentation. Indeed, several heterogeneous oxidation systems were found to convert lignin models to oxygenated aryl monomers (mainly benzoic acids and phenols) using inexpensive primary oxidants (*i.e.*, hydrogen peroxide and molecular oxygen). Reactions were conducted at relatively mild temperatures and at low oxygen concentrations for the purpose of an easy transition to large-scale experiments. Finally, the catalytic systems that resulted in significant cleavage of lignin models were applied to a Kraft lignin. Oxidation of Kraft lignin resulted a mixture of products for which analytical data and increased solubility are consistent with interunit cleavage within the lignin macromolecule.
Keywords: Heterogeneous Catalyst, Lignin Oxidation, Depolymerization, Layered Double Hydroxides, Lignin Model Compound

John Adam Jennings

Date: July 21, 2017
HETEROGENEOUS BASE METAL CATALYZED OXIDATIVE DEPOLYMERIZATION OF LIGNIN AND LIGNIN MODEL COMPOUNDS

By

John Adam Jennings

Dr. Mark Crocker
Director of Dissertation

Dr. Mark Lovell
Director of Graduate Studies

July 21, 2017
This dissertation is dedicated to my wife Cheryl Jennings
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Chapter 1. Introduction to Lignin and Oxidative Depolymerization Routes
1.1. Introduction to Lignin Synthesis and Properties

Lignocellulosic biomass consists of three main biopolymers: cellulose, hemicellulose, and lignin. Other biomass components, such as lipids, terpenes, and saps are minor in lignocellulosic biomass. Although lignin is less abundant than cellulose, its aromatic nature and relatively low oxygen content provides a higher energy density than cellulose. Lignin constitutes 15-30% of biomass by weight and some 40% by energy.\(^1\) The Van Krevelen diagram below (Fig. 1) illustrates the relative energy densities of three biomass components. As a reference, lipids, which are largely saturated, are also shown Fig. 1. Since lignin is aromatic, the atomic H: C ratio is lower than lipids; hence, it possesses a lower energy density. The aromaticity and relatively high energy density of lignin (compared to cellulose), along with its underutilization make it of interest to both the biofuel and fine chemical industries.
In planta, lignin serves as a secondary structural unit in plant cell walls, providing resistance to chemical and biological attack. Lignin lines xylem vessels and facilitates internal water transport due to its hydrophobic nature. Unlike cellulose, which consists of linear repeating glycosidic monomers, lignin is formed by random phenolic radical coupling of three monolignols - coniferyl, sinapyl, and \( p \)-coumaryl alcohol - via the phenylpropanoid pathway (Fig. 2). Monolignols are linked by a series of bonds commonly referred to as lignin linkages. In the naming convention of lignin, the phenol position is labeled the “4” position and the alkyl chain that branches from the “1” position is labeled by Greek letters \( \alpha \), \( \beta \), and \( \gamma \), respectively. This naming convention is transposed from the organic chemistry naming convention, where the phenolic position is referred to as the “1” position. In this contribution, the organic chemistry naming system will not be used.
Monolignols are biosynthesized by deamination of phenylalanine, followed by various other enzymatic processes involving aromatic hydroxylation and \textit{ortho}-phenolic methylation.\textsuperscript{4} For simplicity, these monolignols are abbreviated: coniferyl alcohol, represented by “G,” sinapyl alcohol “S” and \textit{p}-coumaryl alcohol “H.” Contrary to S and G alcohols, H alcohol is all but negligible in lignin types excluding grasses; therefore, lignin is generally characterized by the S/G ratio. The content of S and G alcohols is highly variable with respect to the lignin source. Typical softwood (gymnosperm) lignins contain approximately 80% G-units, whereas typical hardwood (angiosperm) lignins contain approximately 60% G-units.\textsuperscript{5}

![Monolignol alcohols](image)

\textbf{Figure 2.} Monolignol alcohols coupled to form lignin.\textsuperscript{1}

It has been proposed that lignin biosynthesis proceeds through two polymerization pathways, endwise and batchwise polymerization. During endwise polymerization, propagation occurs \textit{via} 4-phenolate radical coupling with the C$_\alpha$-C$_\beta$ \(\pi\)-bond of another monolignol. Alternatively, propagation in batchwise polymerization proceeds \textit{via} coupling of 4-phenolate radical resonance structures with an unreacted C$_\alpha$-C$_\beta$ \(\pi\)-bond (Fig. 3). However, it is the current academic opinion that endwise polymerization is the primary reaction pathway, due to the distribution of lignin linkages discussed below.\textsuperscript{1}
Lignin is comprised of eight main linkages, although others have been discovered in low abundance (Fig. 4). The β-O-4 is the most frequently occurring linkage, followed by the 5-5 linkage, the latter consisting of up to a little under 30% of all linkages. As opposed to the β-O-4 linkage resulting from endwise polymerization, the origin of the 5-5 linkage is a result of radical coupling of two ortho-phenoxy radicals. The formation of 5-5 linkages is the most common example of a batchwise polymerization. Some linkages such as the 5-5, β-5, 4-O-5 and dibenzodioxocin linkages can only occur when one of the monomers is a G-unit. In S-units the 5-position is occupied by a methoxy substituent, therefore it is incapable of forming linkages from the 5-position. Though lignin has been highly researched, the structure of native or protolignin has not been determined, presumptively as a consequence of spectroscopic limitations.
In addition to the linkages shown above, one of the more interesting naturally occurring linkages is the ferulate linkage (Fig. 5). Ferulate linkages are derived from coupling of monolignol $\gamma$-alcohols to produce easily hydrolyzed esters.\(^6\) Ferulate linkages consist of bridging esters, which are favorable for lignin depolymerization by acidic or basic hydrolysis. Unfortunately, this type of linkage is generally only present in grasses in low frequency (up to 3% of all linkages).\(^9\) Efforts to produce more easily extracted/depolymerized lignin via upregulation of the enzyme responsible for ferulate linkages (ferulate 5-hydroxylase (F5H)), have recently been reported by Ralph and co-workers.\(^10\) The authors found that lignin could be bioengineered to synthesize a less robust structure with no significant change in observable plant characteristics (e.g., height, chemical resistance).
While the production of bioengineered lignin is a flourishing area of research, it largely beyond the scope of this work.

The structure of native lignin remains an active area of discussion. Since it is nearly impossible to analyze native lignin on a molecular basis, there is very little information available concerning the molecular weight and degree of branching of lignin before extraction. It has recently been suggested that milled lignin is a linear polymer with relatively low molecular weight, in contrast to the previous suggestions.\textsuperscript{11-12} Often, analytical methods rely on first solubilizing the analyte. If the analyte is not fully solubilized in the analytical medium then misrepresentation of the data is possible. It is also possible that current analytical methods skew lignin agglomerates to appear as high molecular weight macromolecules.\textsuperscript{11} Additionally, it may also be the case that lignin is only extracted after portions of the polymer have been functionalized. It would stand to reason that the most reactive sites are functionalized during extraction. For instance, ferulate linkages are likely easily hydrolyzed during acid or base extraction; therefore, they are not commonly observed in extracted lignins. It is also difficult to determine if reactions between two lignin polymers take place
during extraction, or if some linkages are simply protected by the reaction medium. Lignin functionalization typically leads to a more robust feedstock that is harder to utilize. To remove ambiguity and simplify analysis, lignin models are commonly used.

1.2. Current Lignin Utilization

Cellulose is the most widely utilized biomass component utilized for the production of pulp and paper as well as bioethanol. Hemicellulose, the least abundant component of lignocellulosic biomass, is incorporated into the production of various gums and biodegradable films. In contrast, lignin is underutilized and seldom used for commercial applications.

In an effort to combat economic dependence on the depleting supply of petroleum, renewable energy alternatives must be employed. Lignocellulosic biomass appeals to multiple markets (e.g., fuels, chemical, polymers, etc.) due to its multiple constituents. As discussed above, cellulose, the main component of lignocellulosic biomass, can be converted into ethanol. However, in order to make biorefineries a cost-effective solution, all components of biomass must be utilized. As noted in a review by Ragauskas and co-authors,\textsuperscript{13} the U.S. Energy Security and Independence Act of 2007 mandates that 79 billion liters of second-generation biofuels be produced annually by 2022. The authors go on to estimate that 355 liters of bioethanol can be produced per ton of biomass. Approximately 223 million tons of lignocellulosic biomass would need to be converted into cellulosic bioethanol to satisfy the mandate. Lignocellulosic biomass consists of
≤30 wt.% of lignin, meaning that fulfilling the mandate would result in ca. 62 million tons of lignin annually in addition to current lignin production.\textsuperscript{13} In 2004, pulp and paper industries produced 50 million tons of lignin\textsuperscript{1} while it is estimated that only 40% of lignin was required for on-site heat production.\textsuperscript{13}

The lignin produced by fulfilling the mandated amount of cellulosic bioethanol, in addition to that produced by the pulp and paper industries would result in an excess of 80 million tons of lignin annually with no designated commercial use. Indeed, it has been estimated that for every one liter of cellulosic ethanol, 0.5-1.5 kg of lignin will be produced.\textsuperscript{14} Consequently, integration of lignin utilization into biorefineries and mills is a key step in an economically sustainable biorefinery model.

1.3. Lignin Extraction Processes

Not only is protolignin seemingly randomly assembled, there are many different techniques to fractionate lignin from whole biomass, which further increases the variation of lignin structure. Each extraction method introduces characteristics of the extraction conditions used. Therefore, properties of the lignin are variable based on the extraction technique.

The primary lignin extraction technique is the Kraft process, used to separate cellulose for paper production. It is estimated that Kraft lignin constitutes 85% of lignin produced worldwide.\textsuperscript{15} The Kraft extraction process is performed at high temperature (150 °C-180 °C) in a solution of sodium hydroxide.
and sodium sulfide,\textsuperscript{8} for approximately two hours.\textsuperscript{1} During the cooking process approximately 90-95\% of lignin is dissolved in the aqueous medium to form a bio-oil known as black liquor.\textsuperscript{8} Due to its industrial prevalence, the protocol for this extraction process is well established. Most black liquor utilization is integrated into the production of paper and burned on-site as a low-grade fuel. Kraft derived lignin has a characteristic high sulfur as well as an increased phenolic content as a result of the cooking process. Additionally, the Kraft processing is largely believed to break $\beta$-O-4 linkages, resulting in C-C bond formation. The mechanism for C-C bond formation is shown in Scheme 1. In a mechanism proposed by Lercher and co-workers,\textsuperscript{16} $\beta$-O-4 linkages are cleaved by sodium hydroxide via a six-membered ring transition state. Monomers like acetosyringone are then susceptible to nucleophilic attack by resonance structures of 2,6-dimethoxyhydroquinone resulting in tertiary alcohols that are not further oxidized (Scheme 1). Hydroxylation of protolignin during extraction increases phenol content and leads to ash content of up to 30\% after evaporation of the aqueous medium. Acidification of the black liquor with dilute sulfuric acid treatment, decreases ash content to ca. 5\%, but is rarely performed commercially.\textsuperscript{17-18} One such example of commercial lignin acidification is the Lignoboost process. The Lignoboost process is performed by Innventia, a Swedish company, and is a propriety lignin precipitation process incorporating black liquor acidification. In another example of sulfuric acid pretreatment, Meadwestvaco produced well-characterized Indulin AT lignin. However, lignin
resulting from Kraft black liquor has relatively high sulfur content and it is often severely degraded.

Another popular extraction technique is lignosulfonate processing, also known as the sulfite process. This method involves lignin processing with alkali or alkaline earth metal sulfites and bisulfites. While the Kraft process is strongly basic, sulfite processing can be conducted over a large pH range. One million tons of lignosulfonate dry solid are produced every year. Lignosulfonates exist primarily as metal sulfonates (i.e., calcium and sodium), making them readily water-soluble. The ionic nature of alkali or alkaline earth metal lignosulfonates allows them to be utilized industrially as detergents, stabilizers, and in materials such as pressed wood and glue. Sulfonated lignin has unique characteristics such as increased phenolic content, carboxylic acid content, high polydispersity,
and high ash content. Sulfite lignin is also likely deficient in \( \beta\)-O-4 linkages depending on the temperature and pH, making it a more resilient feedstock than protolignin.

Another popular lignin extraction technique is the organosolv process. Organosolv lignin is the most diverse method of lignin extraction. It is of interest to many researchers because of the lower degree of modification during cooking. The operating principle of organosolv lignin is selective solvation from whole biomass as opposed to precipitation from black liquor. Organosolv processes often involve lignin cooking in an organic acid and water. Other common organosolv processes involve biomass treatment at 180-200 °C in a water/alcohol mixture. This process also yields a more uniform lignin than others (i.e., Kraft and lignosulfonate). When alcohol is used as a solvent some linkages are alkylated (i.e., \( \beta\)-O-4 and \( \beta\)-1 linkages) resulting chemical modification. Only lignin of similar size and composition is dissolved, yielding a more uniform lignin. While the organosolv process yields separate streams of lignin and cellulose, the lignin product usually contains lower hemicelluloses. Hemicellulose can be problematic in some lignin utilization schemes such as hydrodeoxygenation due to preferential coordination to metallic active sites. However, the primary disadvantage of organosolv lignin is the expense of solvent recovery.

The aforementioned processes are the most prevalent lignin extraction methods. However, other lignin extraction techniques such as cellulosic
enzymatic processing, steam explosion processing, acidolysis processing, etc., have also been studied. More complete discussions of lignin extraction techniques as well as the resulting lignin modifications can be found in the literature.¹,¹¹

1.4. Techniques for Lignin Analysis

As previously discussed, lignin is difficult to analyze due to its low solubility in common organic solvents. Therefore, unique analytical methods have been developed and applied to lignin. Classic analytical techniques such as infrared spectroscopy, UV-vis spectroscopy, and gas chromatography provide important structural information, but are not discussed in this contribution. Rather, this work focuses on the benefits and shortfalls of techniques that provide significant information on lignin structure or molecular weight.

1.4.1. Thioacidolysis

Thioacidolysis is a destructive technique employed to determine the S/G ratio of extracted lignins. It is also the most widely used method to determine the frequency of the β-O-4 linkage.¹⁹ Thioacidolysis currently serves as the gold standard for lignin analytical depolymerization techniques. As shown in Fig. 6, thioacidolysis proceeds through a Lewis acid catalyzed reaction with boron trifluoride etherate. After polarization of the carbon-oxygen bond ethanethiol is sufficiently nucleophilic to attack the carbinol forming ethyl thioethers. Thiol ethers resulting from thioacidolysis can then be silylated and analyzed by
GC/MS, showing two distinct molecular weights for S and G units. Silyation is incorporated into the process simply for the purpose of compatibility with instrumentation.

![Proposed mechanism for thioacidolysis modified from Holtman et al.](image)

Figure 6. Proposed mechanism for thioacidolysis modified from Holtman et al.\textsuperscript{19}

While thioacidolysis is the most widely used method to determine S/G ratios, this process is only capable of analyzing the soluble portion of the solution. Any char produced by this process is not analyzed. Furthermore, as discussed above, it is common in the literature to use thioacidolysis to estimate the frequency of the $\beta$-O-4 linkage. While $\beta$-O-4 linkages are indeed converted to ethyl thioesters like the one shown in Fig. 6, the quantification of number of linkages assumes 100% conversion, which is unlikely for such a heterogeneous macromolecule.
1.4.2. Derivatization followed by reductive cleavage (DFRC)

Initially developed by the Dairy Forage Research Center, derivatization followed by reductive cleavage is another method of S/G ratio determination. Shown in Fig. 7, DFRC begins with acetylation of alcohols, specifically the γ-alcohol and any phenols present. It has been proposed by Holtman et al.\textsuperscript{19} that the benzylic alcohol in β-O-4 linkages is also lost due to nucleophilic attack of bromine from acetyl bromide. However, it is likely that the α-position is also acetylated. Coordination of a Lewis acid, in this case zinc, facilitates cleavage of the β-aryl ether bond and acetylation by acetic anhydride. As shown in the mechanism below, the incorporation of a leaving group at the α-position facilitates dehydration of the C\textsubscript{α}-C\textsubscript{β} bond, regardless of whether the leaving group is bromine or an acetate group.

![Figure 7. DFRC mechanism modified by Holtman et al.\textsuperscript{19}](image)

In addition to producing monolignols, acetylation of alcohols has been shown to decrease lignin agglomeration during gel permeation chromatography, which is a method of lignin molecular weight determination.\textsuperscript{20} However, β-O-4 linkages are still present in DFRC treated lignin, indicating that DFRC does not depolymerize lignin to monolignols with 100% efficiency. Holtman \textit{et al.}\textsuperscript{19} speculated that the incomplete depolymerization of lignin may be due to the
rigidity of the macromolecule, which decreases the ability of reagents to functionalize all linkages.

1.4.3. Heteronuclear Single Quantum Coherence (HSQC) Spectroscopy

Currently, one of the most powerful tools for the determination of the distribution and functionality of lignin linkages is non-destructive heteronuclear single quantum coherence (HSQC) spectroscopy. The pulse sequence used for this type of 2-dimensional NMR spectroscopy transfers magnetism from the protons to a heteroatom. Originally described in the 1980’s for protein analysis by transfer of magnetism from hydrogen to nitrogen,\textsuperscript{21} HSQC spectroscopy has recently been applied for the determination of lignin structure and functionality.

Due to the aromatic nature of lignin, HSQC is particularly useful. The aromatic regions of the spectra remain relatively unaffected by the presence of other components of lignocellulosic biomass such as cellulose and hemicellulose. Furthermore, after oxidation the chemical shift of the aromatic protons moves downfield, allowing for quick evaluation concerning the extent of oxidation. In addition, the differing resonances of lignocellulosic biomass components allow the ready characterization of soluble whole biomass with little interference. The analysis of HSQC spectra is discussed in greater detail in section 1.6.3.
1.5. Thermal and Reductive Lignin Densification and Depolymerization

One of the largest problems associated with biomass utilization is the fact that biomass has a low density, making transportation inefficient. The energy cost for transporting biomass is a function of biomass density and the proximity of the biomass source to the biorefinery. In order to maximize energy losses associated with biomass transportation, on-site densification or proximal biorefinery locations are critical. The practice of burning Kraft black liquor as a low-grade fuel is logical when considering transportation costs. Although on-site production of black liquor is cost-efficient, the production of high-value small aromatic molecules is pivotal to the biorefinery model. For the reasons addressed above, the likely solution for lignin underutilization will involve the integration of lignin valorization process into bioethanol or paper production.

Pyrolysis is another common densification technique. Pyrolysis is the thermal treatment of biomass in the absence of oxygen. When lignin is pyrolyzed it results in unselective homolytic bond cleavage. Though the C\(_{\beta}\)-O\(_4\) bond in the \(\beta\)-O-4 linkage is the weakest bond (ca. 248 kJ/mol), additional bonds are broken and formed during bulk treatment. This method of densification results in a phenolic\(^{22}\) and corrosive oil, with a high water content derived from dehydration reactions. Pyrolysis oil often contains persistent radicals from the pyrolysis process and is unstable with respect to long-term storage. Moreover, pyrolysis of lignin produces more char when compared to other biomass components.\(^{22}\) This process is energy intensive, requiring temperatures anywhere from 200-300 °C
(torrefaction)\textsuperscript{23} up to 600 °C (fast pyrolysis). Generally, torrefaction is used to synthesize charcoal and fast pyrolysis yields bio-oil. While charcoal is not easily convertible to monomeric aromatics, the conversion of bio-oil to monomers has been extensively investigated and reviewed.\textsuperscript{1, 22} Industrially, energy intensive processes translate to high production costs; hence, pyrolysis is not currently feasible for large scale utilization.

In addition or in conjunction with pyrolysis, many reports of lignin hydrodeoxygenation (HDO) have been recently published.\textsuperscript{24-25} HDO is the process of removing oxygen from oxygenated compounds by means of hydrogenation. HDO is a catalytic, bulk reductive technique that is performed under a reductive atmosphere at temperatures typically in excess of 250 °C. High pressure hydrogen or inert gas, in the case of ethanolysis and methanolysis, are commonly used for HDO reactions. HDO is effective for a multitude of feedstocks such as lignin and lignin-derived bio-oil. Advancements in lignin HDO have been the subject of multiple reviews.\textsuperscript{26-28} In addition, a book chapter focusing on HDO of model compounds has recently been published.\textsuperscript{29} HDO has yet to be applied to commercial production of lignin-derived molecules, partly due to the high cost of the reductive gas required and significant energy demands of heat production. Additionally, when expensive noble metal catalysts are used, lignin monomers are often reduced to cycloalkanes, representing a lower-value product than aromatic monomers.
Sulfided catalysts (CoMo and NiMo) are also commonplace in reports of lignin HDO. Sulfided catalysts have the potential for incorporation of sulfur into lignin residues and therefore are not the optimal catalysts for lignin HDO. The fact that HDO is a reductive technique makes this process of interest to the biofuels and bulk chemical industries. However, HDO of lignin is not optimal for production of high-value oxygenated small molecules such as vanillin and is primarily appealing for the production of BTXs.

1.6. Oxidative Lignin Depolymerization

As an alternative to thermal and reductive depolymerization strategies, functional group modification via selective oxidation of the abundant $\beta$-O-4 linkage (ca. 60% of linkages) has recently been explored.$^{30-33}$ The most widely studied approach for selective oxidative depolymerization of $\beta$-O-4 linkages involves benzylic oxidation (Scheme 2). Subsequently, the corresponding ketone can be modified by a number of means, such as $\beta$-aryl ether cleavage or Baeyer-Villiger-type oxidation. Ideally, the resulting low molecular weight fractions can be separated and used for applications such as biofuels or as fine chemicals. In fact, the only commercially produced aromatic product of lignin depolymerization, vanillin, is produced via an oxidative reaction with a proprietary copper catalyst.$^{34}$
Scheme 2. An example of a selective oxidation strategy for cleavage of a β-O-4 linkage.

The efficacy of lignin oxidation is to a large degree dependent on the extraction processes mentioned in section 1.3. Incorporation of heteroatoms (e.g. sulfur, sodium) into the isolated lignin and degradation of linkages (formation of C-C bonds) during the extraction process have a large effect on lignin reactivity. Consequently, lignin model compounds are widely used to establish reactivity trends. Models eliminate lignin heterogeneity and enable facile analysis of reaction mixtures and intermediates.

It has been previously calculated\textsuperscript{35} that benzylic oxidation of β-O-4 linkages leads to weakening of the C\textsubscript{β}-O\textsubscript{4} bond while increasing the strength of the C\textsubscript{α}-C\textsubscript{β} bond (Fig. 8). While the decrease in bond energy may provide a more favorable route for thermal bond cleavage, it generally has little implication for reactivity in selective oxidation systems.

Figure 8. Key bond strengths in the β-O-4 linkage and oxidized β-O-4 linkage according to Wang and co-workers.\textsuperscript{35}
1.6.1. Fungal and bacterial enzymatic oxidative deconstruction

To investigate the efficacy of potential depolymerization pathways, it is often beneficial to study natural processes. Fungi, via laccases and peroxidases, efficiently and naturally depolymerize lignin and have been thoroughly investigated over the past 30 years.

White rot fungi are one of the most studied means of natural oxidative lignin degradation. White rot fungi selectively depolymerize lignin leaving the white cellulose fibrils intact. Only a few enzymes have been identified as active in lignin depolymerization. These enzymes are a copper-containing laccase, iron porphyrin lignin peroxidase, manganese dependent peroxidase, and versatile peroxidase.\textsuperscript{11}

Laccase enzymes consist of 2-3 copper centers connected by a series of Lewis-basic amino acids such as histidine and cysteine, which are present in fungi, bacteria, and plants. Laccases alone are not capable of lignin depolymerization, instead they use lignin oxidation products from reactions initiated by peroxidases. Products such as the veratryl radical cation,\textsuperscript{36} serve as electron mediators, which ultimately facilitates depolymerization.\textsuperscript{37} Small radical molecules generated by laccases are then capable of diffusing into the cell wall (Scheme 3).\textsuperscript{38}
The mechanism of laccase initiated lignin depolymerization proceeds using molecular oxygen as the primary oxidant. Laccases first abstract a phenolic proton to form phenolate radicals, albeit native lignin is estimated to contain a low (10%) phenolic content.\textsuperscript{39} Laccases are also believed to participate in lignin biosynthesis, meaning they are active for both depolymerization and repolymerization reactions. Therefore, it is believed that lignin biodegradation is primarily performed by peroxidases.

As opposed to laccases, secreted peroxidases contain an iron heme center and depolymerize lignin using hydrogen peroxide generated by extracellular glucose oxidase (Fig 9).\textsuperscript{39} Peroxidases identified for lignin depolymerization are manganese or manganese dependent peroxidase, lignin peroxidase, and versatile peroxidase. Manganese peroxidases are the most common peroxidase secreted by fungi.\textsuperscript{39} Unlike lignin peroxidase and versatile peroxidase that can oxidize non-phenolic lignin functionality, manganese peroxidase is only active for lignin depolymerization intermediates with phenolic moieties.\textsuperscript{39} After radical formation via hydrogen abstraction, non-enzymatic reactions occur such as bond cleavage, $\alpha$-oxidation and repolymerization.\textsuperscript{39} Lignin peroxidases (LiP) behave in a very similar manner as manganese
peroxidases, but create small radical molecules such as the veratryl radical cation to facilitate depolymerization instead of manganese (II), discussed below. Versatile peroxidases possess features of both manganese peroxidase and lignin peroxidase.\textsuperscript{39} Fig. 9 illustrates a general mechanism for peroxidase-mediated lignin depolymerization.\textsuperscript{41}

Glucose oxidase produces extracellular hydrogen peroxide, which is coordinated to the heme center of the porphyrin. After electron transfer from the porphyrin to form an iron (IV) oxo species and water, manganese (MnP) or an electron mediator (LiP) transfers an electron into the porphyrin aromatic system, yielding a reactive Mn\textsuperscript{3+} species (MnP) or a radical electron mediator (LiP). The active manganese species, generally chelated with carboxylic acids, can then diffuse into the lignin structure where it performs non-enzymatic reactions with free phenols (MnP) or lignin linkages (LiP).
Lignin biodegradation is initiated by one-electron transfer from the lignin Cα-Cβ bond to lignin peroxidase or an electron carrying mediator like veratryl alcohol, which is later oxidized to veratrylaldehyde. This single-electron transfer (SET) effectively cleaves the Cα-Cβ bond, after which aqueous and aerobic reactions lead to lignin-derived aldehydes and phenols (Scheme 4).
The commercial use of extracted or synthesized peroxidases for the production of specialty chemicals has been investigated due to high substrate selectivity. However, the efficacy of peroxidases is limited by several factors such as temperature sensitivity, low solubility of the biomass source in the requisite aqueous phase, and sensitivity to high concentrations of hydrogen peroxide.\textsuperscript{11, 44-45} For these reasons, enzymatic lignin deconstruction is not currently an industrially feasible technique for the production of small aromatic molecules.

Additionally, bacterial lignin depolymerization has been investigated. Although the use of bacteria seems like an unconventional means of natural lignin depolymerization, it has been the focus of several studies and reviews in the past five years.\textsuperscript{46-49} Lignin depolymerization by bacteria also utilizes laccases and other enzymatic processes that have yet to be identified.\textsuperscript{49} In a publication by Huang \textit{et al.},\textsuperscript{49} bacterial degradation of both a lignin model dimer and Kraft lignin was realized. Although the depolymerization pathway was not fully elucidated, this publication serves as an example of other natural lignin depolymerization strategies.

1.6.2. Biomimetic oxidative depolymerization

Undoubtedly inspired by lignin peroxidase and other lignin biodegradation enzymes, researchers have developed biomimetic deconstruction systems. Biomimetic lignin oxidation using copper, manganese, and iron complexes has been an active area of research since the late 1980’s.\textsuperscript{50} Biomimetic reactions have recently been reviewed by Crestini \textit{et al.}\textsuperscript{11}
In a recent example of iron porphyrin oxidation by Patil et al., a lignin model compound susceptible to both benzylic alcohol and benzylic methylene oxidation was subjected to a (tetraphenylporphyrinato)iron (III) chloride (TPPFeCl)/tert-butyl hydrogen peroxide oxidation system along with a phase transfer catalyst (Scheme 5). The authors observed 52% conversion and 33% yield of the benzylic oxidation product. Furthermore, the authors found the oxidation system did not oxidize the γ-carbinol despite obtaining a 12% yield of the product of methylene oxidation. Therefore, the reaction is believed to proceed through a similar reaction pathway as excreted peroxidases.

Scheme 5. Iron porphyrin mediated oxidation of lignin model compounds reported by Patil et al.

Previously the oxidation of benzylic alcohols using TPPFeCl has been proposed to proceed via benzylic hydrogen abstraction forming an iron hydroxide and a benzylic radical. Homolytic cleavage and coupling of the hydroxyl radical with the benzylic radical produce a geminal diol intermediate, that forms a benzylic ketone upon dehydration (Fig. 10).
However, porphyrins have a propensity to form $\mu$-oxo dimers that are catalytically inactive.\(^1\) While the formation $\mu$-oxo dimers can be suppressed by the addition of bulky groups such as aryl rings, this further increases the cost of porphyrin synthesis, which is already prohibitively expensive for industrial applications. Moreover, radical-based mechanisms are capable of both depolymerization as well as condensation reactions; hence, relatively few iron porphyrin/H\(_2\)O\(_2\) oxidations have been studied in the last ten years.

In addition to iron active sites, other metals active in the biodegradation of lignin have been studied. In a recent report by Springer et al.,\(^5\) manganese salen complexes were used to degrade a model compound with $\beta$-O-4 like functionality. The authors observed 91% conversion of the model but only recovered 5% of identifiable products. A modest yield of identifiable products is a common problem in oxidations utilizing homogeneous manganese catalysts. The unselective nature of catalytic systems containing manganese prevents them from being viable catalysts for the production of small molecules from lignin.
1.6.3. Step-wise oxidative catalytic cleavage of lignin model dimers

Classical oxidation reactions have inspired several successful lignin oxidation systems ranging from TEMPO/hypochlorite, Dess-Martin periodinane, Swern, pyridinium chlorochromate, and chromic acid oxidations. These oxidations resulted in varying degrees of success as reported by Stahl and co-workers. The above reactions are examples of selective oxidation systems as opposed to bulk oxidation. In an example of bulk oxidation, ozonolysis has been studied, resulting in direct cleavage of alkenes, including aryl groups. Indeed, ozonolysis treatments are very susceptible to over-oxidation, resulting in loss of the aromatic character of lignin and ultimately forming low-value viscous bio-oils. Obtaining high-value oxidation products from lignin requires retention of aromatic character, whereas over-oxidation results in degradation of potentially high-value aromatic compounds to lower value dicarboxylic acids.

To evaluate the efficacy of textbook oxidations, Stahl and co-workers surveyed several systems known to perform benzylic alcohol oxidation. These oxidation systems consisted of stoichiometric oxidants, metal-free catalytic oxidation systems and metal-catalyzed oxidation systems. The authors found a mild benzylic oxidation strategy using a 4-acetamido-TEMPO/oxygen system, which afforded a benzylic oxidation product in the case of dimeric model compounds in up to 96% yield (Scheme 6).
Scheme 6. Benzylic alcohol oxidation reported by Stahl and co-workers.\textsuperscript{30}

The highest-yielding, most selective result (Scheme 6) was achieved using 5 mol\% 4-acetamido-2,2,6,6-tetramethylpiperidine-N-oxyl (AcNH-TEMPO), with 10 mol\% nitric acid, and 10 mol\% hydrochloric acid as co-catalysts in acetonitrile: water (19:1) under atmospheric oxygen at 45 °C for 24 h.\textsuperscript{30} TEMPO oxidations are believed to proceed through the catalytic cycle shown below (Scheme 7). Similar reports of TEMPO-based benzylic oxidations using “Bobbitt's salt,”\textsuperscript{55} vanadyl sulfate,\textsuperscript{35} and copper (I) chloride\textsuperscript{56} have also been reported.

The optimized conditions for oxidation of lignin model compounds were then applied to a cellulosic enzymatic lignin (CEL). The degree of oxidation was assessed by HSQC spectroscopy. As shown in Fig. 11, the TEMPO-based catalytic system successfully oxidized CEL lignin. As hypothesized, most of the β-O-4 linkages were oxidized as evidenced by the change in chemical shift of the
β-hydrogen (A_{S/G-G}, 4.4/84 ppm (\(^1\)H/\(^{13}\)C) and A_{S/G-S}, 4.2/86 ppm (\(^1\)H/\(^{13}\)C)) after oxidation (the absence of cross-peaks is indicated by dotted lines in Fig. 11, structures A and A’). Additionally, the authors observed oxidation of the γ-carbon of β-β linkages (C\(_{\alpha}\), 4.7/85 ppm (\(^1\)H/\(^{13}\)C), C\(_{\beta}\), 3.0/54 ppm (\(^1\)H/\(^{13}\)C), and C\(_{\gamma}\), 3.9/72 ppm (\(^1\)H/\(^{13}\)C)) as well as oxidation of β-5 (B\(_{\alpha}\), 5.5/88 ppm (\(^1\)H/\(^{13}\)C) units (Fig. 11, structures B and C). β-β and β-5 linkages were likely oxidized to aromatic furans and benzofurans. Indeed, oxidation of β-5 models to their corresponding benzofurans is commonplace in model compound oxidation.
Figure 11. HSQC spectra of oxidized and native lignin as reported by Stahl and co-workers. Copyright (2013) American Chemical Society.
Oxidation was further confirmed by analyzing the aromatic region of the spectra. Specifically, oxidation of G-units was observed as indicated by structures G (G2, 6.8/114 ppm (1H/13C) G5/G6 (6.8/122 ppm (1H/13C)) and G′ (G′2, (7.5/112 ppm (1H/13C), G′5, 7.0/113 ppm (1H/13C), and G′6, 7.6/122 ppm (1H/13C)). However, the authors observed that S-units were more difficult to oxidize as observed in Fig. 11 (structures S2/6 (6.8/103 ppm (1H/13C) and S′2/6 (7.3/107 ppm (1H/13C)). Unfortunately, the reaction was performed on 35 mg of lignin, and scalability was not investigated. While this serves as an excellent example of the oxidation of multiple lignin linkages, it is not industrially scalable as a homogeneous oxidation system.

After benzylic oxidation, Stahl and co-workers performed a Dakin oxidation, resulting in an 88% yield of 3,4-dimethoxybenzoic acid and 42% yield of guaiacol (Scheme 8). The low yield of guaiacol is likely attributed to phenolic radical coupling from exposure of the phenol to hydrogen peroxide, which is capable of both one and two-electron oxidations. Poor isolated yields of phenols is a common problem in the oxidation of aromatic molecules.57

![Scheme 8. Dakin oxidation of lignin model compound performed by Stahl and co-workers.](image)

In a follow up contribution by Stahl and co-workers,31 excess formic acid and sodium formate were used in a redox-neutral system to effectively depolymerize lignin and lignin model compounds to discrete products following
TEMPO oxidation. These discrete molecules include phenols and are reported in excellent yields, ranging from 73%-92% (Scheme 9). Unlike the first report by Stahl and co-workers, this process is redox-neutral and thus requires no formal oxidant.

Model compound cleavage proceeds first by formylation of the γ-carbinol, followed by concerted deprotonation of $C_\beta$ and elimination of formate anion (Scheme 10). The $C_\beta$-$O_4$ bond is then cleaved, resulting in guaiacol and an aryl 1,2-diketone. This example of lignin model depolymerization suffers from a large excess of hazardous formic acid and is homogeneous in nature. Additionally, this reaction is run on a milligram scale with 3 equivalents of sodium formate, making the conditions difficult to scale-up.

To date Stahl and co-workers are the only authors to report a completely metal-free lignin depolymerization. This approach uses low cost reagents, but the above reactions would likely be more efficient if a catalyst (i.e., a Lewis acid
catalyst) was incorporated into the reaction system. In addition, the buffered reaction solution would be difficult to recycle.

Westwood and co-workers\textsuperscript{33} also presented a near quantitative yield of the benzylic oxidation product of lignin model compounds, as well as lignin model polymers. Similarly to Stahl and co-workers,\textsuperscript{30} Westwood also used a metal-free oxidant in 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)/\textit{tert}-butyl nitrite (Scheme 11).

The general catalytic cycle for benzylic oxidation using DDQ/\textit{tert}-BuONO is shown in Scheme 12. The catalytic cycle is initiated by stoichiometric benzylic oxidation, resulting in a ketone and the hydroquinone equivalent of DDQ. Molecular oxygen oxidizes nitric oxide to nitrogen dioxide, which in turn regenerates DDQ with the elimination of one equivalent of water. The DDQ oxidation catalytic cycle is similar to that of the TEMPO oxidation reported by Stahl and co-workers.\textsuperscript{30-31}
However, after one-pot zinc-based reduction/cleavage of the ketone, this method resulted in low yields of unprotected phenols. Zinc-based cleavage is complete within 15 minutes of addition and likely leads to formation of unidentifiable products when the reaction is allowed to continue. In addition, the maximum yield of phenolic monomers is 27%.

Westwood and co-workers\textsuperscript{33} went on to perform a two-step oxidative depolymerization of 1,4-dioxane extracted birch lignin yielding 5% of 3-hydroxypropylsyringol.\textsuperscript{33} While this is a promising report of lignin oxidation, the monomer yield from extracted lignin would likely increase if a two-electron bond or redox-neutral cleavage method were employed. This is the only report of reductive bond cleavage after benzylic oxidation, and employs a modified method published by the Dairy Forage Research Center for evaluating S/G ratios of lignin sources. DFRC was previously described and discussed in section 1.4.2 (Scheme 13).\textsuperscript{59}
HSQC 2-D NMR spectroscopy of the DDQ-treated birch lignin confirmed oxidation (Fig. 12). Oxidation of β-O-4 linkages was evident, as indicated by the disappearance of structure A ($A_\alpha$, 4.8/74 ppm ($^1$H/$^{13}$C), $A_\beta$ S/G-G, 4.4/84 ppm ($^1$H/$^{13}$C), and $A_\beta$ S/G-G, 4.0/86 ppm ($^1$H/$^{13}$C)) indicated by the dotted lines in Fig. 12, spectrum B) and the presence of structure $A'_\gamma$ (Fig. 12, spectrum B, $A'_\gamma$, 43.8/65 ppm ($^1$H/$^{13}$C)). Similar to the findings of Stahl and co-workers, structures B and C were not observed in the spectrum of DDQ oxidized lignin, suggesting that β-5 and β-β linkages are also reactive under the reaction conditions. The products of β-5 and β-β linkages were not discussed in the publication but were likely converted to furans and benzofurans. Aromatization of molecules that are one degree of unsaturation removed from aromaticity is a common issue in lignin depolymerization. The frequent conversion of 2,3-dihydrobenzofurans to benzofuran is due to the favorable resonance stabilization energy of the aromatic benzofuran. Likewise, substituted tetrahydrofuran rings (β-β linkages) can partially aromatize.
After the HSQC spectrum of the oxidized lignin was collected, zinc-based reductive cleavage was performed and the resulting small molecules were analyzed by GC/MS. Similar monomers from the cleavage of lignin model compounds and polymers were observed, albeit in lower yields (Scheme 14). Monomers 1-3 were recovered in a 6% total yield. While this may be a modest yield from the standpoint of the reaction of small molecules, these are excellent yields from an isolated lignin. Product 2, derived from cleavage of an S-unit, accounted for the majority of identifiable monomers and was recovered in 5% yield. Furthermore, DDQ oxidation and reductive cleavage reactions were performed on a 2.5 g scale. Large-scale selective oxidations are crucial for the utilization of lignin for high-value products.
Although much progress has been made in the field of selective benzylic oxidation, an industrially viable selective benzylic oxidation procedure still remains to be developed. Steps toward using more active oxidation systems have been made by incorporating base transition metals that are commonly active in oxidations. Although often less selective than textbook organic oxidants, base metals are inexpensive and are fairly active oxidation catalysts.

1.6.4. Base metal oxidative cleavage of lignin model compounds

In an effort to realize a more robust catalytic system than homogenous organic oxidants, base metals have been applied in catalytic systems to take advantage of their relatively low cost and high stability. Most base metals have stable consecutive oxidation states, making them good oxidation catalysts via activation of molecular oxygen.

One such transition metal is cobalt, which is stable in both the $\text{Co}^{2+}$ and $\text{Co}^{3+}$ oxidation state. Consecutive stable oxidation states allow transition metals
to donate an electron to molecular oxygen, which then actives the superoxide complex. Cobalt salen complexes are also of great interest to the catalysis community given that the oxidation system is tolerant of aqueous media.\textsuperscript{11} In contrast to reports of phenol sensitivity under oxidizing conditions (discussed below), Bozell and co-workers\textsuperscript{60} used a catalyst system specifically targeting phenolic moieties. The authors reported cobalt/Schiff base catalyzed oxidation of \textit{para}-hydroxy substituted phenyl ethanols, benzyl alcohols, and lignin model dimers. Moreover, oxidation of models to benzoquinones proceeded at room temperature in methanol under minimal oxygen pressure (50 psi) reaching a maximum of 86% benzoquinone yield (Scheme 15).

Catalytic oxidation is proposed to proceed via a cobalt/superoxide complex generated \textit{in situ}. The superoxide complex initially abstracts the phenolic hydrogen (Fig. 13). The resulting phenoxide radical is stabilized by aromatic resonance. Cobalt superoxide then forms a cobalt/superoxide-carbon bond in the \textit{para}-position. The C\textalpha-C\textbeta bond is then broken by two-electron cleavage of the peroxide bond, resulting in formation of \textit{para}-benzoquinone and concerted cleavage of the \textbeta-aryl ether bond. Subsequently, after an electron

Scheme 15. Oxidation of a lignin model dimer compound using a Co/Schiff base catalyst as reported by Bozell and co-workers.\textsuperscript{60}
transfer from the resulting phenoxide, a phenoxy radical is formed. In addition to a free phenoxy radical, the cobalt salen complex must be regenerated. The regeneration of the catalyst does not occur by a single step and likely requires a cascade of electron transfer reactions, which were not clearly expressed in the contribution.\(^6^0\)

Figure 13. Proposed mechanism for formation of benzoquinones reported by Bozell and co-workers.\(^6^0\)

In the above example, conversion of both aromatic rings was observed, albeit in a significantly reduced yield for the benzoquinone derived from \(\beta\)-aryl ether cleavage (17% yield as opposed to 86% yield for the phenolic ring). A probable mechanism for the formation of this minor product involves loss of an oxidized three-carbon linear chain, resulting in generation of a second phenol that is then oxidized to the corresponding benzoquinone. The authors speculate that coupling of the benzoquinone reaction intermediates led to low yields of non-phenolic aromatic rings resulting from \(\beta\)-aryl ether cleavage. Unfortunately, this reaction system is only effective for models with a \textit{para}-phenol. Although technical lignins usually contain phenols incorporated by methods of cooking or extraction, processes such as the Kraft process do not selectively produce \textit{para}-phenols. In addition to being homogeneously catalyzed, the above reaction is performed at an oxygen concentration that results in a flammable reaction mixture.\(^6^1\)
In an iron porphyrin catalyzed depolymerization strategy proposed by Patil et al.,\textsuperscript{32} $\beta$-O-4 linkages can be cleaved by a series of oxidation reactions. The authors first investigated several previously reported oxidation systems including (TPPFeCl)/$t$-butyl hydrogen peroxide (discussed previously, section 1.6.2), DDQ/O\textsubscript{2}, and TEMPO/O\textsubscript{2}. The authors then presented a depolymerization strategy focused on selective benzylic oxidation, followed by Baeyer-Villiger oxidation, and finally ester hydrolysis (Scheme 16). Patil et al.\textsuperscript{32} were the first to report well-characterized homogeneous BVO of lignin model dimer compounds. When using a formic acid/hydrogen peroxide oxidation system, oxidation takes place \emph{via in situ} formation of performic acid.

\begin{center}
\begin{tikzpicture}
\node (a) at (0,0) {MeO} ;
\node (b) at (1,0) {O} ;
\node (c) at (2,0) {O} ;
\node (d) at (3,0) {n-Pr} ;
\node (e) at (4,0) {O} ;
\node (f) at (5,0) {MeO} ;
\node (g) at (0,1) {MeO} ;
\node (h) at (1,1) {O} ;
\node (i) at (2,1) {O Me} ;
\node (j) at (4,1) {O} ;
\node (k) at (5,1) {OMe} ;
\node (l) at (4,1.5) {100\% Conversion} ;
\node (m) at (6,0) {H\textsubscript{2}O\textsubscript{2} (8 eq.), HCO\textsubscript{2}H (8 eq.)} ;
\node (n) at (6,1) {DCE, 50 °C, 24 h} ;
\node (o) at (7,0) {MeO} ;
\node (p) at (8,0) {O} ;
\node (q) at (9,0) {OMe} ;
\node (r) at (10,0) {78\% yield} ;
\draw [->] (a) -- (b) -- (c) -- (d) -- (e) -- (f);
\draw [->] (g) -- (b) -- (c) -- (d) -- (e) -- (f);
\draw [->] (b) -- (h) -- (i) -- (j) -- (k);
\end{tikzpicture}
\end{center}

\textbf{Scheme 16.} Lignin depolymerization reaction reported by Patil et al.\textsuperscript{32}

As a consequence of the acidic nature of the reaction mixture, a 78\% yield of 3,4-dimethoxybenzoic acid from hydrolysis of a $\beta$-O-4 model was reported.\textsuperscript{32} Consistent with reported trends observed by Westwood,\textsuperscript{33} Stahl,\textsuperscript{30} Wang,\textsuperscript{35} and Toste,\textsuperscript{62} the phenol product was not isolated. The authors attributed the absence of phenol to polymerization.\textsuperscript{32}

In another report, vanadium was identified as one of the more promising base metals for lignin oxidation. Toste and Son\textsuperscript{62} reported that a vanadium/Schiff base catalyst can selectively oxidize the $\alpha$-position of a $\beta$-O-4 model compound,
producing up to 82% yield of the $\text{C}_\beta$-$\text{C}_\gamma$ unsaturated ketone resulting from $\text{C}_\beta$-$\text{O}_4$ bond cleavage (Scheme 17). In this reaction guaiacol was also recovered, albeit in a maximum yield of 64%.

The reaction was found to proceed under anaerobic conditions. In the absence of oxygen yields of the $\alpha$-$\beta$-unsaturated ketone decreased (yields of 60% and 64% being obtained for the $\alpha$-$\beta$-unsaturated ketone and guaiacol, respectively), and formation of a purple precipitate was observed. However, guaiacol was recovered in similar yields to that of the $\alpha$-$\beta$-unsaturated benzylic ketone, oxidation likely occurring due to the presence of sub-stoichiometric amounts of oxygen dissolved in solution. Although the reaction mixture was prepared in a glovebox, the reaction solvent (acetonitrile) was not sparged prior to the reaction; hence, it is conceivable that dissolved oxygen was present in solution. The precipitate was determined to be a catalytically inactive vanadyl $\mu$-oxo dimer (Scheme 17). The authors observed that under aerobic conditions the $\mu$-oxo dimer is solubilized and appears as a deep purple homogeneous reaction mixture. The authors state that the absence of oxygen results in the precipitation the catalyst, making the reaction readily heterogeneous. Vanadium oxidations are establishing a strong foothold in selective homogeneous benzylic oxidations with multiple reports in the recent literature.
Multiple bonding and electronic interactions provide vanadium-based catalysts with intrinsic activity. Unfortunately, the same activity that makes vanadium complexes active catalysts proves problematic with respect to their immobilization on metal oxide supports. Indeed, vanadium is known to leach into reaction solutions and re-precipitate onto metal oxide supports upon cooling, leaving ambiguity with respect to identification of the active catalyst. While vanadium is re-deposited onto the catalyst support during batch reactions, in a flow reactor the active metal would be leached from the support, resulting in catalyst deactivation.

In a report concerning vanadyl sulfate, Wang and co-workers also reported successful benzylic oxidation (98% yield) using a vanadyl sulfate/TEMPO/oxygen system (Scheme 18). In addition to the expected benzylic
ketone (53% yield), the reaction also yielded an unexpected α-retro aldol product (20% yield). Benzylic ketones that undergo retro aldol reactions are simplified by the loss of formaldehyde.\textsuperscript{35,68} Oxidation of the γ-alcohol to formaldehyde has in fact been shown to increase the reactivity of lignin model compounds likely due to a decrease in steric hindrance. To date no reaction conditions focus on selective benzylic oxidation followed by production of formaldehyde by α-retro aldol reaction. The resulting lignin could then be transformed to specialty chemicals from fragmentation of β-O-4 linkages.

Following vanadium-based benzylic oxidation, Wang et al.\textsuperscript{35} went on to cleave several lignin model dimers with a copper/phenanthroline/superoxide system forming benzoic acid and phenols, with the C\textsubscript{β} being lost as carbon dioxide (Scheme 19). As previously reported, phenols were isolated in lower yields than benzoic acids. The authors noted a significant decrease in the yield of phenols in models with electron-donating methoxy groups.\textsuperscript{35} Both the α-retro aldol product and benzylic ketone were converted to benzoic acids in excellent yields (\textit{i.e.}, the product of selective α-oxidation, in 92% yield and the product of α-retro aldol in 95% yield). It was also found that the retro aldol product was more reactive to the copper/phenanthroline oxidation system than the intended α-oxidation product. Furthermore, the above oxidation was performed in methanol, a solvent readily susceptible to oxidation. However, catalytic compatibility with
polar protic solvents such as methanol is highly desirable from the standpoint of cost-effective dissolution of lignin.

Scheme 19. Lignin model cleavage as reported by Wang et al.\textsuperscript{35}

In another study by Wang and co-workers,\textsuperscript{69} oxidative C-C bond cleavage of models with \( \beta-1 \) like functionality was explored. Contrary to their first publication, the authors found that the presence of an organic ligand (e.g., phenanthroline) was not necessary for catalytic C-C bond cleavage. Indeed, the authors found that \( \beta-1 \) models were converted into their corresponding acids and aldehydes using only copper (II) acetate and boron trifluoride etherate as a catalytic Lewis acid (Scheme 20).

Scheme 20. Oxidation of desoxyanisoin performed by Wang and co-workers.\textsuperscript{69}

In fact, the modified catalytic system increased the activity of the copper/superoxide complex in models that are increasingly difficult to oxidize (Scheme 20). Models like desoxyanisoin are generally more difficult to depolymerize because of the absence of a \( \beta \)-aryl ether linkage. In \( \beta-O-4 \) linkages the \( \beta \)-aryl ether bond is the weakest bond in the bridging connection between monolignols. Despite the \( \beta-1 \) unit not benefiting from weakening of the aryl bond
upon oxidation, a number of these models were converted to benzoic acids in almost quantitative yield. The increased catalytic activity was attributed to the presence of a strong Lewis acid in the form of boron trifluoride etherate. The authors propose that polarization of the carbonyl oxygen to boron sufficiently increases the acidity of the $C_\beta$ protons, which are then more easily removed. In addition to oxidizing $\beta$-1 models, the authors also found this oxidation system effective in fragmenting $\beta$-O-4 models to benzoic acids and phenols.

As in previous reports, Wang and co-workers$^{69}$ found this catalytic oxidation system to be compatible with polar protic solvents such as methanol, which appear to be unreactive towards reactive intermediates. However, in the reaction of anisoin (desoxyanisoin with a $\beta$-carbinol), no conversion was observed. This observation suggests that anisoin is not an intermediate in the oxidation of desoxyanisoin to 4-methoxybenzoic acid. As an alternative the authors propose the reaction may proceed first by nucleophilic attack of peroxide at the $\beta$-carbon, followed by peroxide homolysis. Peroxide homolysis forms a radical oxygen species (Fig. 15). In the cited contribution,$^{69}$ the radical aryl intermediate is converted to benzoic acid presumably by the radical coupling of a hydroxyl radical although it was not clearly mentioned.

While the $\beta$-radical oxygen seems like a reasonable intermediate, hydrogen abstraction yielding anisoin is also likely. The proposed reaction intermediate is particularly likely to abstract a proton from the methanol
considering this reaction is conducted in a polar protic solvent, making protons readily accessible. Due to the high selectivity to benzoic acid, a two-electron process is more likely than the key reaction intermediate proposed by the authors in Fig. 14. Indeed, the benzoic acid and phenol produced by the reaction are consistent with the product of alkyl migration in Baeyer-Villger type oxidations.

$$\text{R} = \text{phenyl (}\beta\text{-1) or phenoxy (}\beta\text{-O-4)}$$

Key reaction intermediate

Figure 14. Mechanism proposed by Wang and co-workers.$^{69}$

Recently Wang and co-workers$^{70}$ published an additional contribution under similar reaction conditions finding that copper nitrate was a sufficiently active catalyst for the aerobic oxidation of acetophenones and lignin model compounds in acetonitrile. In addition to conventional lignin model compounds, the authors also investigated oxidation of molecules such as 3,4-dihydronaphthalenone to 1,3-isobenzofurandione in 98% yield, highlighting the power of this oxidation system (Scheme 21).

Scheme 21. Oxidation of 3,4-dihydronaphthalenone performed by Wang and co-workers.$^{70}$

In a follow up study, Wang et al.$^{71}$ investigated the versatility of a similar catalytic system for the oxidation of benzylic alcohols followed by C-C bond
cleavage (Scheme 22). Using a catalytic system similar to previous reports from the authors, yields of benzoic acids resulting from the oxidation of 1-phenylethanol reached a maximum of 98% in DMSO at 130 °C. Upon kinetic investigation, the authors proposed that the benzylic alcohol is first oxidized to acetophenone. The resulting benzylic ketone contains β-hydrogen atoms of increased acidity and is then deprotonated, resulting in the production of a β-carbinol. The β-carbinol is then oxidized to carbon dioxide by a cascade of oxidation reactions. The formation of carbon dioxide was speculated based on the formation of a gaseous product in the liquid phase.

Scheme 22. Oxidation of phenyl ethanol to benzoic acid reported by Wang et al.71

In addition to 1-phenyl ethanol, the oxidation of several benzylic alcohols and β-O-4 model compounds was explored. The oxidation system above was found to be less active for lignin model compounds that have not been oxidized. The highest yield of benzoic acid resulting from cleavage of a lignin model compound was 79% (Scheme 23). Additionally, as the complexity of the models increased, yields of the corresponding benzoic acids decreased. As in similar publications by this group the yield of phenols was not reported likely due to phenol consumption via phenolic radical coupling reactions.
Despite the excellent yield of benzoic acids reported by the authors, the reactions were conducted in dimethyl sulfoxide (DMSO), from which it is difficult to isolate reaction products. Furthermore, DMSO can be oxidized to dimethyl sulfone, which is a non-volatile solid. However, the potential for solvent oxidation was not discussed. The numerous reports from this group suggest that the reaction mechanism and the catalytically active species are not well known, evidenced by the changes in reaction solvent and ligands in the above publications.

The above reports serve as current examples of copper catalyzed oxidations of lignin models. However, the catalyst is homogeneous, making separation of the catalyst from the reaction products difficult. Additionally, the formation of metallorganic complexes (i.e., copper benzoate) is possible and could lead to catalytically inactive metal species.

In another report of benzylic oxidation, Motteweiler et al.\textsuperscript{72} incorporated an iron DABCO/H\textsubscript{2}O\textsubscript{2} oxidation system and explored the oxidation of lignin model compounds in DMSO/water solvent. Models were oxidized to guaiacol and veratraldehyde in a maximum yield of 46\% and 47\%, respectively (Scheme 24, entry (a)).\textsuperscript{72-73} As noted in a review by Ralph, Bruijnincx, and Weckhuysen,\textsuperscript{73} this
reaction system showed functional group sensitivity when subjected to unprotected phenols, resulting in a 27% yield of guaiacol as the only identifiable product (Scheme 24, entry (b)).

The reaction is believed to proceed through a Fenton type mechanism, involving iron-based hydrogen peroxide activation and subsequent homolysis. After hydrogen peroxide homolysis, phenolic protons are abstracted and polymerization reactions occur.

1.6.6. Heterogeneous oxidation of lignin model compounds

Heterogeneous catalysts present obvious industrial advantages over their homogeneous analogues, namely ease of separation and high stability. However, heterogeneous catalysts present unique challenges to researchers, such as multiple types of active sites, diffusion limitations, and difficult characterization.
Starting around the 1990’s heterogeneous catalysts, in the form of immobilized laccases and peroxidases for lignin oxidation, were studied with limited success. Most immobilized peroxidases are used by the bleaching and dye industries, as well as in waste water treatment. One of the main problems preventing immobilized metalloporphyrins from being industrially feasible is the relatively high synthesis cost. Therefore, many reports focus on supported metal nanoparticles.

In a report by Deng et al., the authors explored supported palladium nanoparticles on various supports for oxidative fragmentation of lignin model compounds. The authors found that ceria was the most effective support for the oxidation of $\beta$-O-4 model compounds (Scheme 25). In this contribution $\beta$-O-4 model compounds were converted to methyl benzoate in 40% yield. Additionally, Deng et al. observed acetophenone and guaiacol in good to excellent yields (38% and 82%, respectively). The ketone dimer and the product of benzylic methylation were not observed. The reaction likely proceeds via benzylic oxidation, after which the ketone is thermally cleaved to form benzoic acid and guaiacol (the $\beta$-carbon likely being lost as carbon dioxide).
Scheme 25. Oxidation of a β-O-4 compounds performed by Deng et al.\textsuperscript{75}

The reaction temperatures used by Deng \textit{et al.}\textsuperscript{75} are capable of thermally converting benzylic ketones to benzoic acid under aerobic conditions in the absence of a catalyst (discussed in Chapter 3). Benzoic acids are functionalized with the reaction solvent yielding methyl benzoate. On the other hand, acetophenone likely results from non-oxidative cleavage of the C\textsubscript{β}-O\textsubscript{4} bond of the benzylic ketone. The presence of acetophenone is somewhat surprising considering the strongly oxidizing conditions. Additionally, the authors reported an 82\% yield of guaiacol. Guaiacol and like phenols are often polymerized, initiated by hydrogen abstraction to form a phenolate radical, which is a common problem in lignin oxidation chemistry. However, in this reaction system only a minor amount (ca. 8\%) of guaiacol was unaccounted for as calculated by subtracting the yield of guaiacol from the total conversion. It is possible that the ceria support slows the consumption of guaiacol by adsorption of molecular oxygen, which can behave as a two-electron oxidant as well as a diradical due to its paramagnetic electron configuration. The mixed oxidation state of cerium (\textit{i.e.}, Ce\textsuperscript{3+}, Ce\textsuperscript{4+}) facilitates oxygen adsorption, and renders the surface oxygen extremely labile.\textsuperscript{76} It has been found that under elevated temperatures guaiacol
can be polymerized under aerobic conditions in the absence of a catalyst, as discussed in Chapter 3.

The authors went on to apply their catalyst to an organosolv lignin, converting it to ca. 8% monomers. The monomer distribution from oxidation of organosolv lignin was found to be vanillin (5.2% yield), guaiacol (ca. 1% yield), and 4-hydroxybenzaldehyde (2.6% yield). While this is an excellent example of the oxidation of lignin and of a lignin model compound, the catalyst uses expensive noble metal nanoparticles and the solvent is partially consumed during the reaction.

Recently, other basic heterogeneous supports have been explored with the goal of avoiding the use of noble metals. Layered double hydroxides comprise one such material, those being anionic clays capable of catalytic activity with or without additional supported metals.

1.6.7. Layered double hydroxides

Layered double hydroxides (LDHs), or hydrotalcites, are brucite-like anionic clays. The hydroxide layer consists of di- and trivalent metals octahedrally coordinated by hydroxide groups. This bonding motif forms stacked, positively charged, two-dimensional sheets, illustrated in Fig. 15. Positive charge is compensated by anions (commonly carbonates), located in the interlayer
region. The result of these interactions is an LDH with a general formula shown in (Equation 1). A representation of the LDH structure is shown in Fig. 15.

Equation 1. Generic LDH formula as reported by Guczi and Erdőhelyi,78

\[
[M^{2+}_1 M^{3+}_x (OH)_2]^x+ (A^{n-})_x \cdot \frac{m}{n} H_2 O
\]

Where \( M \) is a divalent or trivalent metal, \( x \) is the overall charge of the hydroxide sheet, \( A \) is the anion, \( n \) is the anion charge and \( m \) is the number of water molecules in the crystal structure.

Figure 15. Representation of a LDH structure published by Sturgeon et al.79 Red spheres represent hydroxide groups. Copyright (2014) RSC Advances.

These materials have recently attracted much attention due to their anion exchange capacity, as well as inherent properties such as high surface area, catalytic activity, and the well documented “memory effect”.80 Upon thermal pretreatment, LDHs are converted to mixed metal oxides (MMOs) possessing increased surface area and near-atomic dispersion of the metals. Moreover, LDH derived MMOs can be “rehydrated” with aqueous solutions of metal carbonates or bicarbonates to restore the LDH structure (the memory effect). As mentioned above, unlike conventional catalyst supports, LDHs themselves are often catalytically active, giving them a dual function, i.e., support and catalyst.
Additionally, metals can be deposited on the surface of the basic support, which in some cases increases the catalytic activity. Mobley and Crocker\textsuperscript{81} recently reviewed the use of hydrotalcites and hydrotalcite-like compounds for heterogeneous oxidation of alcohols.

In one of the few reports of LDH-derived catalytic oxidation of lignin model compounds, Beckham and co-workers\textsuperscript{82} recently described near quantitative conversion of a lignin model compound using a hydrotalcite-supported nickel (5 wt.\%) catalyst at 270 °C (the reaction gas was not explicitly stated in the publication). Unfortunately, yields were not reported and products were analyzed by concentration in solution. It is likely that β-aryl ether cleavage begins with benzylic deprotonation followed by simple thermal cleavage of the Cβ-O4 bond (Fig. 16). As discussed above, the β-aryl ether is ca. 85 kJ/mol weaker after benzylic oxidation.\textsuperscript{35}

![Figure 16. Potential mechanism for β-aryl ether cleavage performed by Beckham and co-workers.\textsuperscript{79} HTC = hydrotalcite.](image)

Furthermore, similar results were obtained in the reaction of the model with aqueous sodium hydroxide. In all cases, lower yields of acetophenone were observed relative to phenol. The authors attribute this to aldol condensation reactions with the solvent (methyl-isobutyl ketone (MIBK)). Choosing a solvent
for oxidation reaction is difficult due to the requisite high polarity to dissolve lignin and model compounds, while not participating or reacting in catalytic oxidation.

In a follow up study by Beckham and co-workers, nitrate intercalated hydrotalcites and hydrotalcite supported nickel catalysts were explored for their activity in oxidation of lignin model dimers to acetophenones and phenols. Models of increasing complexity were oxidized at 275 °C. As a substitute for MIBK, 3-methyl-3-pentanol (3M3P) was used as the reaction solvent. The incorporation of a tertiary alcohol (3M3P) as the reaction solvent prevents oxidation. Although tertiary alcohols are incapable of being oxidized, they are prone to elimination, which was not discussed in the report. Additionally, 3M3P is prohibitively expensive for industrial scale up.

The authors did not observe the ketone resulting from benzylic oxidation in appreciable amounts during the reaction. Therefore, the Beckham and coworkers concluded that the ketone was not a primary route to formation of acetophenone or phenols resulting from β-aryl ether cleavage. Unfortunately, the authors did not subject the corresponding benzylic ketone to the aforementioned reaction conditions, which could have provided meaningful information regarding a mechanistic evaluation. In contrast to what the authors proposed, it is possible that the reaction does indeed proceed through oxidation to the benzylic ketone, which is then thermally cleaved to afford acetophenone and phenol. However, the authors did speculate that β-aryl ether cleavage may proceed through an
enol ether intermediate. The enol ether intermediate was indicated by the successful dehydration of a simple (more stable) β-1 model to stilbene using the most active catalyst in the contribution (Scheme 26). Although the β-1 model was efficiently converted to stilbene, further oxidation was not observed. Moreover, stilbene represents a linkage increasingly similar to the recalcitrant 5-5 linkage.

The model used to support an enol ether reaction pathway is conjugated after dehydration, unlike β-O-4 models. Resonance stabilization of the stilbene resulting from dehydration may lead to misinterpretation of the reaction mechanism.

![Scheme 26. Dehydration of a β-1 model performed by Beckham and co-workers.](image)

The authors highlight the heterogeneous nature of nitrate ions in the catalytic system, as confirmed by the low catalytic activity of NaNO₃. The authors also speculate that the removal of the benzylic alcohol may proceed via nitration, which would also likely require homogenous nitrate ions. Lignin model compound depolymerization is likely a combination of nitrate and nickel peroxide-mediated β-aryl ether cleavage. Although the mechanism of catalytic formation of lignin model compounds to acetophenone and phenol resulting from β-aryl ether cleavage was not confidently elucidated in this report, it is one of the first reports of oxidative depolymerization of lignin model dimers using hydrotalcite-like catalysts.
In another report of hydrotalcite catalyzed oxidation, Corma and co-workers\textsuperscript{83} reported successful oxidation of lignin model dimers and a variety of technical lignins using a copper and vanadium doped hydrotalcite (Scheme 27). In their initial investigation the authors attempted oxidation with copper on hydrotalcite, converting 77\% of starting material. Upon addition of vanadate into the interlayer spacing, they observed near quantitative conversion. Unfortunately, the reaction continued after hot filtration of the catalyst, implying that the active metal species leached into solution. The main reaction products were veratraldehyde and veratric acid, which were obtained in various ratios with no obvious trend, likely due to auto-oxidation of veratraldehyde. The minor co-products observed are likely reaction intermediates preceding retro-aldol based cleavage of the C$_{\beta}$-O$_{4}$ bond. It would be interesting to see the influence of increased reaction time on product distribution. It would be reasonable for the dimeric models isolated in 5\% and 3\% yields to continue to react, perhaps at the expense of decreased guaiacol yields.

![Scheme 27: Oxidation of a lignin model dimer as reported by Corma and co-workers.]

The authors also confirmed that the reaction proceeded with homogeneous analogues of the active metal species. When the reaction time was increased (17 h), 97\% conversion was observed with 2.5 mol\% vanadyl
acetylacetonate and 1 mol% copper (II) nitrate. This is a valuable example of hydrotalcite-based lignin oxidation, but metal-support interactions must be improved in order to develop an industrially viable oxidation system.

1.7. Conclusions and Outlook

Lignin utilization is still in its infancy despite being an active area of research for over a century. However, recent reports of selective benzylic oxidation provide relatively unexplored routes to the production of small molecules from lignin. From the literature reports summarized above, it would appear that benzylic oxidation represents a key step towards industrial lignin utilization. Benzylic oxidation generally proceeds at relatively low temperatures (cf. HDO) and often uses inexpensive and widely available oxidants (i.e., molecular oxygen and peroxides). Although the reports summarized in this work represent groundbreaking advances in lignin utilization, many of them are performed on a small scale using homogenous catalysts. Industrially, homogeneous catalysts are sub-optimal due to the difficulty of separating them from depolymerization products. Therefore, more work must be conducted to make the reaction systems discussed in this work economically feasible.

After benzylic oxidation, a majority of reports continue down an oxidative pathway leading to a variety aromatic monomers. To our knowledge, heterogeneous reductive cleavage (HDO) of oxidized lignin has not been studied. It can be speculated that oxidized lignin may prove to be an increasingly versatile
feedstock (cf. protolignin or extracted lignins) that can undergo further oxidation to fine chemicals and reduction to form BTXs. Indeed, the oxidation of lignin linkages should render oxidized lignin a more labile biorefinery feedstock than extracted and native lignins by providing a comparatively reactive carbonyl moiety. Considering the process of lignin fragmentation, the presence of one-electron oxidants should be limited to prevent lignin repolymerization reactions. Although most of the processes reviewed here are not commercially feasible, they represent steps toward an effective lignin strategy, this being a necessity if biorefineries are to realize their full economic potential.

Ultimately the daunting task of efficient lignin utilization will be a cooperative multidisciplinary effort. Synergistic application of bioengineered lignins with established chemical modifications would provide a more easily manipulated feedstock for scaling up and separating into discrete molecules. Moreover, even after methods for the production of discrete molecules from lignin have been developed, the efficient separation of monomers must be investigated.
Chapter 2. Regioselective Baeyer-Villiger Oxidation of Lignin Model Compounds with Tin Beta Zeolite Catalyst and Hydrogen Peroxide

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2.1. Introduction

Lignin is biosynthesized to defend plant-life against chemical and biological attack. As the largest natural source of aromatics, products of lignin depolymerization have potential as both renewable fuel (e.g., benzene, toluene, and xylenes (BTX)) and fine chemicals (e.g., vanillin). However, most lignin produced by the pulp and paper industries is currently burned on-site as a low-grade fuel. Due to lignin’s characteristic irregularity and poor solubility, lignin is challenging to utilize on an industrial scale.

In lieu of using lignin, which is difficult to analyze, models of various linkage motifs are commonly used to investigate depolymerization strategies. The most abundant of these linkages is the β-O-4 structure, which represents up to 60% of the linkages found in lignin. A benzylic alcohol moiety and a bridging aryl ether bond are characteristic of the β-O-4 linkage. Many lignin depolymerization strategies focus on cleaving the bridging ether groups using thermal and/or reductive techniques, requiring high temperatures and pressures. As an alternative, Stahl and co-workers performed an extensive study of stoichiometric oxidants, metal-catalyzed aerobic oxidation and metal-free catalytic aerobic oxidations. The authors found the most selective and efficient benzylic oxidation system to be 4-acetamido-2,2,6,6-tetramethylpiperidine-N-oxyl/oxygen, yielding almost quantitative benzylic oxidation for “dimeric” model compounds (i.e., compounds containing two aromatic groups linked in β-O-4 fashion). The authors also reported that in some less selective oxidation
systems, after γ-oxidation, models were converted to substituted aldehydes via retro aldol reactions. According to Stahl and co-workers, the utility of this retro aldol reaction is limited due to formation of unidentified products, presumably phenolic radical coupling products. Retro aldol reactions have been reported for both α and γ-ketones.

After benzylic oxidation, Stahl and co-workers cleaved the β-O-4 linkage via Dakin oxidation, affording an 88% yield of 3,4-dimethoxybenzoic acid and 42% yield of guaiacol (Scheme 28). The low yield of guaiacol is derived from phenolic radical coupling initiated by hydrogen peroxide, which is capable of both one and two-electron oxidations. Indeed, poor isolated yields of phenolic compounds is a common problem in the oxidation of aromatic molecules.

![Scheme 28. Dakin oxidation of a lignin dimer model compound performed by Stahl and co-workers.](image)

Westwood and co-workers also reported almost quantitative benzylic oxidation of lignin model compounds using a 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)/oxygen system. After zinc-based reduction/cleavage the authors obtained up to 92% isolated yields of substituted propylarenes, although the yields of phenolic moieties were not reported.
Wang and co-workers\textsuperscript{35} also observed almost quantitative benzylic oxidation of lignin model compounds using vanadyl sulfate/TEMPO/oxygen (Scheme 29). In addition to benzylic ketones, the reaction also yielded an unexpected $\alpha$-retro aldol product (20\% yield). Benzylic (C$_\alpha$) retro aldol reactions simplify models by elimination of formaldehyde, increasing the reactivity in oxidizing systems.\textsuperscript{35,68} Indeed, Wang \textit{et al.}\textsuperscript{35} found that models with no $\gamma$-carbon were more active to further oxidation.

Following benzylic oxidation, Wang \textit{et al.} depolymerized the ketone with a copper/phenanthroline/superoxide system to form a benzoic acid and a phenol, the authors noting a significant decrease in phenol yields in models with electron-donating methoxy groups.\textsuperscript{35}

![Scheme 29. Benzylic oxidation performed by Wang \textit{et al.}\textsuperscript{35}](image)

In one of the few reports resulting in high yields of phenols, Stahl and co-workers\textsuperscript{31} used a redox-neutral system (excess formic acid and sodium formate) to effectively depolymerize oxidized lignin and lignin model compounds to discrete products. Depolymerization products of models included phenols, which were obtained in excellent yields (Scheme 30). The absence of a one-electron reactant supports the hypothesis that phenols produced in a peroxide-free environment can be isolated in excellent yields. However, this very successful
example of β-O-4 cleavage suffers from a large excess of formic acid and is homogeneous in nature.

![Scheme 30. Depolymerization of a lignin model compound performed by Stahl and co-workers.](image)

Although selective benzylic oxidation is a rather facile first step, there are few methods for which the phenolic portions of models produced by Cβ-O4 bond cleavage are isolated in high yield. To avoid the production of phenolate radicals, which readily repolymerize, benzylic ketones can be converted directly to esters via Baeyer-Villiger Oxidation (BVO), and subsequently hydrolyzed in a one-electron free medium. In another publication concerning benzylic oxidation of lignin model compounds, Patil et al. reported the first well-characterized homogeneous BVO of an aromatic ketone using an oxidation system generating performic acid in situ (Scheme 31).
As a consequence of the acidic nature of the reaction, a high yield of 3,4-dimethoxybenzoic acid from hydrolysis of the β-O-4 model was reported (Scheme 31, entry (a)). The complete absence of the phenol co-product was attributed to polymerization. In the same report a BVO product (not hydrolyzed in-situ) was reported in 10% yield (>99% selectivity) (Scheme 31, entry (b)).

Recently, several heterogeneous systems for the oxidation of lignin model compounds have been identified. However, these catalysts do not yield ester products resulting from oxygen insertion. Rather, reports of heterogeneous oxidation result in small molecules resulting from Cα-Cβ or Cβ-O4 bond cleavage. In the present study an oxidation system consisting of hydrogen peroxide (a weaker oxidant than performic acid) and a heterogeneous tin beta zeolite catalyst was explored in an effort to avoid phenolic polymerization. The nature of this reaction system was anticipated to facilitate ready isolation of the desired products.
Most reports of heterogeneously catalyzed BVO concern cyclic ketones,\textsuperscript{87} with few reports of acyclic ketones, and even fewer of benzylic ketones. BVO of aromatic aldehydes to formate esters using hydrothermally synthesized tin beta zeolite has been reported,\textsuperscript{88} but employed highly active peroxyimidic acids. Panchgalle \textit{et al.}\textsuperscript{89} reported BVO of acetophenone derivatives using an ionic liquid as co-oxidant, but provided no details of the catalyst synthesis, characterization, or role of the ionic liquid. Hydrothermally synthesized tin beta zeolite has also been reported as being active in several other Lewis acid catalyzed reactions such as Meerwein-Ponndorf-Verley (MPV) reductions.\textsuperscript{90} However, synthetic challenges such as long crystallization times (\textit{e.g.}, 20 days), and hazardous synthetic reagents (hydrofluoric acid) make large-scale hydrothermal synthesis of tin beta zeolite problematic.\textsuperscript{91}

As an alternative to hydrothermal synthesis, tin beta zeolite has recently been synthesized using post-synthetic (PS) modification strategies.\textsuperscript{91-95} Indeed, PS incorporation of tin into beta zeolite has presented numerous advantages over hydrothermal synthesis, \textit{e.g.}, higher tin loading, introduction of multiple active sites, and smaller beta particle size.\textsuperscript{91} PS tin beta zeolite has been used for many of the same heterogeneously catalyzed reactions as its hydrothermally synthesized analogue, including BVO,\textsuperscript{87, 91, 93-95} MPV reductions,\textsuperscript{87} Oppenauer oxidations (OPO),\textsuperscript{87} hydration of epoxides\textsuperscript{93} and glucose isomerization.\textsuperscript{92} In this
work, we applied a PS tin beta zeolite/hydrogen peroxide oxidation system to acetophenone derivatives and dimeric lignin model compounds.

2.2. Experimental Methods

2.2.1. Catalyst Characterization

X-ray diffractograms were collected on a Phillips PW 3040 X-ray diffractometer using Cu Kα radiation (\(\lambda = 1.54184 \, \text{Å}\)) and a step size of 0.02°. X-ray diffractograms were referenced to the International Centre for Diffractogram Data (ICDD) database. Elemental concentrations were determined by Proton-Induced X-ray Emission (PIXE) (Elemental Analysis Inc., Lexington, KY). Room temperature solid state NMR spectra were acquired using a Tecmag Redstone spectrometer (Tecmag, Inc., Houston, TX) operating at 111.917 MHz for \(^{119}\text{Sn}\) (7.05 T static magnetic field). Samples were packed into 7.5 mm zirconia rotors and sealed with Teflon or Kel-F end caps (Revolution NMR, LLC, Fort Collins, CO). Experiments were performed using a 7.5 mm double resonance MAS probe (Varian, Palo Alto, CA). All \(^{119}\text{Sn}\) spectra were acquired under MAS at 5 kHz at ambient conditions. \(^{119}\text{Sn}\) chemical shifts are reported relative to samarium stannate at -102.6 ppm with an accuracy of ±0.4 ppm. \(^{119}\text{Sn}\) spectra were collected with a single pulse on \(^{119}\text{Sn}\) followed by acquisition. All spectra were acquired with a 50 second recycle delay and a 2.56 msec acquisition time. Dehydrated samples were heated to 473 K in vacuo overnight, prior to data collection. Scanning electron microscopy (SEM) was performed on a Hitachi S-2700 microscope equipped with a LaB₆ gun and a PGT EDS analyzer with thin
window detector. Samples were gold-coated prior to imaging. Brunauer–Emmett–Teller (BET) surface area and micropore volume measurements were determined by nitrogen adsorption at 77 K using a Micromeritics Gemini VII analyzer. Prior to measurement, samples were degassed at 423 K under nitrogen. X-ray Photoelectron Spectroscopy (XPS) was performed on a Kratos Axis HSi X-ray photoelectron spectrometer equipped with a charge neutralizer and magnetic focusing lens, using a monochromated Mg Kα X-ray source ($hν = 1253.6$ eV). Spectra were referenced to the adventitious C 1s peak at 284.6 eV. Prior to analysis, XPS samples were dried under high vacuum at 303 K and then transferred to an in situ stage where they were dried at 673 K in vacuo for 1 h. UV-vis Diffuse Reflectance spectra were collected on a Varian Cary 5000 spectrometer using barium sulfate as a reference. Ammonia temperature programmed desorption (NH₃-TPD) experiments were performed on a Micromeritics AutoChem II analyzer using 0.500 g of sample. In each case the sample was first dehydrated at 673 K under argon for 1 h, cooled to 363 K and saturated with NH₃ (1% in helium, 50 sccm) for 1 h. Next, the sample was purged with He (120 sccm) for 1 h. The sample was then heated to 1023 K at 10 K/min. Effluent gas was analyzed using a mass spectrometer (Pfeiffer Thermostat GSD301), the signal at $m/z = 15$ being used to monitor NH₃. Single crystal X-ray diffraction data were collected at 90.0(2) K on a Bruker-Nonius X8 Proteum diffractometer with graded-multilayer focused Cu Kα x-rays. Raw data were integrated, scaled, merged and corrected for Lorentz-polarization effects using the APEX2 package. Corrections for absorption were applied using SADABS.
The structure was solved by direct methods (SHELXT)\textsuperscript{98} and refined against F^2 by weighted full-matrix least-squares (SHELXL-2014).\textsuperscript{99} Hydrogen atoms were found in difference maps but subsequently placed at calculated positions and refined using a riding model. Non-hydrogen atoms were refined with anisotropic displacement parameters. The final structure model was checked using an R-tensor\textsuperscript{100} and by Platon/checkCIF.\textsuperscript{101} Atomic scattering factors were taken from the International Tables for Crystallography.\textsuperscript{102}

2.2.2. Synthesis of grafted tin beta zeolite (Si:Al ratio = 25:1)

Commercial H-beta-zeolite (25 g), obtained from Clariant\textsuperscript{®} (Si:Al ratio = 25:1), was treated with 13 M nitric acid and heated at 353 K overnight (solid/liquid ratio = 1 g/ 20 mL). The mixture was filtered and washed with deionized water until neutral. This dealumination procedure was repeated a second time. Two batches were mixed and dried in vacuo overnight at 343 K, yielding De-Al beta (42.8 g). De-Al beta was added to a solution of butyltin trichloride (7.6 mL, 45.6 mmol) in anhydrous toluene (150 mL) under nitrogen and stirred at room temperature for 1 h. The solution was neutralized by addition of triethylamine (17.6 mL, 126.2 mmol) and stirred for 1 h. The suspension was then filtered, washed with toluene (500 mL), and dried overnight in a vacuum oven. The catalyst was heated in air to 623 K for 30 min followed by calcination at 773 K for 3 h, yielding 37.3 g of Sn-beta zeolite.
2.2.3. Synthesis of lignin model compounds

Model compounds 6\textsuperscript{103} and 7\textsuperscript{104} were synthesized according to literature procedures which are included in the Appendix I.

2.2.4. Procedure for Baeyer-Villiger Oxidations

All reagents were purchased from Fisher Scientific or Sigma Aldrich and were used without further purification, unless stated otherwise. In a typical reaction, tin beta zeolite (0.150 g), 4-methoxyacetophenone, 3 (0.451 g, 3 mmol), 1,2-dichloroethane (3 g) and 30% hydrogen peroxide (2 mL, 20 mmol) were added to a 50 mL round-bottomed flask equipped with a jacketed water-cooled condenser, and heated at the desired temperature with stirring for 24 h. After completion of the reaction, the suspension was filtered through a Nylon\textsuperscript{®} membrane (0.45 μm pore size). The catalyst was rinsed with dichloroethane (5 mL x 2) and water (5 mL x 2). The biphasic mixture was separated and the aqueous layer was extracted with dichloroethane (2 mL x 3) and dried over magnesium sulfate. In the case of reusability experiments, the catalyst was calcined at 500 °C for 3 h and allowed to cool to room temperature prior to being reused. For the hydrolysis of 3a, potassium carbonate (0.455 g, 3.3 mmol) in methanol (3 g) was added to the reaction mixture. The mixture was stirred for 30 min at room temperature and was then neutralized with hydrochloric acid to afford 4-methoxyphenol 9b (0.307 g, 98% yield).
Baeyer-Villiger Oxidation of 2-(4-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (6)

Tin beta zeolite (0.15 g), 2-(4-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (0.41 g, 1.5 mmol), 1,2-dichloroethane (3 g) and 30% hydrogen peroxide (2 mL, 20 mmol) were added to a 50 mL round-bottomed flask equipped with a jacketed water-cooled condenser, and heated at the desired temperature with stirring (80 °C, 24 h). BVO product 6a was isolated as described above as brown/orange crystals. GC/MS: m/z 288.1 (24%), 260.1 (10%), 137.1 (100%), 123.1 (17%), 107.1 (24%) and \(^1\)H-NMR (400 MHz, CDCl\(_3\)) δ: 7.05-7.00 (m, 2H), 6.95-6.92, (m, 2H), 6.90-6.85 (m, 2H), 4.80 (s, 2H), 3.80 (s, 3H), 3.78 (s, 3H). 13C-NMR (100 MHz, CDCl\(_3\)) δ: 168.3, 157.7, 155.0, 152.2, 143.8, 122.3, 116.3, 115.0, 114.9, 66.7, 55.9, 55.8. Ferrocene (10 mg/mL) was used as an internal standard to quantify the yield of products in the crude product mixture. HRMS (ESI) m/z [M+H] calculated for C\(_{16}\)H\(_{16}\)O\(_5\) = 289.1076, experimental = 289.1072.

Baeyer-Villiger Oxidation of 2-(2-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (7)

Tin beta zeolite (0.150 g), 2-(2-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (0.41 g, 1.5 mmol), 1,2-dichloroethane (3 g) and 30% hydrogen peroxide (2 mL, 20 mmol) were added to a 50 mL round-bottomed flask equipped with a jacketed water-cooled condenser, and heated at the desired temperature with stirring (80 °C, 24 h). BVO product 7a was isolated as pale yellow crystal. GC/MS: m/z 288.1 (16%), 260.1 (17%), 137.1 (100%), 122.1 (49%), 109.1 (15%) and \(^1\)H-NMR (400 MHz, CDCl\(_3\)) δ: 7.04-7.00 (m, 2H), 6.98-6.86 (m, 6H), 4.92 (s, 2H), 3.90 (s, 3H), 3.79 (s, 3H). 13C-NMR (100 MHz, CDCl\(_3\)) δ: 168.3, 157.7,
Ferrocene (10 mg/mL) was used as an internal standard to quantify the yield of products in the crude product mixture. HRMS (ESI) m/z [M+H] calculated for C_{16}H_{16}O_5 = 289.1076, experimental = 289.1070.

Baeyer-Villiger Oxidation of Desoxyanisoin (8)

Tin beta zeolite (0.15 g), desoxyanisoin (0.39 g, 1.5 mmol), 1,2-dichloroethane (3 g) and 30% hydrogen peroxide (2 mL, 20 mmol) were added to a 50 mL round-bottomed flask equipped with a jacketed water-cooled condenser, and heated at the desired temperature with stirring (80 °C, 24 h). BVO product 8a was isolated as a white solid. GC/MS: m/z 272.1 (4%), 148.1 (100%), 121.1 (95%) and 'H-NMR (400 MHz, CDCl_3) δ: 8.06-8.03, 7.31-7.29 (m, 2H), 6.98-6.96 (m, 2H), 6.89-6.87 (m, 2H), 3.88 (s, 2H), 3.81 (s, 3H), 3.71 (s, 3H). 13C-NMR (100 MHz, CDCl_3) δ: 170.9, 159.1, 144.5, 131.1, 130.6, 128.8, 122.4, 114.6, 114.4, 114.0, 55.8, 55.5, 40.7. Ferrocene (10 mg/mL) was used as an internal standard to quantify the yield of products in the crude product mixture. HRMS (ESI) m/z [M+H] calculated for C_{16}H_{16}O_4 = 273.1127, experimental = 273.1122.

Baeyer-Villiger Oxidation of Anisoin (9)

Tin beta zeolite (0.15 g), anisoin (0.41 g, 1.5 mmol), 1,2-dichloroethane (3 g) and 30% hydrogen peroxide (1 mL, 10 mmol) were added to a 50 mL round-bottomed flask equipped with a jacketed water-cooled condenser, and heated at the desired temperature with stirring (80 °C, 24 h). 4-Methoxybenzoic acid (9b) was isolated as colorless crystals. Ferrocene (10 mg/mL) was used as an
internal standard to quantify the yield of products 9a in the crude product mixture.

2.2.5. Determination of phenyl acetate yields using Gas Chromatography Mass Spectrometry (GC/MS)

GC/MS analyses were performed using an Agilent 7890 GC with a tandem Agilent 5975C MS detector. The column used was a DB-1701 (60 m × 0.25 mm × 0.25 μm) and the temperature program was as follows: 45 °C for 3 min, ramp to 280 °C at 4 °C/min, and hold for 10 min. The flow rate was set to 1 mL/min using helium as the carrier gas. The inlet was maintained at 260 °C, and the MS source was set at 70 eV. An external calibration curve of anisole or dodecane was used to calibrate BVO products in the reaction mixture. Analysis of lignin model dimer compounds proved difficult (due to the low response factors observed for oxidized dimer model compounds). In lieu of calibrated GC/MS yields, 1H-NMR spectroscopy with a ferrocene internal standard was used to determine product yields.

2.3. Results and Discussion

2.3.1. Tin Beta Synthesis and Characterization

Beta zeolite (Si:Al, 25:1) was first treated with 13 M nitric acid to afford dealuminated beta zeolite (De-Al beta) with a Si/Al ratio of >1800 (Table 1). The De-Al beta was treated with butyltin trichloride in toluene, followed by
triethylamine to promote formation of Sn-O-Si bonds via hydrochloric acid elimination (procedure modified from Corma and co-workers).\textsuperscript{107} The catalyst was then calcined at 500 °C for 3 h to remove remaining organic ligands, yielding tin beta zeolite with a Si/Sn ratio of 12 (Sn-beta, 3.7 wt.% Sn) (Table 1).

Table 1. Si/Al ratio, surface area and pore-size distribution of zeolite samples. Tin loading is 3.7 wt.%\textsuperscript{a}

<table>
<thead>
<tr>
<th>Zeolite</th>
<th>Si/Al Ratio</th>
<th>Surface Area\textsuperscript{c} (m\textsuperscript{2} g\textsuperscript{-1})</th>
<th>Pore Volume\textsuperscript{d} (cm\textsuperscript{3} g\textsuperscript{-1})</th>
<th>NH\textsubscript{3} ads. (μmol g\textsuperscript{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>H-beta</td>
<td>25</td>
<td>480</td>
<td>0.142</td>
<td>0.253</td>
</tr>
<tr>
<td>De-Al beta</td>
<td>&gt;1800\textsuperscript{a}</td>
<td>472</td>
<td>0.135</td>
<td>0.227</td>
</tr>
<tr>
<td>Sn-beta</td>
<td>&gt;1800\textsuperscript{ab}</td>
<td>479</td>
<td>0.142</td>
<td>0.158</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Determined by ICP analysis.\textsuperscript{b} Determined by PIXE.\textsuperscript{c} Determined by BET method.\textsuperscript{d}Micropore volume calculated from \textit{t}-plot.

The surface area and micropore volumes measured at each step of tin beta zeolite synthesis (Table 1) showed little variation, indicating removal of framework aluminum did not lead to collapse of the zeolite lattice. Ammonia temperature programmed desorption (NH\textsubscript{3}-TPD) was performed to measure the relative acidity of De-Al beta zeolite and tin beta zeolite. De-Al beta zeolite adsorbed a minimal amount of ammonia, consistent with near complete removal of Al from the framework, while tin beta zeolite adsorbed 28.4 μmol of ammonia per gram of catalyst. Most of the ammonia desorbed below 525 K during TPD, indicating that tin incorporation resulted in weakly acidic sites. Pore-size distribution measurements on the tin beta zeolite showed that 55% of the total pore volume corresponded to the mesopore range. This is noteworthy given that the presence of mesopores is critical to the reaction of bulky lignin model compounds, and ultimately lignin itself.
The preservation of beta zeolite structure was verified via XRD (Fig. 17). Additionally, subtle changes in the d_{302} interlayer spacing confirmed that first dealumination had occurred, with subsequent inclusion of tin. Indeed, the interlayer spacing of H-beta zeolite was reduced from 3.864 Å (2θ = 22.54°) to 3.817 Å (2θ = 22.82°) upon dealumination but increased to 3.856 Å (2θ = 22.59°) after incorporation of tin, consistent with the findings of Tang et al.\textsuperscript{93} In addition to incorporation of tin into the beta zeolite framework, the presence of crystalline extra framework (EFW) tin was also observed (2θ = 26.7° and 34.0°).\textsuperscript{92} Application of the Scherrer equation indicated the average tin dioxide particle size to be 48 nm. EFW species are incorporated as a consequence of tin hydrolysis by adventitious water during grafting, or from calcination due to the high tin loading (3.7 wt.%). The presence of water before calcination hydrolyzes Sn-Cl bonds, forming low-coordinate Sn-OH species; upon calcination, Sn-OH bonds in close spatial proximity dehydrate forming catalytically inactive SnO\textsubscript{2} crystals as opposed to framework Sn-O-Si bonds. Dijkmans et al.\textsuperscript{94} found the maximum tin loading for the PS tin beta zeolite used in their report without formation of EFW species to be approximately 2%. 
Fig. 18 shows SEM images of De-Al beta and Sn-beta. SEM images of the dealuminated beta zeolite show highly textured particles characteristic of beta zeolite. Images of beta zeolite following tin incorporation show textured particles as well as a smaller (~40 nm) secondary phase that is structurally different and which can be assigned to EFW tin dioxide.
In an effort to evaluate tin speciation, $^{119}$Sn magic-angle-spinning (MAS) nuclear magnetic resonance (NMR) spectroscopy was employed. $^{119}$Sn MAS NMR spectroscopy has been reported to effectively distinguish between EFW and framework tin species based on coordination number. Removal of water aids in the elucidation of open tetrahedral, closed tetrahedral and octahedral tin species present in the catalyst. To remove adsorbed water, tin beta zeolite was heated at 200 °C overnight in vacuo prior to data collection. Spectra of both the hydrated and dehydrated samples were collected, effectively monitoring the dehydration process.
As shown in Fig. 19, $^{119}$Sn MAS NMR spectra for hydrated and dehydrated tin beta zeolite contain resonances for both octahedral and tetrahedral tin. The observed resonances in the spectrum of hydrated tin beta zeolite at -630 ppm to -720 ppm are assigned to the presence of hexa-coordinate hydrated tetrahedral tin species. Davis and co-workers observed similar resonances centered at -688 ppm and -700 ppm for hydrated species. Penta-coordinate hydrous tin species present in the spectrum of hydrated tin beta zeolite resonate at -579 ppm, and are absent after dehydration. In a recent report, Yakimov et al. observed penta-hydrated tin species at -581 ppm. Crystalline tin dioxide resonating at -606 ppm was also observed.

In the spectrum of the dehydrated tin beta zeolite (Fig. 19), a broad resonance at -437 ppm indicates the presence of both open and closed tetrahedral tin species, which were previously hydrated. Tetrahedrally coordinated tin species reported by Davis and co-workers were centered at -424 ppm and -443 ppm after dehydration. Furthermore, the authors assigned the downfield resonance to open tin sites (strongly acidic, SnOH(OSi)$_3$) and the upfield resonance to closed tin sites (weakly acidic, Sn(OSi)$_4$). Following dehydration, crystalline tin dioxide was still present as indicated by a resonance centered at -604 ppm corresponding to EFW tin (Fig. 19).
Diffuse reflectance UV-vis spectroscopy is a sensitive technique that can distinguish between octahedral and tetrahedral Sn$^{4+}$ to O$^{2-}$ ligand to metal charge transfer. A local intensity maximum at 200 nm suggests incorporation of tin into tetrahedral sites (Appendix I, Fig. S1), consistent with the finding of Davis et al. who reported an intensity maximum at 203 nm. However, a broad intensity maximum at 281 nm arises from the presence of hexa-coordinate polymeric tin (EFW tin), which largely dominates the spectrum. Consequently, the spectrum of tin beta zeolite is similar to that of bulk tin dioxide (maximum at 270 nm).

Tin speciation was also investigated by X-ray photoelectron spectroscopy (XPS). The spectrum of tin beta zeolite contained broad signals centered around 486.0 eV and 494.6 eV corresponding to tin 3d$^{3/2}$ and 3d$^{5/2}$ photoelectrons (Fig. 20). In comparison, the 3d$^{3/2}$ and 3d$^{5/2}$ photoelectrons of crystalline tin dioxide produced signal maxima at 487.0 eV and 495.5 eV, the signals being much
narrower (FWHM = 1.6 eV) than the corresponding signals for dehydrated tin beta (FWHM = 3.7 eV). We propose that line broadening in the spectrum of dehydrated tin beta is due to the presence of overlapping signals from a mixture of octahedral and tetrahedral Sn⁴⁺ species, consistent with the data presented above.

![XPS spectra of tin beta zeolite and tin dioxide in the Sn 3d region.](image)

In summary, characterization of the synthesized tin beta zeolite confirmed the presence of tetrahedral Sn⁴⁺ species. Given that Lewis acid sites are believed to be responsible for Baeyer-Villiger catalysis, such low coordinate Sn species should function as active sites. These correspond to the "open" and "closed" tetrahedral tin sites observed by \(^{119}\)Sn MAS NMR spectroscopy,
although other coordinatively unsaturated amorphous tin species on the catalyst surface could also contribute to catalysis.

2.3.2. BVO of Simple Cyclic and Acyclic Ketones

In nearly all cases, literature reports of heterogeneous BVO concern cyclic ketones. Thus, in order to compare the catalyst in this work with those reported in the literature, 2-adamantanone was oxidized using the tin beta zeolite/H$_2$O$_2$ system (Scheme 32). 2-Adamantanone is less susceptible to direct hydroxylation side-reactions discussed below, which makes 2-adamantanone a valuable probe molecule to aid in discerning reactivity trends. After 24 h at 80 °C the corresponding lactone was obtained in 83% yield (>99% selectivity), comparable to previous reports for tin beta zeolite/H$_2$O$_2$.$^{91, 95}$

![Scheme 32. BVO of 2-adamantanone.](image)

The tin beta zeolite/hydrogen peroxide oxidation system was then used to investigate BVO of acetophenone 1 (Table 2). Low yields of phenyl acetate (1a, 33%) were observed as a result of poor electron donation to the carbonyl oxygen, slowing nucleophilic addition of hydrogen peroxide.$^{110-111}$ Alkyl migration from the Criegee intermediate is considered to be the rate-limiting step, however, when using weak oxidants such as hydrogen peroxide, the rate-limiting step can become nucleophilic addition.$^{112}$ While this result is disappointing, angiosperm
and gymnosperm lignins are the result of coniferyl (G) and sinapyl (S) alcohol polymerization, these monolignols containing one and two methoxy group(s), respectively. Therefore, addition of an electron-donating group (EDG) was investigated to determine if it positively affects catalyst activity.\textsuperscript{110-111} Indeed, when EDGs were present (i.e., methyl and methoxy groups, corresponding to 2 and 3, respectively), a higher yield of the corresponding phenyl acetate (2a, 3a) was observed. Due to an EDG influenced increase in the basicity of the carbonyl oxygen,\textsuperscript{111} 3 was converted in 81% yield to 3a at 45 °C after 24 h. When the temperature was increased to 80 °C selectivity decreased from 90% to 83%, and a notable darkening of the reaction mixture was observed, implying formation of phenolic resins. To demonstrate facile cleavage of the ester, after BVO 4′-methoxyphenyl acetate (3a) was hydrolyzed to 4-methoxyphenol (9b, 98% yield) using potassium carbonate and methanol at room temperature for 30 min.\textsuperscript{113}

Considering that 4 contains an EDG in the ortho-position, surprisingly, low yields of 4a were observed (Table 2). This could be due to hindrance of the ortho-substituent to both coordination of 4 to the catalyst surface, and alkyl migration. A similar effect was observed for 5, which contains both meta and para-methoxy groups, and which gave 5a in 58% yield. In reactions with poor selectivity, such as the BVO of 1 and 4, water-soluble resins were also obtained. Likely the product of direct hydroxylation (discussed below) or phenolic radical coupling following ester hydrolysis, resin formation was much more prevalent at 80 °C than 45 °C (as in the case of model 3), presumably due to the increased
rate of hydrogen peroxide homolysis. Additionally, mequinol was detected in 9% yield from hydrolysis of model 3a at 45 °C (Table 2). Hydrolysis could have occurred during the reaction, during reaction work up, or in the gas chromatograph inlet.

Table 2. BVO of acetophenone derivatives using tin beta zeolite/hydrogen peroxide oxidation system.

<table>
<thead>
<tr>
<th>Model Number</th>
<th>Model</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield (%)</th>
<th>Product Number</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="image" /></td>
<td>54</td>
<td>41</td>
<td>33</td>
<td>1a</td>
<td><img src="image2" alt="image" /></td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="image" /></td>
<td>99</td>
<td>60</td>
<td>59</td>
<td>2a</td>
<td><img src="image4" alt="image" /></td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="image" /></td>
<td>90</td>
<td>90</td>
<td>81</td>
<td>3a</td>
<td><img src="image6" alt="image" /></td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="image" /></td>
<td>58</td>
<td>47</td>
<td>27</td>
<td>4a</td>
<td><img src="image8" alt="image" /></td>
</tr>
<tr>
<td>5</td>
<td><img src="image9" alt="image" /></td>
<td>91</td>
<td>64</td>
<td>58</td>
<td>5a</td>
<td><img src="image10" alt="image" /></td>
</tr>
</tbody>
</table>

All reactions were performed in 1,2-dichloroethane at 80 °C for 24 h unless otherwise noted. °Reaction was conducted at 45 °C. Control reactions were run with crystalline tin oxide (2% conversion) and de-aluminated beta zeolite (1% conversion), yielding only trace amounts of 4′-methoxyphenyl acetate, 3a, at 80 °C. Mequinol, 9b, was observed in 9% yield in the reaction of model 3. Phenol was observed in 23% yield in the reaction of model 1.

Given the high yield of 3a, compound 3 was selected for a catalyst reusability study (Fig. 21). After each sequential cycle the catalyst was thermally regenerated at 500 °C in air for 3 h. Minimal loss in activity (3% yield) was observed after the 3rd catalytic cycle.
Using 3 as a probe molecule, solvent effects in the tin beta zeolite/H$_2$O$_2$ oxidation system were explored at 45 °C (Table 3). Initially, water-miscible solvents were evaluated (e.g., ethanol), however they generally afforded modest yields. Acetonitrile was also tested, since in the presence of H$_2$O$_2$ it forms peroxylimidic acid, a more powerful oxidant/nucleophile than H$_2$O$_2$. However, results were disappointing, a 24% yield of 4-methoxyphenol being obtained from ester hydrolysis. Other solvents (e.g., toluene) were also determined to be compatible with this oxidation system. They were not considered further in this study due to the low solubility of lignin in non-polar solvents, but provide potential for other heterogeneous BVO applications.
Table 3. BVO of 3 using tin beta zeolite/hydrogen peroxide in different solvents.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield 3a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,4-Dioxane</td>
<td>48</td>
<td>95</td>
<td>45</td>
</tr>
<tr>
<td>Acetonitrile</td>
<td>40</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Toluene</td>
<td>72</td>
<td>95</td>
<td>68</td>
</tr>
<tr>
<td>Ethanol</td>
<td>55</td>
<td>&gt;99</td>
<td>55</td>
</tr>
<tr>
<td>Ethanol&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>99</td>
<td>49</td>
<td>49&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>1,2-Dichloroethane</td>
<td>90</td>
<td>90</td>
<td>81</td>
</tr>
<tr>
<td>1,2-Dichloroethane&lt;sup&gt;b&lt;/sup&gt;</td>
<td>99&lt;sup&gt;b&lt;/sup&gt;</td>
<td>83&lt;sup&gt;b&lt;/sup&gt;</td>
<td>83&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Selectivity and yields are expressed in terms of 4′-methoxyphenyl acetate, 3a. Reactions were conducted at 45 °C unless otherwise noted. In the case of BVO with acetonitrile, ester hydrolysis resulted in 24% yield of 4-methoxyphenol, 9b. Reaction conducted at 80 °C. 9b was observed in 31% yield.

Of the solvents evaluated, 1,2-dichloroethane (which is water immiscible) gave the highest yield of phenyl acetate. The resistance to oxidation and immiscibility of chlorinated solvents has previously been reported to yield high conversions in BVO reactions as demonstrated with chlorobenzene. The use of a biphasic system limits the solubility of hydrogen peroxide in the organic solvent, decreasing the prevalence of side reactions such as direct ring hydroxylation and ester hydrolysis, which occur readily at temperatures above 45 °C. In BVO, hydrogen peroxide acts as a two-electron oxidant, performing nucleophilic addition to form the Criegee intermediate. However, as the temperature is increased hydrogen peroxide decomposition is accelerated. Homolysis of the peroxide bond forms hydroxide radicals that are very active one-electron oxidants. Hydroxide radicals can perform direct ring hydroxylation as well as many other side-reactions. In competition with BVO, direct ring-hydroxylation reactions can involve both starting material and BVO products. Without the presence of an organic layer (i.e., using a single aqueous phase at 80 °C), reactions resulted in the production of a dark insoluble phenolic resin or tar, as has been reported for similar reactions (i.e., hydrogen peroxide mediated...
oxidation of benzene to phenol).\textsuperscript{57} Interestingly, at low temperatures the highest selectivity was obtained when ethanol was the solvent. However when the reaction temperature was increased, lower selectivity and an increased yield of unidentified products was observed. In the case of ethanol at 80 °C, mequinol (9b) was obtained in 31\% yield, whereas 9b was not observed when the solvent was DCE, consistent with decreased ester hydrolysis in the biphasic system.

2.3.3. BVO of Lignin Model Compounds

Using the tin beta zeolite/hydrogen peroxide oxidation system, selected lignin dimer model compounds, similar to the retro aldol products of \( \alpha \)-position oxidation observed by Wang \textit{et al.},\textsuperscript{35} were oxidized in good to moderate yields. In the reaction of these lignin model compounds, increased amounts of hydrogen peroxide were used due to their lower reactivity as compared to acetophenone derivatives, which can be attributed to their increased steric bulk. Ketone compounds representing the product of benzylic alcohol oxidation in \( \beta \)-O-4 and \( \beta \)-1 linkages were converted to their respective BVO products as shown in Table 4.
Table 4. BVO of lignin dimer model compounds using tin beta zeolite/hydrogen peroxide oxidation system.

<table>
<thead>
<tr>
<th>Model Number</th>
<th>Model</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield (%)</th>
<th>Product Number</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td><img src="image1.png" alt="Image" /></td>
<td>86</td>
<td>37</td>
<td>32</td>
<td>6a</td>
<td><img src="image2.png" alt="Image" /></td>
</tr>
<tr>
<td>7</td>
<td><img src="image3.png" alt="Image" /></td>
<td>81</td>
<td>26</td>
<td>21</td>
<td>7a</td>
<td><img src="image4.png" alt="Image" /></td>
</tr>
<tr>
<td>8</td>
<td><img src="image5.png" alt="Image" /></td>
<td>41</td>
<td>22</td>
<td>9</td>
<td>8a</td>
<td><img src="image6.png" alt="Image" /></td>
</tr>
<tr>
<td>9</td>
<td><img src="image7.png" alt="Image" /></td>
<td>94</td>
<td>23</td>
<td>22*,15</td>
<td>9a, 9b</td>
<td><img src="image8.png" alt="Image" /></td>
</tr>
</tbody>
</table>

Product yields were determined by 1H-NMR spectroscopy using an internal standard. Mequinol, 9b was observed in 3% and 2% yields in the reaction of models 6 and 7, respectively. \*Isolated product yield.

Small amounts of the corresponding phenol were detected in the reactions of 6 and 7, likely resulting from hydrolysis of the ester during aqueous workup or thermal cleavage upon injection during gas chromatography. In the case of compounds 6-8, no 4-methoxybenzoic acid resulting from alkyl migration was present.

The crystal structure of the BVO product of lignin dimer 6 is shown below (Fig. 22, (a)). The crystal structure confirms that the product, 6a, is the result of aryl migration. 6a is over twice the length (15.3 Å) of the pore openings in zeolite beta (7 Å), inhibiting its diffusion through the micropore system. Although in some confirmations (via rotation about the C8-C9 bond) 6a may be able to enter the pore system, conformational requirements of the reaction intermediates (specifically the Criegee intermediate) make the occurrence of BVO in micropores unlikely. Consequently, catalysis likely takes place at tin centers located in mesopores. The crystal structure of BVO product 7a was also
determined (Fig. 22, entry (b); see also Tables S1-S9 in the Supplementary Information).

Figure 22. (a) Crystal structure of the Baeyer-Villiger oxidation product 6a of 2-(4-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (6). (b) Crystal structure of the Baeyer-Villiger oxidation product 7a of 2-(4-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (7). Crystals of 7a were twinned by non-merohedry, and there were two molecules in the asymmetric unit. For the sake of clarity, only one of the independent molecules is shown.

The occurrence of selective aryl migration is contrary to the findings of Patil and co-workers\textsuperscript{32} who found that alkyl migration was preferred over aryl migration for all lignin model compounds in their homogeneous oxidation system. In our work the \textit{p}-methoxybenzene migrating group was presumably better able to stabilize positive charge accumulation in the Criegee intermediate, consistent with DFT studies of acetophenones.\textsuperscript{111}

Regioselective aryl migration was observed for all cases excluding BVO of anisoin 9, where mixed selectivity was observed. Anisoin, 9, was converted almost quantitatively to products consistent with BVO with 7 eq. of hydrogen peroxide at 80 °C, the reaction resulting primarily in alkyl migration. The
observed change in selectivity is a result of polarization of the Cβ-OH group that stabilizes the partial positive charge during Cβ alkyl migration in the Criegee intermediate. Hemiacetal decomposition followed by aldehyde oxidation after BVO resulted in 4′-methoxybenzoic acid, \textbf{9a} (22%). Mequinol, \textbf{9b}, was also detected (15%), from aryl migration.

Patil \textit{et al.} first reported homogenous BVO of lignin model dimer compounds under a formic acid/hydrogen peroxide environment, achieving a maximum yield of 10% of the BVO product of alkyl migration (Scheme 4).\textsuperscript{32} In the same report, using a more complex model they reported a 78% yield of benzoic acid from cleavage of the ester but observed polymerization of the phenolic co-product. In this work we obtained ester yields of respectively 32% and 21% in the BVO of β-O-4 model compounds \textbf{6} and \textbf{7} using tin beta zeolite/H\textsubscript{2}O\textsubscript{2}, which can be cleaved in a second step to recover phenolic moieties. Furthermore, β-1 model compounds were also successfully oxidized. Moreover, the heterogeneous nature of this catalytic system makes this reaction more industrially applicable due to generation of water as a co-product and separation of the catalyst by filtration.

On the other hand, the effects of direct hydroxylation of the aromatic groups are reflected in the moderate yields. Ester yields were found to be affected by reaction time, temperature and hydrogen peroxide concentration. Low yields can be caused by hydrolysis of BVO products to form phenols that are
susceptible to multiple hydroxylations, as well as \( \text{H}_2\text{O}_2 \) homolysis, which limits the conversion of the ketone reactant. In an effort to improve product yields, staging of the \( \text{H}_2\text{O}_2 \) addition was investigated. However, the addition of aliquots of \( \text{H}_2\text{O}_2 \) over a three-day period (14 eq. initially and 7 eq. after 24 h) led to mass balances as low as 14%, due to formation of insoluble phenolic resins.

2.4. Conclusions

The tin beta zeolite/\( \text{H}_2\text{O}_2 \) oxidation system was applied to 2-adamantanone, several acetophenone derivatives and oxidized \( \beta\)-O-4 and \( \beta\)-1 linkage models. Selective aryl migration was observed in all cases excluding anisoin, where both aryl and alkyl migration were observed. The oxidation system presented in this work yields esters that can be cleaved in a simple hydrolysis reaction, yielding phenolic moieties that are typically difficult to isolate from \( \beta\)-O-4 oxidation reactions. Yields of ester products derived from \( \beta\)-O-4 and \( \beta\)-1 lignin models were generally modest due to the formation of polymeric material stemming from direct ring hydroxyl. While preventing the formation of byproducts is challenging, if the reaction were run at low conversion (shorter residence time and/or lower temperature) then the selectivity should increase due to decreased ring hydroxylation and resin formation. Naturally, this would require a means for separating the products and starting material, so that the latter could be recycled. To our knowledge, this is the first report of heterogeneous BVO of lignin model dimer compounds.
Chapter 3. Oxidation of Benzylic Alcohols and Lignin Model Compounds with Layered Double Hydroxide Catalysts

Disclaimer: The work provided in this chapter is the result of collaboration with Justin Mobley, a recent graduate of the University of Kentucky Chemistry Department. Justin Mobley was responsible for some of the reactions and characterization described in sections 3.3.1 through 3.3.2.5.
3.1. Introduction

Lignin is one of the most abundant biopolymers on earth and potentially the largest source of renewable aromatic chemicals.\textsuperscript{114} While delignification of woody biomass has been carried out for more than a century by the pulp and paper industry,\textsuperscript{115} relatively little progress has been made towards lignin deconstruction for the production of value-added chemicals. Rather, lignin is burned on-site as a component of black liquor resulting from cellulose separation. Given the renewed focus on biofuels and the biorefinery concept, interest has grown in the depolymerization of lignin for its valorization.\textsuperscript{114} The majority of this work has focused on the deconstruction of lignin via reductive or thermal pathways, oxidative deconstruction having, until recently, received little attention. Oxidative deconstruction of the lignin polymer is highly desirable due to the potential for producing oxygenated aromatics, which are valuable to the pharmaceutical, perfume, and flavor industries. Indeed, several research groups have identified potential catalytic systems for oxidative lignin deconstruction. The most heavily studied systems are organometallic vanadium\textsuperscript{116-118} and cobalt salen complexes\textsuperscript{60, 119} along with biomimetic porphyrin complexes.\textsuperscript{120-122} Common to all of the aforementioned studies is the desire for single step oxidative deconstruction of lignin or lignin model compounds, commonly through C-C or C-O bond cleavage.

While single step or one-pot deconstruction of the polymer is ideal, stepwise oxidative deconstruction may hold greater promise due to the potential
for selective bond cleavage, which would generate fewer products. To this end, several groups have designed stepwise oxidative processes for lignin deconstruction. Westwood and co-workers identified a process by which benzylic alcohol moieties in model $\beta$-O-4 compounds were selectively oxidized to the corresponding ketones using DDQ/$t$-BuONO/O$_2$ followed by reductive cleavage with Zn.$^{123}$ When this process was applied to Organosolv lignin, the authors were able to isolate small phenolic products in 6% yield. Stahl and co-workers screened a series of stoichiometric and catalytic reagents, finding that 4-acetamido-TEMPO/O$_2$ is an effective catalyst for the selective oxidation of the benzylic alcohol moieties found in lignin.$^{30}$ In a follow-up contribution, Stahl and co-workers$^{124}$ reported that treatment of 4-acetamido-TEMPO/O$_2$ oxidized lignin with HCOOH/HCOONa is an effective process for selective cleavage of the $\beta$-O-4 linkage, yielding up to 60% low molecular weight aromatics. Additionally, our group has recently demonstrated benzylic oxidation followed by Baeyer-Villiger oxidation (BVO) using HCOOH/H$_2$O$_2$ to be an effective route for deconstruction of a lignin $\beta$-O-4 model compound (Scheme 33).

![Scheme 33. Stepwise oxidative cleavage of a $\beta$-O-4 like linkage of a lignin model compound$^{125}$](image)

While these systems have proven effective, they all suffer from the use of homogeneous catalysts and/or stoichiometric reagents and therefore from inherent difficulties in catalyst separation and reuse and/or poor atom economy. Indeed, several heterogeneous oxidative lignin depolymerization strategies have
been recently published.\textsuperscript{126-130} Specifically, heterogeneous layered double hydroxide (LDH) catalysts (also known as hydrotalcite-like compounds) constitute a potential replacement for homogeneous oxidation systems. LDHs are an interesting choice for oxidation reactions given their tunability, relatively high surface area, and near-atomic dispersion of metal ions. Indeed, the LDH structure can accommodate most $M^{2+}$ and $M^{3+}$ metal ions with ionic radii similar to $Mg^{2+}$ (i.e., most $1^{\text{st}}$ row transition metals), while retaining mesoporosity and specific surface areas of ca. 100 m\textsuperscript{2}g\textsuperscript{-1}. For these reasons, many reports have focused on transition metal substituted LDHs for the oxidation of benzylic and aliphatic alcohols to their corresponding ketones and aldehydes.\textsuperscript{131-137} We were particularly interested by a report by Choudary \textit{et al.} \textsuperscript{131} who found Ni-Al-LDHs to be effective catalysts for the oxidation of benzylic alcohols in toluene with $O_2$ as the terminal oxidant. Unfortunately, this catalyst proved ineffective when used in polar solvents (e.g., DMSO), which would be necessary to solubilize lignin.\textsuperscript{137}

Recently, other LDH catalysts have been reported for the deconstruction of lignin model compounds. Sturgeon \textit{et al.}\textsuperscript{128} reported Ni$^{2+}$ supported on the surface of Mg-Al-LDH to be an effective catalyst for deconstruction of benzenemethanol, $\alpha$-(phenoxy)methyl to acetophenone and phenol under inert atmosphere in methyl isobutyl ketone, albeit these reactions require high temperatures (270 °C). In a follow up study, Beckham and co-workers\textsuperscript{82} studied more complicated lignin model dimers using the previously reported Ni-HTC catalyst resulting in modest to excellent yields of the corresponding
acetophenones and phenols. Generally, the authors found that as model complexity increased, yields of monomeric compounds decreased.

Additionally, Corma and co-workers\textsuperscript{138} achieved significant depolymerization of Organosolv lignin using a copper- and vanadium-containing LDH catalyst in pyridine with O\textsubscript{2} as the terminal oxidant. However, it was found that this catalyst suffered from significant metal leaching and was therefore not recyclable. Nevertheless, we were encouraged by the aforementioned examples of benzylic oxidation and lignin deconstruction. In this contribution, a series of transition metal LDHs were synthesized and evaluated for aerobic benzylic oxidation of lignin model compounds in a polar solvent.

3.2. Experimental

3.2.1. Catalyst preparation

Catalysts were prepared by co-precipitation under conditions of low supersaturation. In general, two solutions, one containing metal nitrates and the other containing a mixture of NaOH and Na\textsubscript{2}CO\textsubscript{3}, were added simultaneously and stirred while maintaining a constant pH (generally 8-10). The concentration of the metal nitrate solution used was typically ca. 1.5 M (total metals), while the base solution contained Na\textsubscript{2}CO\textsubscript{3} (ca. 1.0 M) and the calculated amount of NaOH (ca. 3 M) required for complete reaction with the divalent and trivalent metal ions. The solutions were mixed at room temperature at an addition rate of ca. 3 mL min\textsuperscript{-1}, with vigorous mechanical stirring. Unless otherwise stated, the precipitate was aged in the synthesis solution overnight at 70 °C and isolated by a cycle of
centrifuging/decanting/washing with deionized water until neutral pH was obtained. The resulting solid was dried at 60 °C in vacuo. Additional synthetic details can be found in the Appendix II. All catalysts were stored under atmospheric conditions. Unless otherwise specified, catalysts were used without further pretreatment.

3.2.2. Catalyst characterization

Surface area, average pore diameter, and pore volume were determined using a Micromeritics Tristar 3000 porosity system using the Brunauer–Emmett–Teller (BET) method by N₂ adsorption at -196 °C or using a Micromeritics Gemini VII analyzer. Samples were outgassed under vacuum or nitrogen for at least 6 hours at 160 °C prior to measurement. Powder X-ray diffraction measurements were performed on a PANalytical X’Pert system using Cu Kα radiation (λ = 1.5406 Å) and a step size of 0.02°. Elemental analysis was performed on a Varian 720-ES inductively coupled plasma-optical emission spectrometer. Scanning electron microscopy (SEM) was performed on a Hitachi S-2700 instrument equipped with a PGT EDS analyzer with a thin window detector and a LaB₆ electron gun. FTIR spectroscopy was performed on a Nicolet 6700 FTIR instrument equipped with a smart iTR diamond ATR. In all cases 32 scans were taken with a resolution of 4 cm⁻¹. Pulsed CO₂ chemisorption and NH₃-TPD were performed on a Micromeritics AutoChem II analyzer using 200 mg of sample. In each case the sample was first outgassed at 120 °C under argon for 1 h. For pulsed CO₂ chemisorption measurements the sample was then cooled to room temperature and pulsed with CO₂ (100%, 30 sccm) until saturated as indicated
by a thermal conductivity detector (TCD). CO$_2$ was assumed to titrate base sites on a 1:1 molar ratio. In the case of NH$_3$-TPD, the pre-treated sample was cooled to room temperature and then saturated with NH$_3$ (1% in helium, 50 sccm) for 1 h. Next the sample was purged (helium 100%, 120 sccm) for 1 h. The sample was then heated to 750 °C at 10 °C/min. Effluent gas was analyzed using a mass spectrometer (Pfeiffer Thermostat GSD301), the signal at $m/e = 15$ being used to monitor NH$_3$. NH$_3$ was assumed to titrate acid sites in a 1:1 molar ratio.

3.2.3. General procedure for oxidation of 1-phenyl ethanol derivatives

In a typical reaction, the lignin model compound (2 mmol), solvent (10 mL), and catalyst (0.5 g) were added to a 3-neck flask equipped with an oxygen bubbler, a reflux condenser, and a glass stopper. The reaction mixture was stirred at 150 °C for 24 h, after which it was cooled to room temperature and dichloromethane (ca. 10 mL) was added. The reaction mixture was then filtered through Whatman 1 filter paper. The catalyst was washed with dichloromethane or tetrahydrofuran and the washings added to the filtrate. When model compound 3 (1-(4-hydroxy, 3-methoxyphenyl) ethanol) was used as the substrate, 1,4-dimethoxybenzene (0.25 g, 1.8 mmol) was added to the reaction mixture prior to reaction as an internal standard. Conversion, selectivity, and yield were determined using GC (for details see Appendix II).

3.2.4. General procedure for oxidation of lignin model dimer compounds

Reactions were performed in batch mode using a Parr reactor (50 mL, Hastelloy body) equipped with a magnetic stirrer. The catalyst (0.5 g), solvent (16
mL), lignin model compound (2 mmol), and dodecane (0.25 g, internal standard) were added prior to sealing the reactor. Before each run the system was purged three times with the reaction gas (ca. 50 bar). After cooling the reaction mixture was filtered through Whatman 1 filter paper and washed with tetrahydrofuran. The filtrate and washings were then analyzed by GC/MS.

3.2.5. Derivatization procedures for GC/MS samples

For reactions involving lignin model dimer compounds (4-5), product solutions were esterified using trifluoroborate etherate (0.09 mL, 0.7 mmol) as a catalyst to facilitate quantification by GC/MS. A 1 mL aliquot of the reaction mixture was diluted with 4 mL of methanol and purged under an inert atmosphere for 10 minutes before being capped and heated at 100 °C for 6 h, similar to previous reports.38

In order to enhance chromatographic mobility of model 6, a 1 mL sample aliquot of the reaction mixture was derivatized with N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA, 0.4 mmol, 0.1 mL). In order to complete derivatization a catalytic amount of pyridine was added and the sample was heated at 60 °C overnight in a sealed container. The derivatized sample was then analyzed by GC/MS.
3.2.6. Synthesis of enol ether intermediate

To a reaction flask containing 4-methoxyacetophenone (3.0 g, 20.3 mmol) dissolved in ethyl acetate (120 mL) was added pyridinium tribromide (90% technical grade, 7.1 g, 20.0 mmol) at 0 °C. The reaction mixture was stirred for ca. 2 hours at room temperature and then quenched with saturated NaHCO₃ (200 mL). The organic fraction was then removed and the aqueous fraction was extracted with dichloromethane (33 mL). The combined organic layers were washed with 1 M HCl (35 mL, x2) and brine (33 mL) and dried over anhydrous Na₂SO₄. The combined organic layers were then concentrated in vacuo. The crude brominated product (4.47 g, 19.5 mmol, assuming 100% conversion) was then dissolved in acetone and guaiacol (2.24 mL, 20.3 mmol) was added along with K₂CO₃ (11.12 g, 80.47 mmol) and NaI (0.18 g, 1.21 mmol). The reaction mixture was stirred 80 °C for 190 minutes. The reaction mixture was then cooled and concentrated via rotary evaporation. The dried product mixture was then reconstituted in EtOAc (200 mL) and deionized water (75 mL). The organic fraction was washed with 1 M HCl (75 mL) and brine (40 mL) and dried over anhydrous Na₂SO₄ and concentrated in vacuo. The carbonyl product was then isolated via recrystallization from hot/cold ethanol (4.073 g, 73.7% yield). The isolated carbonyl compound (2 g, 7.35 mmol) was then added to sodium borohydride (0.28 g, 7.38 mmol) in THF/MeOH (60 mL, 5:1) at room temperature, the reaction mixture being allowed to stir for 90 min. The solution was concentrated via rotary evaporation and the dried mixture was reconstituted in EtOAc (300 mL) and 1 M HCl (200 mL). The organic fraction was then washed
with 1 M hydrochloric acid (200 mL) and brine (200 mL) and dried over Na₂SO₄. The product was then concentrated *in vacuo* (1.91 g, 1.94 mmol, 94.5% yield). The alcohol product (1.34 g, 4.87 mmol) was then subjected to dehydration with methanesulfonic anhydride (0.96 g, 5.52 mmol) and Et₃N (1.48 mL, 10.60 mmol) in dichloromethane. The solution was stirred at 0 °C for 30 minutes and then allowed to reach room temperature overnight. The reaction mixture was then diluted with deionized water (74 mL) and extracted with CH₂Cl₂ (35 mL, x2). The combined organic fractions were then washed with 1 M hydrochloric acid (100 mL) and brine (50 mL) and dried over Na₂SO₄ and concentrated *in vacuo*. The *cis*-product (0.48 g, 1.87 mmol, 38.4 % yield) was isolated via fraction column chromatography (100 g SiO₂) using 0→15% EtOAc/hexanes as the eluent over 20 column volumes. ¹H NMR (500 MHz, CDCl₃, 7.26 ppm): δ 7.68-7.66 (d, 2H, Ar₂,6, J = 8.86 Hz), δ 7.1-7.06 (m, 2H, Ar), δ 6.98-6.97 (dd, 1H, Ar, J = 8.13, 1.50 Hz), δ 6.95-6.92 (ddd, 1H, Ar, J = 7.61, 1.5 Hz), δ 6.88-6.87 (d, 2H, Ar₃,5, J = 8.91 Hz), δ 6.47-6.45 (d, 1H, Cₐ, J = 6.80 Hz), δ 5.57-5.55 (d, 1H, C₈, J = 6.82 Hz), δ 3.90 (s, MeO, 3H), δ 3.81 (s, MeO, 3H). ¹³C NMR (500 MHz, CDCl₃, 77.16 ppm): δ 158.27, 150.24, 146.91, 141.40, 130.11, 128.00, 124.08, 121.07, 117.81, 113.84, 112.84, 109.82, 56.27, 55.38. GC/MS: m/z 256.1 (100%), 121.1 (72%), 77.1 (33%).
3.3. Results and Discussion

3.3.1. Catalyst characterization

Generally, LDHs are expected to form under basic conditions as long as the metal cations (M$^{2+}$ and M$^{3+}$) have an ionic radius similar to Mg$^{2+}$ and the trivalent metal ratio ($\chi$) is between 0.2 and 0.4 as noted in Equation 1. In this study all catalysts were synthesized with the theoretical $\chi$ value within the aforementioned limits. The metal ratios of prepared catalysts, their physical properties, as well as their respective acidity and basicity measurements are summarized in Table 5. Elemental analysis revealed that the catalysts returned a similar molar metal ratio to that of the solutions used for LDH synthesis. SEM images of Ni-Al-LDH-1 and Ni-Cr-LDH are shown in Appendix II, Fig. S1-S2, and illustrate typical LDH platelet morphology.

\[
0.2 \leq \frac{M^{3+}}{M^{2+} + M^{3+}} \leq 0.4
\]

Equation 2. Trivalent metal ratio ($\chi$) calculation
Table 5. Elemental analysis and gas adsorption data for LDH catalysts

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Target Formula</th>
<th>Actual Formula</th>
<th>Trivalent Metal Ratio</th>
<th>BET SA (m²/g⁻¹)</th>
<th>Av. Pore Volume (cm³/g⁻¹)</th>
<th>Av. Pore Diameter (nm)</th>
<th>Basicityᵃ (μmol CO₂ ads./g catalyst)</th>
<th>Acidityᵇ (μmol NH₃ ads./g catalyst)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mg-Al-LDH-1</td>
<td>Mg₀.75A1₀.25</td>
<td>Mg₀.68A₁₀.32</td>
<td>0.32</td>
<td>100.5</td>
<td>0.429</td>
<td>17.1</td>
<td>71.6</td>
<td>136.0</td>
</tr>
<tr>
<td>2</td>
<td>Mg-Al-LDH-2</td>
<td>Mg₀.80A₁₀.20</td>
<td>Mg₀.73A₁₀.27</td>
<td>0.27</td>
<td>36.4</td>
<td>0.211</td>
<td>23.2</td>
<td>40.5</td>
<td>75.3</td>
</tr>
<tr>
<td>3</td>
<td>Ni-Al-LDH-1</td>
<td>Ni₀.65A₁₀.35</td>
<td>Ni₀.65A₁₀.35</td>
<td>0.35</td>
<td>136.6</td>
<td>0.249</td>
<td>7.3</td>
<td>79.2</td>
<td>281.4</td>
</tr>
<tr>
<td>4</td>
<td>Ni-Al-LDH-2</td>
<td>Ni₀.73A₁₀.27</td>
<td>Ni₀.73A₁₀.27</td>
<td>0.27</td>
<td>127.8</td>
<td>0.286</td>
<td>9.0</td>
<td>157.4</td>
<td>271.1</td>
</tr>
<tr>
<td>5</td>
<td>Ni-Cr-LDH</td>
<td>Ni₀.65Cr₀.33</td>
<td>Ni₀.63Cr₀.32</td>
<td>0.32</td>
<td>76.6</td>
<td>0.055</td>
<td>2.9</td>
<td>51.8</td>
<td>383.1</td>
</tr>
<tr>
<td>6</td>
<td>Ni-Cu-Cr-LDH</td>
<td>Ni₀.34Cu₀.32Cr₀.34</td>
<td>Ni₀.35Cu₀.33Cr₀.33</td>
<td>0.33</td>
<td>103.2</td>
<td>0.251</td>
<td>9.5</td>
<td>14.3</td>
<td>39.7</td>
</tr>
<tr>
<td>7</td>
<td>Cu-Cr-LDH</td>
<td>Cu₀.67Cr₀.33</td>
<td>Cu₀.68Cr₀.32</td>
<td>0.32</td>
<td>134.2</td>
<td>0.177</td>
<td>5.1</td>
<td>27.8</td>
<td>51.5</td>
</tr>
</tbody>
</table>

ᵃDetermined by pulsed CO₂ chemisorption.ᵇEvaluated by ammonia temperature programmed desorption (NH₃-TPD).
Cavani et al.\textsuperscript{140} noted that in order to incorporate copper (II) into LDH structures, it must be present with another bivalent metal in a Cu\textsuperscript{2+}/M\textsuperscript{2+} ratio of less than or equal to 1. This empirical rule is attributed to the tendency of Cu\textsuperscript{2+} compounds to undergo Jahn-Teller distortions causing elongation of the octahedral coordination sphere. Therefore, Cu\textsuperscript{2+} ions must be accompanied by another M\textsuperscript{2+} metal such that the coordination sphere is undistorted as required by the brucite-like LDH structure. Whereas the Cu\textsuperscript{2+}/M\textsuperscript{2+} rule was followed for the synthesis of Cu-Ni-Cr-LDH, the rule was disregarded in the synthesis of Cu-Cr-LDH. In the case of the Cu-Cr LDH the presence of a minor crystalline phase, which is in good agreement with the mineral malachite, was apparent (Fig. 23). However, it was inferred that the potential for Jahn-Teller distortions in the crystal lattice had a minimal effect on the catalysts prepared in this work due to the presence of the LDH phase in all Cu\textsuperscript{2+} containing catalysts.
In addition, acidity and basicity measurements were conducted on all catalysts (see Table 5, and Appendix II, Fig. S3-S7). Notably, the Ni-Al-LDHs had the highest number of base sites, adsorbing 157.4 μmole CO₂ g⁻¹ of catalyst and 79.2 μmole CO₂ g⁻¹ for Ni-Al-LDH-2 and Ni-Al-LDH-1, respectively. According to NH₃-TPD experiments, Ni-Cr-LDH possessed the highest number of acid sites of the samples analyzed. While Mg-Al-LDH-1 had relatively few acid sites, it contained a higher relative proportion of strong acid sites (NH₃ desorbed >450 °C, see Appendix II, Fig. S5). While both Ni-Al-LDH-1 and Ni-Al-LDH-2 had a similar number of total acid sites, Ni-Al-LDH-2 had a higher proportion of medium (NH₃ desorbed at 250-450 °C) and strong acid sites (Appendix II, Fig. S3 and S4). Indeed, strong and medium acid sites were virtually absent in Ni-Al-LDH-1.

Figure 23. XRD analysis of LDH catalysts
FT-IR analysis (Appendix II, Fig. S8) revealed that all catalysts displayed bending and stretching bands characteristic of LDH structures. Specifically, bands corresponding to the bending mode of interlayer water and asymmetric carbonate stretching were observed at ca. 1633 cm\textsuperscript{-1} and at ca. 1345 cm\textsuperscript{-1}, respectively (Appendix II, Fig. S8).\textsuperscript{141} A similar band ca. 1635 cm\textsuperscript{-1} has been reported for Ni-Al-LDHs\textsuperscript{142-145} and Ni-Cr-LDH.\textsuperscript{146}

3.3.2. Catalytic oxidation of lignin model compounds

3.3.2.1. Solvent screening

Inspired by the work of Choudary et al.,\textsuperscript{131} we endeavored to find a solvent system that would be suitable for the oxidation of lignin model compounds. While Choudary found toluene to be an effective solvent for the oxidation of a multitude of benzylic and allylic alcohols, when 4-nitrobenzyl alcohol was oxidized in polar solvents such as methanol and acetonitrile only 5\% and 30\% of the substrate was converted to 4-nitrobenzaldehyde, respectively. Likewise, other researchers have noted decreased activity for alcohol oxidation in polar solvents using LDH catalysts.\textsuperscript{132, 147} The observed decrease in catalytic activity in polar solvent is likely the result of competitive coordination to active sites by the solvent, preventing reactant binding. However, given the polar nature of lignin, it is crucial to find a polar solvent in which lignin can be dissolved and that can act as an effective solvent for alcohol oxidations using LDH catalysts. Therefore, utilizing Ni-Al-LDH-1, which has a similar composition to the Ni-Al-LDH used by Choudary et al.,\textsuperscript{131} a series of solvents varying in polarity were screened for the oxidation of
1-phenyl ethanol, 1. As shown in Table 6, only limited conversions of 1 were obtained in most polar solvents (Table 6, entries 5-10). Acetophenone, 1a, was obtained in a near quantitative yield in toluene (Table 6, entry 4) and α,α,α-trifluorotoluene (Table 6, entry 3), while reaction in 1,4-dioxane (Table 6, entry 8) yielded only 8% of 1a. Unfortunately, α,α,α-trifluorotoluene lacks sufficient polarity to dissolve lignin. In an attempt to amalgamate the polar ether properties of 1,4-dioxane with the electron-rich, aromatic character of toluene, phenyl ether (Table 6, entry 1) was trialed, resulting in 49% conversion of 1 to 1a. Separate experiments confirmed that Organosolv lignin is somewhat soluble in phenyl ether.

Table 6. Conversion of 1-phenyl ethanol (1) to acetophenone (1a) in selected solvents

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Temperature (°C)</th>
<th>1a Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phenyl Ether</td>
<td>6</td>
<td>90</td>
<td>49</td>
</tr>
<tr>
<td>2</td>
<td>Phenyl Ether</td>
<td>24</td>
<td>150</td>
<td>66</td>
</tr>
<tr>
<td>3a</td>
<td>α,α,α-Trifluorotoluene</td>
<td>6</td>
<td>Reflux</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>6</td>
<td>85</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>Dimethyl Sulfoxide</td>
<td>6</td>
<td>120</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>Chloroform</td>
<td>6</td>
<td>60</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Hexachloroacetone</td>
<td>6</td>
<td>85</td>
<td>&lt;1</td>
</tr>
<tr>
<td>8</td>
<td>1,4-Dioxane</td>
<td>6</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>9</td>
<td>Benzonitrile</td>
<td>24</td>
<td>90</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>1,2-Dichlorobenzene</td>
<td>6</td>
<td>85</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

*aCatalyst was calcined at 175 °C for 3 h.

3.3.2.2. Oxidation of 1 over LDH catalysts

Having identified a suitable solvent for benzylic alcohol oxidation, LDH catalysts containing metals that are traditionally used in oxidation chemistry (copper and chromium) were synthesized (section 3.3.1) and screened for
activity in the oxidation of 1. As shown in Table 7, Ni-Cr-LDH (entry 7), Ni-Al-LDH-1 (thermally pretreated at 175 °C for 3 hours, entry 5), and Ni-Al-LDH-2 (entry 6) gave high yields of 1a (>90%). Notably, Mg-Al-LDH-1 and Mg-Al-LDH-2 showed relatively little conversion of 1, indicating that activity is not the result of catalyst basicity. Likewise, conversion of model compound 1 did not trend with acidity. Indeed, Ni-Cr-LDH, which had the highest number of acid sites, did not show the highest conversion of 1 to 1a. Moreover, while Cu-Cr-LDH had neither the most acid or base sites it demonstrated the highest conversion of 1 to 1a, suggesting a reaction mechanism not related simply to the acidity or basicity of the catalyst.

Table 7. Conversion of 1-phenyl ethanol, 1 to acetophenone, 1a in phenyl ether with various LDH catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mg-Al-LDH-1</td>
<td>8</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>Mg-Al-LDH-2</td>
<td>12</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>Ni-Al-LDH-1</td>
<td>66</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4&lt;sup&gt;a&lt;/sup&gt;,&lt;sup&gt;b&lt;/sup&gt;,&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Ni-Al-LDH-1</td>
<td>91±3</td>
<td>&gt;99</td>
</tr>
<tr>
<td>5</td>
<td>Ni-Al-LDH-2</td>
<td>91</td>
<td>&gt;99</td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Ni-Cr-LDH</td>
<td>92±5</td>
<td>&gt;99</td>
</tr>
<tr>
<td>7</td>
<td>Ni-Cu-Cr-LDH</td>
<td>80</td>
<td>&gt;99</td>
</tr>
<tr>
<td>8</td>
<td>Cu-Cr-LDH</td>
<td>&gt;99</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

<sup>a</sup>24 h reaction time, 10 mL of phenyl ether as solvent. <sup>b</sup>Calcined at 175 °C/3 h, reaction time 23 h. <sup>c</sup>Average of 3 reactions ± st. dev.

3.3.2.3. Catalyst loading study

In order to elucidate the optimal amount of catalyst needed, a catalyst loading study was performed using Ni-Cr-LDH. The amount of catalyst was incrementally increased while keeping the amount of starting material constant at
2 mmol. As can be seen from Table 8, using 0.5 g of Ni-Cr-LDH for every 2 mmol of starting material proved to be optimal (entry 4). While this is a large amount of catalyst, it is not uncommon in the literature.\textsuperscript{147, 148} The need for a large amount of catalyst relative to starting material suggests that the active site corresponds to defect sites that are present in low concentration on the catalyst surface.

Table 8. Ni-Cr-LDH catalyst loading study\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst Loading (g)</th>
<th>Conversion (%)</th>
<th>Selectivity (%) to 1\textsubscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.05</td>
<td>18</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>0.1</td>
<td>37</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>0.25</td>
<td>69</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4\textsuperscript{b}</td>
<td>0.5</td>
<td>92±5</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

\textsuperscript{a}2 mmol of starting material, 10 mL phenyl ether. \textsuperscript{b}Average of 3 reactions ± st. dev.

3.3.2.4. Leaching study

In order to determine whether conversion was the result of leached metal in the solution, a hot filtration experiment was performed in which the Ni-Cr-LDH catalyst was hot filtered from the reaction mixture after 1 h. A sample was taken, after which the filtrate was transferred to a fresh flask and allowed to react for an additional 23 h at 150 °C. Analysis of the reaction mixture indicated a 39% conversion at 1 h with no additional conversion post-filtration, suggesting that catalysis occurred on the LDH surface and not via free metal species in solution. Elemental analysis of the reaction mixture at 24 h post-filtration did not reveal significant amounts of metal leached into solution (<1 ppm Cr and 3 ppm Ni).
3.3.2.5. Oxidation of compounds 2 and 3 over LDH catalysts

In order to determine the efficacy these catalysts with electron-rich substrates that are increasingly similar to lignin, model compound 2 was used as a substrate. As well as having an electron-donating group (EDG), the methoxy group serves to represent the ether linkage present in the β-O-4 motif. Catalysts that returned a yield of >80% in the conversion of 1 to 1a were screened for catalytic activity in the oxidation of 2. Additionally, Ni-Al-LDH-1 was also used in the reaction for comparison purposes.\textsuperscript{131} Oxidation of 2 with the aforementioned catalysts afforded two products, the expected ketone, 2a, as well as the alcohol elimination product, 2b. As can be seen from Table 5, catalysts containing nickel yielded higher amounts of the dehydration product 2a. Dehydration was found to be most prominent for Ni-Al-LDH-2. On the other hand, copper-containing catalysts tended to be more selective towards the ketone product, 2a. In an attempt to elucidate the relationship between catalyst functionality and alcohol dehydration, acidity and basicity measurements were compared to catalyst performance. No clear trend between acidity or basicity and conversion was elucidated, suggesting that the mechanism is dependent on more than the number of acid or base sites. Mechanistically this may occur via an E2-type mechanism in which the metal alkoxide is formed on the catalyst surface, followed by deprotonation of the β-carbon and subsequent elimination of the metal oxide to form the alkene. While production of 2b was unexpected, the analogous elimination in the β-O-4 linkage would result in the formation of enol ethers, which are capable of being cleaved under acidic conditions.\textsuperscript{149} Although
Ni-Al-LDH catalysts both performed well, overall, oxidation with Ni-Cr-LDH resulted in the highest yield of \(2a\). In the case of Cu-Cr-LDH near quantitative conversion of 2 was observed. However, the selectivity to 2a (ca. 50%), which was the only identifiable compound by GC/MS, is significantly lower than other LDH catalysts (entries 2-6, Table 9) presumably due to the conversion of 2 to unidentifiable products, evidenced by the darkening of the reaction mixture.

Table 9. Conversion of 2 over various LDH catalysts in phenyl ether with \(\text{O}_2\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Ketone Yield (%)</th>
<th>Alkene Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>2a</td>
<td>2b</td>
</tr>
<tr>
<td>1</td>
<td>None (BLANK)</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Ni-Al-LDH-1</td>
<td>92</td>
<td>74</td>
<td>18</td>
</tr>
<tr>
<td>3(^a)</td>
<td>Ni-Al-LDH-1</td>
<td>83</td>
<td>75</td>
<td>8</td>
</tr>
<tr>
<td>4(^b)</td>
<td>Ni-Al-LDH-2</td>
<td>99±0</td>
<td>71±8</td>
<td>27±7</td>
</tr>
<tr>
<td>5</td>
<td>Ni-Cr-LDH</td>
<td>99</td>
<td>96</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>Ni-Cu-Cr-LDH</td>
<td>90</td>
<td>88</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>Cu-Cr-LDH</td>
<td>&gt;99</td>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^a\)Calcined at 175 °C for 3 h. \(^b\)Average of 3 reactions ± st. dev.

In order to further increase lignin-like functionality on the substrate and explore functional group sensitivity, the phenolic model compound 3 was chosen. As shown in Table 10, the use of Ni-containing catalysts for the oxidation of 3 favored the formation of the dehydration product 3b, similar to the results obtained for compound 2. Unfortunately, poor mass balances were obtained for the oxidation of compound 3 due to suspected polymerization (chromatographically immobile material). This suggests that phenolic groups may need to be protected, e.g., by alkylation, prior to benzylic oxidation.\(^{14}\) Unexpectedly, a small amount of benzaldehyde 3c was also formed during the
oxidation of 3 as a result of Cα-Cβ bond cleavage. Aldehyde formation was most prevalent when the Ni-Cu-Cr-LDH was used as the catalyst. Moreover, Cu-Cr-LDH was active in the oxidation of 3 but did not yield identifiable products. The production of 3b likely results in phenolic or styrenic coupling reactions leading to high molecular weight polymers.

Table 10. Conversion of 3 over LDHs in phenyl ether with O₂

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Ketone Yield 3a (%)</th>
<th>Alkene Yield 3b (%)</th>
<th>Aldehyde Yield 3c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None (Blank)</td>
<td>27</td>
<td>8</td>
<td>18</td>
<td>1</td>
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<tr>
<td>2a</td>
<td>Ni-Al-LDH-1</td>
<td>99</td>
<td>3</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>Ni-Al-LDH-2</td>
<td>99</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Ni-Cr-LDH</td>
<td>58</td>
<td>8</td>
<td>29</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Ni-Cu-Cr-LDH</td>
<td>98</td>
<td>9</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>Cu-Cr-LDH</td>
<td>&gt;99</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*C Calcined at 175 °C for 3 h.

3.3.2.5. Catalyst reusability study

Catalyst reusability was studied using Ni-Al-LDH-1 and Ni-Cr-LDH in the oxidation of 1 (Table 11). After the reaction, the catalysts were filtered and washed with THF and hexanes, and then dried in a vacuum oven prior to re-use. Re-usability tests for Ni-Al-LDH-1 and Ni-Cr-LDH demonstrated a significant decrease in activity upon successive use. The X-ray diffractogram of the spent Ni-Cr-LDH (Appendix II, Fig. S9) displayed similar peaks to the fresh catalyst with the exception of a new highly crystalline peak corresponding to chromium (III) oxide, while N₂ physisorption analysis revealed a significant decrease in surface area (27.8 m²g⁻¹ post reaction) believed to be the result of phase segregation in
the LDH, in addition to adsorbed organics blocking pores. Similarly, Ni-Al-LDH-1 displayed the characteristic LDH diffraction pattern but also a highly crystalline peak corresponding to Al(OH)_3 (Appendix II, Fig. S10).

Table 11. Catalyst reusability study in the oxidation of 1 (phenyl ether as solvent)

<table>
<thead>
<tr>
<th>Cycle #</th>
<th>Catalyst</th>
<th>Temperature (°C)</th>
<th>Time (h)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ni-Cr-LDH</td>
<td>150</td>
<td>24</td>
<td>78</td>
</tr>
<tr>
<td>2</td>
<td>Ni-Cr-LDH</td>
<td>150</td>
<td>24</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>Ni-Cr-LDH</td>
<td>150</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>4^b</td>
<td>Ni-Cr-LDH</td>
<td>150</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>1^a</td>
<td>Ni-Al LDH-1</td>
<td>150</td>
<td>24</td>
<td>72</td>
</tr>
<tr>
<td>2^a</td>
<td>Ni-Al LDH-1</td>
<td>150</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>3^a,b</td>
<td>Ni-Al LDH-1</td>
<td>150</td>
<td>24</td>
<td>100</td>
</tr>
</tbody>
</table>

^aCatalyst thermally pretreated at 175 °C for 3 hours. ^bCatalyst regeneration with Na_2CO_3 Solution.

Other researchers have reported that full activity in benzyl alcohol oxidation is regained upon washing LDH catalysts with aqueous sodium carbonate. After washing Ni-Cr-LDH with Na_2CO_3 a small amount of activity was regained. It is believed that inability to completely regenerate the Ni-Cr-LDH catalyst may be related to the phase segregation observed by X-ray diffraction (Appendix II, Fig. S9). The effect of carbonate washing was even more pronounced in the case of Ni-Al-LDH-1. Indeed, Ni-Al-LDH-1 showed no activity for the oxidation of compound 1 after the first use. However, after washing with carbonate solution, activity was completely regained. In fact, conversion increased from 72% to 100% possibly due to an increase in the number of defect sites after reconstitution with Na_2CO_3.

Other workers have reported that LDH anions may play an integral role in alcohol oxidation as evidenced by the reduced catalyst activity when anions are absent or substituted by another anion in the LDH. In order to ascertain whether carbonate acts as a stoichiometric base, the amount of CO_3^2− present in
each LDH was calculated based on the idealized LDH formula \([M^{2+\times}xM^{3+\times}(OH)_{2}]^{+\times}(A^n)_{x/n}\), where \(x\) is the trivalent metal ratio, \(A\) is the anionic species, and \(n\) is the charge of the anionic species. The water content was purposefully ignored as this can vary between LDHs.\(^{139}\) As can be seen in Table 12, \(\text{CO}_3^{2-}\) is present in a sub-stoichiometric amount compared to the substrate \(1\); hence, carbonate does not act as a stoichiometric base in these oxidation reactions.

Table 12. Formulae of LDH catalysts and molar ratio of carbonate to \(1\)

<table>
<thead>
<tr>
<th>LDH</th>
<th>Formula</th>
<th>mmol (\text{CO}_3^{2-})/mmol (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mg-Al-LDH-1</td>
<td>([\text{Mg}<em>{0.68}\text{Al}</em>{0.32}(\text{OH})_2]^{0.32+}(\text{CO}<em>3^{2-})</em>{0.16}]</td>
<td>0.58</td>
</tr>
<tr>
<td>Mg-Al-LDH-2</td>
<td>([\text{Mg}<em>{0.73}\text{Al}</em>{0.27}(\text{OH})_2]^{0.27+}(\text{CO}<em>3^{2-})</em>{0.135}]</td>
<td>0.50</td>
</tr>
<tr>
<td>Ni-Al-LDH-1</td>
<td>([\text{Ni}<em>{0.65}\text{Al}</em>{0.35}(\text{OH})_2]^{0.35+}(\text{CO}<em>3^{2-})</em>{0.175}]</td>
<td>0.47</td>
</tr>
<tr>
<td>Ni-Al-LDH-2</td>
<td>([\text{Ni}<em>{0.73}\text{Al}</em>{0.27}(\text{OH})_2]^{0.27+}(\text{CO}<em>3^{2-})</em>{0.135}]</td>
<td>0.37</td>
</tr>
<tr>
<td>Ni-Cr-LDH</td>
<td>([\text{Ni}<em>{0.68}\text{Cr}</em>{0.32}(\text{OH})_2]^{0.32+}(\text{CO}<em>3^{2-})</em>{0.160}]</td>
<td>0.43</td>
</tr>
<tr>
<td>Ni-Cu-Cr-LDH</td>
<td>([\text{Ni}<em>{0.35}\text{Cu}</em>{0.33}\text{Cr}_{0.33}(\text{OH})_2]^{0.33+}(\text{CO}<em>3^{2-})</em>{0.163}]</td>
<td>0.40</td>
</tr>
<tr>
<td>Cu-Cr-LDH</td>
<td>([\text{Cu}<em>{0.68}\text{Cr}</em>{0.32}(\text{OH})_2]^{0.32+}(\text{CO}<em>3^{2-})</em>{0.160}]</td>
<td>0.39</td>
</tr>
</tbody>
</table>

3.2.6. Mechanistic considerations

Given that catalytic activity is regained and even enhanced after washing with sodium carbonate, it follows that catalysis likely occurs on the catalyst edge sites (110 plane) in LDHs or an equivalent site where interlamellar carbonate anions are exposed to the reactants. Fig. 24 shows a plausible mechanism, which is a modified version of that proposed by Tang et al.,\(^{135}\) in which the alcohol is first deprotonated by carbonate to form an alkoxide, which coordinates to an unsaturated metal site. Hydroperoxide oxidation of the metal alkoxide with a concomitant hydride shift from the alkoxide to the hydroperoxide results in net alcohol oxidation and the regeneration of metal hydroxide. Deprotonation of
bicarbonate by the metal hydroxide forms water and regenerates a coordinatively unsaturated metal site.

Figure 24. Plausible mechanism for LDH-catalyzed aerobic alcohol oxidation

In order to determine whether oxidation proceeds via a two-electron or radical pathway, 1-cyclopropy-1-phenylcarbinol was used as a probe molecule. If oxidation proceeds via a benzylic radical then the highly strained cyclopropyl ring would open, yielding a linear propyl chain. On the other hand, if the reaction proceeds through a hydride shift (as shown in Fig. 24) the cyclopropyl ring would remain after benzylic oxidation. Analysis of the reaction mixture post-oxidation
revealed the presence of cyclopropyl phenyl ketone in 64% yield, with no
evidence of the ring-opening product (Scheme 34). This suggests that the
oxidation of benzylic alcohols to ketones proceeds through a two-electron
pathway. The moderate yield of product obtained is a result of evaporation during
the reaction (the boiling point of both starting material and product being ca. 130
°C).

Scheme 34. Oxidation of 1-cyclopropyl 1-phenylcarbinol

3.3.2.7. Oxidation of lignin model dimer compounds over LDH catalysts

While promising results were obtained when benchtop reactions were
performed on compounds 1-3, no conversion was observed when lignin model
dimer 4 was subjected to optimized reaction conditions. Thus, in order to
increase the oxygen solubility, a pressurized reaction system was used. Indeed,
when lignin model dimer compounds were reacted under slightly elevated
temperatures (i.e., 180 °C) and oxygen partial pressures (8%) significant
conversion was observed (Tables 13-15).

It should be noted that the use of pressurized oxygen significantly
increases safety concerns for reactions in organic media. Indeed, Stahl and co-
workers recently reported limiting oxygen concentrations (LOC) for nine
organic solvents, finding that ca. 8% O2 counter-balanced with inert gas was
generally non-combustible. Thus in this study 8% oxygen counter-balanced with nitrogen was used, which provides a nearly stoichiometric amount of oxygen (ca. 3 eq., at 50 bar) for the oxidation of lignin model dimers. In addition to addressing safety concerns, near stoichiometric amounts of oxygen limits over-oxidation to dicarboxylic acids, these being common products of aromatic ring over-oxidation.\textsuperscript{151}

Although modest amounts of the ketone resulting from benzylic oxidation were detected, small molecules resulting from cleavage of the model linkages were observed in more substantial yield (Table 13). Wang \textit{et al.}\textsuperscript{35} previously reported that lignin $\beta$-O-4 models oxidized at the benzylic position are more easily fragmented than the benzylic alcohol, due to the weakening of the C$\beta$-O$_4$ bond by approximately 85 kJ/mol. The modest yields of 4d are explained by the ready cleavage of the C$\beta$-O$_4$ bond, as indicated by the observation of the phenol 4b. Product 4a, which results from oxidative cleavage of 4d, was generally present in higher yield than 4b. In addition, enol ether product 4c was observed, resulting from benzylic alcohol dehydration as a consequence of the catalyst basicity. Additionally, products 4e and 4f, that likely result from non-oxidative cleavage of 4d were observed as minor co-products. Products such as 4e and 4f are commonly observed in heterogeneous oxidation reactions of lignin model compounds.\textsuperscript{126, 128-130}
Table 13. Conversion of 4 over LDH catalysts in phenyl ether with O₂

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>--</td>
<td>22</td>
<td>4 a</td>
</tr>
<tr>
<td>Ni-Al-LDH-1</td>
<td>&gt;99</td>
<td>5 a</td>
</tr>
<tr>
<td>Ni-Al-LDH-1a</td>
<td>&gt;99</td>
<td>10 a</td>
</tr>
<tr>
<td>Ni-Al-LDH-1b</td>
<td>53</td>
<td>0 a</td>
</tr>
<tr>
<td>Cu-Cr-LDH</td>
<td>72</td>
<td>3 a</td>
</tr>
<tr>
<td>Cu-Cr-LDHa</td>
<td>87</td>
<td>4 a</td>
</tr>
<tr>
<td>Ni-Cr-LDH</td>
<td>22</td>
<td>3 a</td>
</tr>
<tr>
<td>Ni-Cr-LDHa</td>
<td>92</td>
<td>0 a</td>
</tr>
</tbody>
</table>

*Reaction time 24h. *Reaction was performed under an argon atmosphere

Surprisingly, the Ni-Cr-LDH catalyst, which successfully oxidized compounds 1-3, produced modest conversions in the cases of dimer models 4-6. The observed loss in catalytic reactivity may be due to the catalyst’s small average pore diameter (2.9 nm). Unlike compounds 1-3, which are monomeric, dimer model compounds 4-6 (ca. 1.5 nm),\(^{127}\) approach the pore diameter of Ni-Cr-LDH (Table 5). Moreover, other catalysts with larger pore diameters showed increased conversion of compounds 4-6. Indeed, Ni-Al-LDH-1, with a pore diameter of 7.3 nm, was found to be the most active catalyst for conversion of dimer model compounds, resulting in >99% conversion of models 4 and 5 (Table 13-14). Moreover, the increased conversion of dimeric compounds by Ni-Al-LDH may be due a combination of pore size (7.3 nm pore diameter) and the basicity
(79.2 μmol CO$_2$ g$^{-1}$ catalyst) of the catalyst, which likely favors enol ether formation. Likewise, oxidations conducted using Cu-Cr-LDH typically resulted in high yields of enol ether products 4c and 5c.

Given the high conversion of models 4 and 5 under oxygen atmosphere, and in order to validate the importance of oxygen in the reaction system, an experiment was performed under an inert atmosphere. Under anaerobic conditions, Ni-Al-LDH-1 afforded a decreased conversion of 4 (Table 13). Specifically, a 53% conversion was obtained, compared to 100% conversion under aerobic reaction conditions. Additionally, compounds 4a-4d were observed in ca. total 7% yield under inert conditions while products of 4a-4d was observed in 56% yield under oxygen atmosphere. One would expect that under inert conditions 5 would largely be converted into the products of non-oxidative bond cleavage (i.e., 4e, 4f).
Table 14. Conversion of 5 over LDH catalysts in phenyl ether with O$_2$

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>--</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Ni-Al LDH-1$^a$</td>
<td>&gt;99</td>
<td>15</td>
</tr>
<tr>
<td>Cu-Cr-LDH</td>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td>Cu-Cr-LDH$^b$</td>
<td>99</td>
<td>19</td>
</tr>
<tr>
<td>Ni-Cr-LDH</td>
<td>14</td>
<td>2</td>
</tr>
</tbody>
</table>

$^a$Calcined at 175 °C for 3 h $^b$Reaction time = 24h

With the promising results from oxidation of model 4, models with similar functionality were explored. Although similar in structure to model 4, model 5 resulted in significantly higher yields of 4a and the enol ether, 5c, for both Ni-Al-LDH and Cu-Cr-LDH. The substitution pattern of 5 in the 1-position of the aryl ether (B-ring) may be the cause of the observed increase in conversion. If formation of 4c proceeds via base catalysis, the $\beta$-hydrogen must be deprotonated. The substitution of 4 at the 3-position may provide steric hindrance, whereas 5 remains unhindered. However, while model 4 is a plausible lignin model compound, model 5 is unrealistic due to the B-ring substitution. This highlights the importance of using realistic lignin model compounds. That is to say, the results seen with model compound 5, while more favorable, are less likely to be seen in native lignin.
Relatively high yields of enol ethers (4c and 5c) were observed over Cu-Cr-LDH and Ni-Al-LDH-1. Enol ethers resulting from dehydration of the benzylic alcohol were most likely produced because of the relatively high basicity of the catalyst in the case of Ni-Al-LDH-1. However, similar results were obtained when Cu-Cr-LDH was used as the catalyst, again suggesting that the reaction does not simply depend on availability of acid and base sites. For both 4 and 5, when the reaction time was increased from 16 h to 24 h, the yield of the enol ether (4c and 5c) obtained over Cu-Cr-LDH decreased while the yield of the benzoic acid 4a increased. However, when 4c was used as the feedstock in a control experiment, 4a was not produced. Rather, 4c was converted to a multitude of minor products, some of which appeared to involve coupling with the solvent and others which eluded identification. Therefore, the increase in yield of 4a upon increase of the reaction time is likely a result of increased conversion of 4 (72% to 99% yield).

Phenols resulting from β-aryl ether cleavage were recovered in low yields. As commonly reported for oxidation of lignin model compounds, phenols are often converted into unidentifiable products.\(^{30, 35, 123}\) In order to investigate the stability of phenols under the reaction conditions, guaiacol (4b) was subjected to the same conditions in the absence of catalyst. After 16 h at 180 °C under 8% \(\text{O}_2/\text{N}_2\), 76% of guaiacol was converted to unidentifiable products and evident darkening of the reaction solution was observed. This leads us to the conclusion that polymerization of phenols in the presence of oxygen is responsible for their low yields.
While models 4 and 5 serve as sufficiently complex models to establish reactivity trends, they do not accurately represent lignin linkages. Consequently, model complexity was increased by the addition of a γ-carbinol group, to better reflect native and technical lignins (compound 6; see Table 15). The addition of a γ-carbinol provides another alcohol that can be oxidized. Once oxidized at the α- or γ-position, 6 can undergo retro-aldol reactions further complicating the product slate. Retro-aldol reactions at the oxidized α-position produce products similar to 4 and 5, alternatively, oxidation at the γ-position produces 4e and 4b that can also undergo further oxidation.

The oxidative fragmentation of model 6 was investigated using Ni-Al-LDH-1, Cu-Cr-LDH, and Ni-Cr-LDH. Unexpectedly, Ni-Al-LDH-1 catalyzed oxidation resulted in only 31% conversion (Table 15), whereas Cu-Cr-LDH afforded similar conversion as for models 4 and 5. In contrast, Ni-Cr-LDH, which showed similar reactivity trends for models 4 and 5, showed no conversion for 6.

Table 15. Conversion of 6 over LDH catalysts in phenyl ether with O₂

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>--</td>
<td>Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>Ni-Al-LDH-1</td>
<td>31</td>
<td>Trace</td>
</tr>
<tr>
<td>Cu-Cr-LDH</td>
<td>79</td>
<td>14</td>
</tr>
<tr>
<td>Ni-Cr-LDH</td>
<td>Trace</td>
<td>Trace</td>
</tr>
</tbody>
</table>

Trace is defined as ≤6% due to spectroscopic limitations
The benzoic acid (4a) resulting from cleavage of the Cα-Cβ bond was observed in trace amounts in the catalytic oxidation system using Ni-Al-LDH. Furthermore, molecules similar to those produced after the oxidation of 4 and 5 (i.e., 6c, 6d, and 4f) were not observed when 6 was subjected to the same reaction conditions. In the run using Cu-Cr-LDH, 6 was converted to 4a in 14% yield. The increased yield of 4a along with the absence of 6c suggests that the enol ether is more difficult to form in models with γ-carbinols.

The difference in the reactivity of 6 compared to 4 and 5 may be due to diverging reaction pathways. It is hypothesized that reaction intermediates include both benzylic ketones formed via oxidation and enol ethers via dehydration. Basic sites are likely responsible for the deprotonation of the benzylic carbinol for catalysts such as Ni-Al-LDH-1. After the substrate is coordinated to the catalyst surface, base sites likely deprotonate the β-carbon. Substitution at the β-carbon (by addition of a γ-carbinol) likely makes deprotonation of the β-carbon more difficult, as suggested by the absence of 6c in the product mixture.

3.3.2.8. Oxidation of model ketone compounds

To investigate the poor yields of the ketone resulting from benzylic oxidation, models 4d-6d were subjected to the same reaction conditions as 4-6. When subjected to the same reaction conditions, sans catalyst, described in Tables 13-15, oxidized lignin model dimers 4d-6d were converted near quantitatively (Table 16); this indicates that lignin models, once oxidized, are easily depolymerized under oxidative conditions at 180 °C. Moreover, 4a was
obtained in a maximum 62% yield, indicating that the primary pathway for the production of 4a begins with benzylic oxidation. The hypothesis that 4d-6d were converted to 4a as a result of oxidation by molecular oxygen was confirmed by the finding that in the absence of O₂, 4d was not converted to products. Evidentially, oxygen is a strong enough oxidant at elevated temperatures to produce 4a. Notably, in non-catalytic oxidation of 6d, 4a was not observed. This implies that though yields were modest, Cu-Cr-LDH is likely responsible for the oxidation of 6 and it is involved in the subsequent conversion of 6d to 4a.

Table 16. Conversion of 4d 6d in phenyl ether with O₂

<table>
<thead>
<tr>
<th>Model</th>
<th>Conversion (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4d</td>
<td>&gt;99</td>
<td>53</td>
</tr>
<tr>
<td>4d³</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5d</td>
<td>&gt;99</td>
<td>62</td>
</tr>
<tr>
<td>6d</td>
<td>&gt;99</td>
<td>0</td>
</tr>
</tbody>
</table>

³Reaction was performed under an argon atmosphere

3.4. Conclusions

LDH materials containing a variety of first row transition metal ions were found to be active catalysts for the oxidation of benzylic alcohols and lignin model dimer compounds using phenyl ether as solvent and O₂ as the terminal oxidant. Upon repeated use, catalyst activity declined, although washing the spent catalyst (i.e., Ni-Al-LDH-1 and Ni-Cr-LDH) with aqueous Na₂CO₃ was found to restore or enhance activity in the oxidation of 1; hence, this suggests that
carbonate species plays an essential role in the oxidation reaction. In the oxidation of 2 and 3, Ni-containing LDH catalysts were found to show significant activity for alcohol dehydration, which is likely attributed to complex reaction mechanisms and not only to catalyst basicity. Cu-Cr-LDH was found to effectively oxidize phenyl ethanol derivatives 1 and 2 as well as β-O-4 models 4-6. Phenyl ethanol derivative 3 was completely converted to unidentifiable products, suggesting that phenol protection is a necessity for the isolation of oxidation products. Oxidation of lignin dimers using Cu-Cr-LDH is believed to proceed mainly through an enol ether intermediate, subsequent reaction of the enol ether leading to unidentifiable products. Typically, for all catalysts only trace amounts of the product of benzylic alcohol oxidation were observed for the model dimers. Rather, monomeric products arising from β-aryl ether cleavage were observed. This observation is consistent with the high reactivity of the ketones, resulting from weakening of the Cβ-O4 bond which was shown to be aerobically cleaved at 180 °C in the absence of catalyst. Future work will focus on depolymerization of benzylic ketones under milder conditions.
Chapter 4. Heterogeneous Cleavage of Oxidized $\beta$-O-4 and $\beta$-1 Model Compounds Using Layered Double Hydroxide Catalysts

Disclaimer: The work provided in this chapter is the result of collaboration with Justin Mobley, a post-doctoral scholar at the University of Wisconsin-Madison (Supervisor: John Ralph). Justin Mobley was responsible for collecting the heteronuclear single quantum coherence (HSQC) 2D-NMR spectra and gel permeation chromatograms (GPC) described in section 4.3.5.
4.1. Introduction

Due to the projected depletion of non-renewable fuel sources, processes for the production of renewable fuels from biomass have recently gained much attention. One of the most abundant renewable fuel sources is lignocellulosic biomass. Lignocellulosic biomass is a feedstock composed of three distinct biopolymers: cellulose, hemicellulose, and lignin. While cellulose and hemicellulose can be converted to bioethanol, lignin is currently underutilized due to its low heating value and a lack of cost-efficient processes for its valorization. It has been estimated by Blanch and co-workers\textsuperscript{152} that in order for cellulosic bioethanol to meet the current market price for ethanol, lignin would need to be converted to compounds with a minimum value of $1 (US) per kilogram. Consequently, the development of an economically viable biorefinery model is intrinsically linked to lignin valorization.\textsuperscript{153}

Lignin utilization by depolymerization has been an ongoing area of research for almost a century. Most depolymerization strategies center around cleavage of the β-O-4 linkage, which is characterized by a bridging β-aryl ether bond and an α-benzylic alcohol. Additionally, this linkage is the weakest and most abundant linkage in lignin (ca. 60% of all linkages).\textsuperscript{1} However, most strategies employ energy intensive thermal or reductive linkage cleavage. Alternatively, depolymerization of lignin and lignin models by means of oxidation has recently been reported.\textsuperscript{30-32, 35, 53, 81}
Frequently, reports concerning lignin model compound oxidation target conversion of benzylic alcohols, which are present in both $\beta$-O-4 and $\beta$-1 linkages, to carbonyls. Oxidation of this moiety results in a significant weakening of the $C_{\beta}$-$O_4$ bond in $\beta$-O-4 linkages (by approximately 85 kJ/mol). For $\beta$-1 models that do not contain a linking $\beta$-aryl ether bond, oxidation of the benzylic alcohol results in a significant increase in $\beta$-hydrogen acidity, which facilitates $C_{\beta}$ deprotonation. Thus, benzylic oxidation is believed to be pivotal to oxidative deconstruction of lignin.

Two of the most successful examples of catalytic benzylic oxidation in lignin use the homogenous catalysts 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ). The reduced forms of both TEMPO and DDQ are catalytically oxidized by molecular oxygen via a concurrent NO/NO$_2$ catalytic cycle, regenerating the active oxidation catalyst. Other benzylic oxidation systems include metals such as vanadium and copper but frequently require the use of TEMPO.

In contrast to the well-studied $\beta$-O-4 linkage, other benzylic alcohol-containing linkages such as the $\beta$-1 linkage (more prevalent in hardwood lignin sources) are less explored. Among the few reports in the literature, Hanson and co-workers reported quantitative conversion of models with $\beta$-1 linkage functionality to their corresponding benzylic ketones using a homogeneous vanadium-based catalyst. In the same report, the authors also investigated
oxidation of β-1 linkages using a soluble copper/TEMPO/O2 catalytic system, which resulted in excellent yields of aldehydes derived from Cα-Cβ and Cβ-Cγ oxidative bond cleavage.

Moreover, in reports by Wang et al.,35,69-70 near quantitative conversion of model β-O-4 and β-1 ketones was realized using copper catalysts under aerobic conditions (Scheme 35). Although this oxidation system produced excellent yields of benzoic acids, the catalyst was a homogeneous copper salt, which would be difficult to recover on an industrial scale. In addition, the reaction conditions reported are above the limiting oxygen concentration (LOC) for methanol, raising safety concerns with respect to process scalability.61

Scheme 35. Oxidation of a β-O-4 lignin model dimer performed by Wang et al.70

In a previous report, our group described heterogeneous Baeyer-Villiger oxidation (BVO) of models with β-O-4 and β-1 functionality using a post-synthetically modified tin-β zeolite/hydrogen peroxide oxidation system. It was found that dimers with ketone functionality could be directly converted to esters, which in turn could be hydrolyzed to the corresponding carboxylic acids and alcohols. In this work, layered-double hydroxides (LDHs) were employed as
heterogeneous catalysts for cleavage of lignin and lignin model compounds, incorporating molecular oxygen as the primary oxidant.

LDHs or hydrotalcite-like catalysts have received significant attention for their ability to perform heterogeneous oxidative transformations, including BVO, benzylic oxidations, etc. LDHs are interesting due to their ease of synthesis and tunability with respect to composition and basicity. LDHs are synthesized using base metals with similar ionic radii to magnesium (II), making them a relatively inexpensive catalyst. Upon thermal pretreatment, LDHs are converted to their mixed metal oxides (MMOs) possessing increased surface area and near-atomic dispersion of the metals. Moreover, LDH derived MMOs can be “rehydrated” with aqueous solutions of metal carbonates or bicarbonates to restore the LDH structure (the so-called “memory effect”). Furthermore, while LDHs are active in catalytic reactions, they can also serve as basic supports.

Previously, Beckham and co-workers reported nickel supported on hydrotalcite (Ni/HTC) to be active for benzylic oxidation and cleavage of lignin model compounds. This serves as the first demonstration of oxidation of benzenemethanol, α-(phenoxy)methyl) to acetophenone and phenol over an LDH catalyst (Scheme 36).
However, the reaction required high temperatures (270 °C) and a simple model was investigated. The authors did not comment on the reaction pathway but observed improved conversion when sodium hydroxide was used in lieu of Ni/HTC, suggesting that the reaction was base-catalyzed. In a follow up report by Beckham and co-workers, the authors explored more complex models using a nitrate-intercalated Ni/HTC catalyst. Unfortunately, while the authors observed significant conversion, mass balances decreased as models became more complex.

In another report concerning HTC-mediated oxidation by Corma and co-workers, copper and vanadium were incorporated into a hydrotalcite. The authors demonstrated near quantitative conversion of complex lignin model dimers to a mixture of veratraldehyde and veratric acid with minor dimeric co-products. Guaiacol resulting from β-aryl ether cleavage was not observed, likely due to secondary reactions resulting in the formation of "a complex mixture of unidentifiable products." However, the authors also noted that after hot filtration of the catalyst the reaction continued, confirming the catalytic species was homogeneous.
As demonstrated by our group (Chapter 3), selective oxidation of 1-phenyl ethanol derivatives to acetophenones was observed in near quantitative yields over several LDH catalysts. Additionally, oxidation of β-O-4 models occurred under aerobic conditions below the typical LOC of organic solvents. However, when β-O-4 model compounds were investigated, it was found that models were converted directly to benzoic acids and phenols in moderate yields rather than to their corresponding benzylic ketones. Although high conversions were realized, modest yields of benzoic acids and phenols were obtained due to formation of unknown products. In addition, after benzylic oxidation, it was observed that β-O-4 model ketones underwent cleavage under aerobic conditions at 180 °C in the absence of a catalyst. Non-catalytic cleavage of β-aryl ether bonds in β-O-4 model ketones resulted in good yield of 4′-methoxybenzoic acid, although the yield of corresponding phenolic products was poor. In this study, LDH catalysts were applied and mild temperatures were used in an effort to achieve high conversions of β-O-4 model ketones to benzoic acids. Based on their ability to form active metal-peroxo or metal-superoxide species, which are commonly active in oxidation reactions, LDHs consisting of nickel, copper, and chromium were explored in the oxidation of β-O-4 and β-1 model ketones.
4.2. Experimental

4.2.1. Catalyst Synthesis and Characterization

4.2.1.1. Synthesis of Ni-Al LDH and Ni-Cr LDH

Details of the synthesis Ni-Al LDH and Ni-Cr LDH via coprecipitation are provided in Appendix II.

4.2.1.2. Synthesis of Ni-Cu-Al LDH

A solid mixture of Ni(NO₃)₂•□□□□(17.5 g, 60 mmol), Cu(NO₃)₂•3□□□□(3.7 g, 15 mmol), and Al(NO₃)₃•□□□□(9.4 g, 25 mmol) was dissolved in a 1:1 ethanol/water solution by volume (40 mL) and stirred for 24 h. The metal solution was then concentrated by rotary evaporation and dried in vacuo at 40 °C. A saturated aqueous solution of NaOH (3 g) and NaCO₃ (7.7 g) was added drop-wise to the dry metal salts. A NaOH solution (1 M) was used to adjust the pH to 7.8. The resulting suspension was stirred for 24 h, concentrated by rotary evaporation, and dried in vacuo at 40 °C. The resulting solid was treated with a series of cycles of centrifuging, decanting, and suspending in water until the washings were neutral, affording Ni-Cu-Al LDH (10.4 g).

4.2.1.3. Catalyst Characterization

Surface area, average pore diameter, and pore volume were determined using a Micromeritics Tristar 3000 porosity system using the Brunauer–Emmett–Teller (BET) method by N₂ adsorption at -196 °C or using a Micromeritics Gemini VII analyzer. Samples were outgassed under vacuum or nitrogen for at least 6
hours at 160 °C prior to measurement. Powder X-ray diffraction measurements were performed on a PANalytical X’Pert system using Cu Kα radiation (λ = 1.5406 Å) and a step size of 0.02°. Elemental analysis was performed on a Varian 720-ES inductively coupled plasma-optical emission spectrometer. Scanning electron microscopy (SEM) was performed on a Hitachi S-2700 instrument equipped with a PGT EDS analyzer with a thin window detector and a LaB₆ electron gun. Pulsed CO₂ chemisorption and NH₃-TPD were performed on a Micromeritics AutoChem II analyzer using 200 mg of sample. In each case the sample was first outgassed at 120 °C under argon for 1 h. For pulsed CO₂ chemisorption measurements the sample was then cooled to room temperature and pulsed with CO₂ (100%, 30 sccm) until saturated as indicated by a thermal conductivity detector (TCD). CO₂ was assumed to titrate base sites on a 1:1 molar ratio. In the case of NH₃-TPD, the pre-treated sample was cooled to room temperature and then saturated with NH₃ (1% in helium, 50 sccm) for 1 h. Next the sample was purged (helium 100%, 120 sccm) for 1 h. The sample was then heated to 750 °C at 10 °C/min. Effluent gas was analyzed using a mass spectrometer (Pfeiffer Thermostar GSD301), the signal at m/e = 15 being used to monitor NH₃. NH₃ was assumed to titrate acid sites in a 1:1 molar ratio.

4.2.2. Model Compound Synthesis

Syntheses of models 1-3 have been previously reported and are included in Appendix I. Models 4 and 5 were purchased from VWR and used without further purification.
4.2.2.1. Synthesis of 4,4′-dimethoxybenzil (6)

A suspension of Au/Li-Al LDH (252 mg, 2.9 wt.%), anisoin, (5, 1.1 g, 4 mmol), and toluene (30 mL) were stirred in a 100 mL 3-necked flask equipped with an oxygen bubbler, a reflux condenser, and a glass stopper. The suspension was then heated and stirred at 100 °C under bubbling O₂ for 15 hours, after which the reaction vessel was cooled to room temperature. The reaction mixture was then filtered through Whatman 1 filter paper. The catalyst was washed with THF (2 x 5 mL). The filtrates were combined and concentrated in vacuo to afford a yellow solid (926 mg, 86% yield). GC/MS: m/z 269.0 (10.3%), 253.0 (4.6%) 135.1 (100%).

4.2.3. Procedure for Oxidation of Lignin Model Compounds

Reactions were conducted in batch mode using a Parr reactor (50 mL, Hastelloy C body) equipped with a magnetic stirrer. The reaction mixture was added before sealing the reactor, purging with the reaction gas at pressure, and heating to the desired temperature. The reactor was allowed to build autogenous pressure. After the reaction, the contents of the reactor were filtered and washed with THF. Conversion and yield data were determined by GC/MS.
4.2.4. Determination of 4-methoxybenzoic acid (1a) yields using Gas Chromatography Mass Spectrometry (GC/MS)

Following reaction, an aliquot of the reaction mixture (1 g) was derivatized with a solution of boron trifluoride etherate (0.1 g) in methanol (4 g) for 6 h at 100 °C under nitrogen. The resulting methyl benzoate was analyzed by GC/MS using dodecane as the internal standard.

4.2.5. Procedure for Oxidation of Indulin Lignin

4.2.5.1. Procedure for Benzylic Oxidation of Indulin Lignin using DDQ

A mixture of 2-ethoxyethanol (14 mL), 1,2-dimethoxyethane (21 mL), DDQ (250 mg), and tert-butyl nitrite (250 mg) was added to Indulin lignin (2.5 g). The reaction mixture was heated to 80 °C for 14 h under bubbling O₂. After cooling to room temperature, the lignin product was precipitated with ether (450 mL), was filtered, and washed with hexane (100 mL). The resulting lignin was dried in vacuo at 50 °C. Drying afforded oxidized lignin in near quantitative yield (2.5 g, 99% yield) similar to previous reports.³³

4.2.5.2. Procedure for Depolymerization of DDQ-oxidized Lignin using Ni-Cu-Al LDH

Ni-Cu-Al LDH (400 mg), DDQ-oxidized lignin (400 mg), and methanol (16 mL) were loaded into a Parr reactor (50 mL, Hastelloy C body) equipped with a magnetic stirrer. The reactor was then sealed and purged three times with 6% O₂
(N₂ counterbalance) (1450 psi). The reactor was then heated to 150 °C for 48 h. The reactor was then cooled, a gas fraction was collected, the reactor contents were washed with THF, and the solids present were removed by filtration. The THF layer was concentrated in vacuo to afford 165 mg of lignin (41% soluble fraction yield).

4.2.6. Procedure for Lignin Molecular Weight Determination

Relative molecular weights of lignins were determined by size exclusion chromatography using a Shimadzu LC20-AD LC pump equipped with a Shimadzu SPD-M20A UV-Vis detector set at 280 nm and a Polymer Standard Services GPC column and guard column (PSS PolarSil 8 mm ID x 5 cm, 5 μm ➔ PSS PolarSil 8 mm ID x 30 cm, 5 μm, 100 angstrom porosity). The samples and column compartment were held at 40 °C during analysis. The mobile phase for SEC analysis was DMF with 0.1 M lithium bromide. A conventional calibration curve using a ReadyCal Kit from Sigma-Aldrich (Aldrich # 76552, M(p) 250-70000) and Wyatt ASTRA 7 software were used to determine the molecular weight distribution for each sample.

4.2.7. Procedure for collection of HSQC 2-D NMR Spectra

Lignin samples were placed directly into NMR tubes (ca. 25 mg for each sample) and dissolved using DMSO-d₆/pyridine-d₅ (4:1).¹⁵⁹⁻¹⁶⁰ NMR spectra were acquired on a Bruker Biospin (Billerica, MA) Avance 700 MHz spectrometer equipped with a 5-mm quadruple-resonance ¹H/³¹P/¹³C/¹⁵N QCI gradient
cryoprobe with inverse geometry (proton coils closest to the sample). The central DMSO solvent peak was used as an internal reference (δC 39.5, δH 2.5 ppm). The 1H–13C correlation experiment was an adiabatic HSQC experiment (Bruker standard pulse sequence 'hsqctgpsisp2.2'; phase-sensitive gradient-edited-2D HSQC using adiabatic pulses for inversion and refocusing). HSQC experiments were carried out using the following parameters: acquired from 11.5 to -0.5 ppm in F2 (1H) with 3366 data points (acquisition time 200 ms), 215 to -5 ppm in F1 (13C) with 620 increments (F1 acquisition time 8 ms) of 16 scans with a 1 s interscan delay; the d24 delay was set to 0.86 ms (1/8J, J = 145 Hz). The total acquisition time for a sample was 3 h. Processing used typical matched Gaussian apodization (GB = 0.001, LB = -0.1) in F2 and squared cosine-bell and one level of linear prediction (32 coefficients) in F1. Volume integration of contours in HSQC plots used Bruker’s TopSpin 3.5pl5 (Mac version) software and used spectra reprocessed without linear prediction.

4.3. Results and Discussion

4.3.1. Catalyst Characterization

Ni-Al and Ni-Cr LDHs were found to have BET surface areas of approximately 100 m²g⁻¹ (Table 17, entry 2 and 3). Ni-Cr LDH was found to have a rather small average pore diameter of 2.9 nm, with a high concentration of acid sites, which are presumably associated with the presence of coordinatively unsaturated metallic species on the catalyst surface. In addition to having a significantly larger surface area than Ni-Cu-Al LDH, both Ni-Al and Ni-Cr
LDH possessed more acid and base sites, as measured by NH$_3$ temperature programmed desorption (TPD) and pulsed CO$_2$ chemisorption, respectively. The surface area of Ni-Cu-Al LDH, prepared by a modified procedure, was approximately 1.5 m$^2$g$^{-1}$, which is very low for typical LDHs. The low surface area is likely responsible for the relatively low number of acid and base sites on the Ni-Cu-Al LDH. However, the average pore diameter was determined to be 22.1 nm, much larger than the pores of the other catalysts studied, which is particularly well-suited for lignin depolymerization given the need for facile diffusion of the lignin macromolecule.

Table 17. Characterization data for LDH catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Actual Formula$^a$</th>
<th>BET SA (m$^2$g$^{-1}$)</th>
<th>Pore Volume (cm$^3$g$^{-1}$)</th>
<th>Pore Diameter (nm)</th>
<th>Basicity$^b$ (μmol CO$_2$ ads./g LDH)</th>
<th>Acidity$^c$ (μmol NH$_3$ ads./g LDH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ni-Cu-Al LDH</td>
<td>Ni$<em>{0.54}$Cu$</em>{0.14}$Al$_{0.32}$</td>
<td>1.50</td>
<td>0.011</td>
<td>22.1</td>
<td>&lt;1</td>
<td>27.7</td>
</tr>
<tr>
<td>2</td>
<td>Ni-Al LDH</td>
<td>Ni$<em>{0.66}$Al$</em>{0.35}$</td>
<td>136.6</td>
<td>0.249</td>
<td>7.3</td>
<td>79.2</td>
<td>281.4</td>
</tr>
<tr>
<td>3</td>
<td>Ni-Cr LDH</td>
<td>Ni$<em>{0.65}$Cr$</em>{0.32}$</td>
<td>76.6</td>
<td>0.055</td>
<td>2.9</td>
<td>51.8</td>
<td>383.1</td>
</tr>
</tbody>
</table>

$^a$Determined by ICP. $^b$Determined by pulsed CO$_2$ chemisorption experiments. $^c$Evaluated by ammonia temperature programmed desorption experiments.

The low surface area of the Ni-Cu-Al LDH is potentially a consequence of the synthesis method. In order to evaluate the effect of the synthesis protocol on LDH properties, an analogous Ni-Al LDH was synthesized using the same method. N$_2$ physisorption revealed that the resulting Ni-Al LDH had a surface area of 151 m$^2$g$^{-1}$. Therefore, it can be concluded that the incorporation of copper is likely responsible for the low surface area. Indeed, it has been previously reported that inclusion of Cu$^{2+}$ increased mesoporosity and uniformity while
decreasing the surface area compared to an analogous Mg$^{2+}$ LDH, albeit the effect is less profound.

When synthesizing Ni-Cu-Al LDH, the Ni$^{2+}$/Cu$^{2+}$ ratio was fixed at 4:1 due to the propensity of copper to form a separate phase, resulting from Jahn-Teller distortions, at high concentrations. Although the incorporation of copper had an effect on the catalyst surface area, no effect on the formation of the LDH phase was observed, as demonstrated by the x-ray diffractograms (Fig. 25). In fact, Ni-Cu-Al LDH appears to be more crystalline than Ni-Al LDH, consistent with previous reports that also observed high structural uniformity in Cu-containing LDHs. Both Ni-Al and Ni-Cu-Al LDHs displayed typical LDH diffraction patterns, while the Ni-Cr LDH displayed rather poor crystallinity.
To confirm the morphology of the Ni-Cu-Al LDH, the catalyst was further characterized by SEM. Micrographs confirmed a platelet morphology, as commonly observed for LDHs (Fig. 26). In addition, the metal dispersion was investigated by energy dispersive x-ray (EDX) spectroscopy. Specifically, copper was found to be well dispersed throughout the LDH structure (Fig. 26, image (d)), indicating that Jahn-Teller distortions did not result in the formation of a separate Cu$^{2+}$ containing phase.

*Layered Double Hydroxide

Figure 25: X-ray diffractograms of LDH catalysts.
4.3.2 Catalytic Oxidative Depolymerization of β-O-4 Lignin Model Ketones

4.3.2.1 Solvent screening

In order to determine an appropriate solvent for the oxidation of lignin model dimers, a previously reported system, Cu$^{2+}$/1,10-phenanthroline, was investigated. Diphenyl ether (DPE) was selected for its ability to solubilize lignin at elevated temperatures (Chapter 3). Additionally, methanol and ethanol were evaluated as solvents due to literature precedent and their high polarity. In all cases, initial solvent screening reactions were fixed at 8% O$_2$-slightly below the flammability limit for DPE-to provide equal oxygen partial pressures to each system. Using molecular oxygen as a primary oxidant is ideal for many reasons (e.g., availability, expense). However, the use of O$_2$ greatly increases safety.
considerations due to its oxidizing capabilities. Therefore, in this work, non-flammable \( \text{O}_2/\text{N}_2 \) gas mixtures were used to oxidize lignin and lignin models.

Common problems in oxidation reactions include solvent oxidation and coordination of polar solvents to the catalytically active sites. However, methanol, ethanol, and DPE were found to be stable under the reaction conditions and did not undergo significant oxidation. Using the \( \text{Cu}^{2+}/\text{phenanthroline} \) oxidation system, model 1 was converted to 4-methoxybenzoic acid (1a) in high yields (Table 18). The oxidation of 1 in methanol to 1a was observed in a moderate yield (55%) after 3 h. When ethanol and DPE were used as solvents, 49% and 41% yields of 1a were obtained, respectively, albeit the reaction in DPE was run for 16 h.

Table 18. Conversion of 1 over copper/phenanthroline under aerobic conditions in DPE.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80</td>
<td>MeOH</td>
<td>3</td>
<td>&gt;99</td>
<td>55</td>
</tr>
<tr>
<td>120</td>
<td>EtOH</td>
<td>3</td>
<td>99</td>
<td>41</td>
</tr>
<tr>
<td>120</td>
<td>DPE</td>
<td>16</td>
<td>&gt;99</td>
<td>49</td>
</tr>
</tbody>
</table>

4.3.2.2. Oxidative depolymerization of \( \beta\)-O-4 lignin model ketones in DPE

Initially, DPE was investigated as the solvent for oxidative fragmentation of lignin model ketones over LDHs catalysts. As shown in Table 19, in the absence of catalyst 1a was obtained in moderate yield (32%, 55% conversion). Similar
conversions and yields of 1a were obtained in reactions with Ni-Cr LDH (38% yield) and Ni-Al LDH (29% yield), implying that the catalysts did not participate in the oxidation of 1 to 1a. However, Ni-Cu-Al LDH resulted in near quantitative conversion of 1, with the formation of 1a in good yield (59%), confirming that Ni-Cu-Al LDH was catalytically active in the oxidative fragmentation of 1. The promotion of catalytic oxidation is similar to previous reports concerning the aerobic oxidation of glycerol over Cu-containing LDHs.162

Table 19. Conversion of 1 over various LDHs under aerobic conditions in DPE.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>--</td>
<td>16</td>
<td>58</td>
<td>55</td>
<td>32</td>
</tr>
<tr>
<td>120</td>
<td>Ni-Cr LDH</td>
<td>16</td>
<td>68</td>
<td>55</td>
<td>38</td>
</tr>
<tr>
<td>120</td>
<td>Ni-Al LDH</td>
<td>16</td>
<td>50</td>
<td>58</td>
<td>29</td>
</tr>
<tr>
<td>120</td>
<td>Ni-Cu-Al LDH</td>
<td>&gt;99</td>
<td>&gt;99</td>
<td>60</td>
<td>59</td>
</tr>
</tbody>
</table>

Although it was not investigated in this contribution, previous publications35,82 found that electron donating groups (EDGs) on the β-aryl ether ring exerted an effect on the recovery of the phenol product resulting from C₆-O₄ bond cleavage. Specifically, Wang et al.35 observed that when one or more methoxy groups activated the β-aryl ether ring, yields of phenol decrease to ca. 30% as opposed to ca. 90% when the β-aryl ether ring was unactivated. Modest yields of phenols from β-aryl ether cleavage are a common problem in the oxidation of lignin model compounds due to reactions such as phenolic radical coupling.30,32-33,35
In this oxidation system, phenols were recovered in poor yields (ca. 5%) and are not reported. In order to investigate the consumption of phenols, a reaction using guaiacol/DPE solution was conducted in the absence of catalyst at 180 °C. After 16 h, guaiacol was recovered in 24% yield and a significant amber coloration of the reaction solution was observed, suggesting the possible formation of polymeric material, as discussed in Chapter 3. Therefore, it can be concluded that phenols resulting from β-aryl ether cleavage are unstable in the presence of O₂ at elevated temperatures, even in the absence of catalyst.

After oxidation of 1 over Ni-Cu-Al LDH, an aliquot of the reaction mixture was analyzed by ICP, revealing negligible leaching of metals (<1 ppm Ni, <1ppm Cu). The absence of metals in the reaction solution suggests that catalysis occurs heterogeneously and not by dissolved metal ions.

When model 2 was investigated under the same reaction conditions in the absence of catalyst, the conversion of 2 was only 22%, contrary to the 58% conversion for 1 (Table 20). Furthermore, significantly higher conversions were observed in Ni-Cr LDH and Ni-Al LDH catalyzed reactions (97% and 72% conversion, respectively). Conversion of 2 increased in all cases, with the exception of Ni-Cu-Al LDH for which conversions of 1 and 2 were near quantitative in both cases. While conversions generally increased, after oxidation
over Ni-Al LDH the yield of 1a decreased from ca. 30% for 1 to approximately 15% for 2. The yield of 1a over Ni-Cr LDH increased from 38% for 1 to 53% for 2.

Table 20. Conversion of 2 over various LDHs under aerobic conditions in DPE.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Catalyst</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120</td>
<td>--</td>
<td>16</td>
<td>22</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>120</td>
<td>Ni-Cr LDH</td>
<td>16</td>
<td>97</td>
<td>55</td>
<td>53</td>
</tr>
<tr>
<td>120</td>
<td>Ni-Al LDH</td>
<td>16</td>
<td>72</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>120&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Ni-Cu-Al LDH</td>
<td>16</td>
<td>91</td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data was collected using a modified GC/MS method (inlet temperature was decreased to 280 °C)

As previously discussed in Chapter 3, it is important to use models that accurately represent lignin’s connectivity in order to evaluate the efficacy of lignin depolymerization. Indeed, model 2 is not a possible lignin model compound due to the substitution pattern of the 4-position (only possible when methoxy groups are in the 3 and 5 positions). The subtle changes in the substitution pattern of 2 had a noticeable effect on conversions when compared to 1. Electronically 1 and 2 are almost identical, thus the observed changes in conversion are likely due to steric effects involving the ortho-substitution pattern of 1.

4.3.2.3. Oxidative depolymerization of β-O-4 lignin model ketones in methanol

Although oxidations in DPE resulted in significant yields of 1a from cleavage of β-O-4 models, minor co-products stemming from solvent hydroxylation and guaiacol-DPE coupling were observed. Undesired reactions
such as ring hydroxylation consume molecular oxygen and solvent, and generate complex product mixtures. Furthermore, the high boiling point (ca. 258 °C) of DPE renders it a difficult medium for small molecule extraction. For the above reasons, methanol was also explored as an aerobic oxidation solvent.

To prevent complete conversion of 1, reactions were initially conducted at 80 °C and reaction times were reduced to 3 h (Table 21). Additionally, the O₂ concentration was decreased to 6% so as to be below the flammability limit (limiting oxygen concentration) for methanol. Indeed, in the uncatalyzed reaction of 1 no conversion was observed. In the case of Ni-Cr LDH, conversion of 1 to 4-methoxybenzoic acid (1a) was also not observed, this being a consequence of increased solvent polarity (catalyst inhibition likely occurred due to solvent coordination to active sites). Due to its low activity in the oxidation of 1 and 2 in DPE, the oxidation over Ni-Al LDH in methanol was not explored. However, oxidation of 1 over Ni-Cu-Al LDH (6% O₂/N₂) resulted in 58% conversion to 1a (19% yield). When the oxygen concentration was increased 8%, oxidation over Ni-Cu-Al LDH resulted in increased conversion of 1 (73%) and increased yield of 1a (48%). The increase in conversion and yield is perhaps a result of limited availability of oxygen in the reaction solution at 50 bar. In order to further increase the equivalents of oxygen available while maintaining oxygen concentrations below the LOC of methanol, the pressure was increased to 100 bar, providing ca. 4 eq. of the primary oxidant.
Table 21. Conversion of 1 over various LDHs under aerobic conditions in methanol.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>[O$_2$] (wt.%)</th>
<th>Pressure (bar)</th>
<th>Approximate eq. of O$_2$</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>--</td>
<td>6</td>
<td>50</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ni-Cr LDH</td>
<td>6</td>
<td>50</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Ni-Cu-Al LDH</td>
<td>6</td>
<td>50</td>
<td>2</td>
<td>58</td>
<td>33</td>
<td>19</td>
</tr>
<tr>
<td>Ni-Cu-Al LDH</td>
<td>8</td>
<td>50</td>
<td>2.7</td>
<td>73</td>
<td>66</td>
<td>48</td>
</tr>
</tbody>
</table>

Similar to results using the Cu/phenanthroline oxidation system, the oxidation of 1 with Ni-Cu-Al LDH in methanol for 3 h (8% O$_2$/N$_2$) was comparable to reactions performed in DPE (16 h). Therefore, to increase the yield of 1a, the oxidation temperature and pressure were increased incrementally. As shown in Table 22, an uncatalyzed reaction was conducted at 100 bar and 120 °C, resulting in 51% conversion of 1 and 0% yield of 1a. Furthermore, in oxidations over Ni-Cu-Al LDH as reaction time and pressure were increased, higher conversions were obtained reaching a maximum of 100% conversion and 0% yield of 1a. The highest yield of 1a was obtained at 80 °C under 100 bar 6% O$_2$/N$_2$ gas mixture (26%), which suggests further reaction of 1a may occur at higher temperatures (120 °C).
Table 22. Conversion of 1 over Ni-Cu-Al LDH under aerobic conditions in methanol.

<table>
<thead>
<tr>
<th>Oxygen concentration (wt.%)</th>
<th>Pressure (bar)</th>
<th>Approximate eq. of O\textsubscript{2}</th>
<th>Temperature (°C)</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6\textsuperscript{a}</td>
<td>100</td>
<td>4</td>
<td>120</td>
<td>51</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>1</td>
<td>80</td>
<td>0</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>75</td>
<td>3</td>
<td>80</td>
<td>93</td>
<td>--</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>4</td>
<td>80</td>
<td>80</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>4</td>
<td>120</td>
<td>100</td>
<td>--</td>
<td>0</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reaction proceeded without catalyst.

After optimization of the reaction conditions for 1 in methanol, the oxidation of model 3 was investigated using Ni-Cu-Al LDH (Scheme 37). The addition of a γ-carbinol makes model 3 a more realistic lignin model compound. However, γ-carbinol models are often converted to monomeric molecules in lower yields\textsuperscript{35, 82} and can yield an increasingly complicated reaction mixture as a result of α-retro-aldo\textsuperscript{30} and γ-retro-aldo\textsuperscript{35, 68} reactions.

Indeed, modest conversion (27%) was observed in the oxidation of 3 over Ni-Cu-Al LDH, resulting in a poor yield of 1a (6%). To obtain increased conversion of 3, more forceful temperatures may need to be used (e.g., 150 °C). Increasing the temperature has been proven to be effective in the oxidation of more complicated lignin model compounds\textsuperscript{35}. 
Having obtained promising results in both protic and aprotic solvents, the effect of light calcination on catalyst performance was investigated. Previously, it has been reported that light calcination resulted in increased LDH activity for base catalyzed reactions. Changes in activity are associated with the removal of weakly absorbed water, which increases the number of coordinatively unsaturated (catalytically active) metal sites. However, in this work, we found that thermal pretreatment at 175 °C for 3 h resulted in a significant decrease in catalytic activity for Ni-Cu-Al LDH. Indeed, after calcination, the conversion of 1 decreased from 73% to 15%. In addition, 1a was observed in only trace amounts after oxidation using calcined Ni-Cu-Al LDH (Scheme 38). The observed loss of activity is likely a result of partial thermal elimination of interstitial carbonates by conversion of the LDH surface to a mixed-metal oxide (MMO). As previously reported by Beckham and co-workers, interstitial anions likely play a role in β-aryl ether bond cleavage. Furthermore, Dragoi et al. previously reported that nickel-based LDHs begin to decompose to their corresponding metal oxides at temperatures as low as 150 °C, albeit under reductive conditions. Moreover, the authors noted that LDH decomposition was more facile for copper containing Mg-Ni-Al LDHs. In summary, the presence of accessible anions in the LDH appears to be critical in the oxidation of lignin model compounds.
4.3.3. Catalytic Oxidative Depolymerization of β-1 Lignin Model Ketones

In order to completely utilize lignin, catalysts need to be active for fragmentation of multiple linkages. Having established that uncalcined Ni-Cu-Al LDH is an effective oxidation catalyst for β-O-4 model compounds, its efficacy for the conversion of β-1 models to benzoic acids was investigated (Table 23). Although they are less frequent than β-O-4 linkages, β-1 linkages can comprise up to ca. 8% of all lignin linkages. Therefore, β-1 model compounds were subjected to the same reaction conditions as β-O-4 models. Initially, β-1 models were investigated at 80 °C in methanol to facilitate the comparison of catalysts at <100% conversion. Due to the symmetry of β-1 models explored in this work, benzoic acid yields are calculated on the basis of a 2:1 product to β-1 model molar ratio.

Table 23. Conversion of 4 over LDH catalysts under aerobic conditions in methanol.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Temperature (°C)</th>
<th>Pressure (bar)</th>
<th>Time (h)</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>--</td>
<td>80</td>
<td>50</td>
<td>3</td>
<td>41</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Ni-Cr LDH</td>
<td>80</td>
<td>50</td>
<td>3</td>
<td>38</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Ni-Al LDH</td>
<td>80</td>
<td>50</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ni-Cu-Al LDH</td>
<td>80</td>
<td>50</td>
<td>3</td>
<td>48</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ni-Cu-Al LDH</td>
<td>120</td>
<td>100</td>
<td>16</td>
<td>&gt;99</td>
<td>27</td>
<td>27</td>
</tr>
</tbody>
</table>
In contrast to β-O-4 model compound 1, when β-1 model 4 was subjected to the previously established oxidation system, modest conversion was observed. At 80 °C conversion reached a maximum of approximately 50% (Table 23). Additionally, all of the catalytic systems examined (Ni-Cr LDH, Ni-Al LDH, and Ni-Cu-Al LDH) with 4 resulted in similar conversion as the reaction in the absence of an LDH catalyst. In order to realize higher conversions, the reaction temperature was increased to 120 °C for the Ni-Cu-Al LDH (Table 23). At 120 °C the conversion of 4 was near quantitative, a 27% yield of 1a being obtained (2:1 substrate to product ratio). Although the yield of 1a was modest, the oxidation of 4 highlights the versatility of this catalytic system. As mentioned above, in order to effectively depolymerize lignin, the catalytic oxidation system should be active for multiple linkages.

4.3.4. Mechanistic investigation

In order to investigate the pathway for Ni-Cu-Al LDH catalyzed bond cleavage, several potential β-1 oxidation intermediates were oxidized at 120 °C (Table 24). Initially, anisoin (5) was investigated as a potential reaction intermediate. It has been previously proposed that β-aryl ether cleavage begins by oxidation of the β-carbon, which is ultimately lost as carbon dioxide.35 Surprisingly, the model representing β-oxidation (5) did not result in formation of 1a. Instead the oxidation of (5) resulted in benzylic oxidation of the β-carbon, yielding 6 in 76% yield. While the reaction intermediate may in fact be a copper-oxygen complex, it would stand to reason that the β-alcohol would be easily
deprotonated or hydrogen abstraction may take place, resulting in a similar mechanism to that suggested previously.\textsuperscript{35}

Table 24. Conversion of 4-6 over Ni-Cu-Al LDH under aerobic conditions in methanol.

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
<th>Yield of 1a (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>&gt;99</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>5</td>
<td>&gt;99\textsuperscript{a}</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Yields of benzoic acids were calculated on the basis of a 2:1 product/substrate ratio due to the symmetry of reaction intermediates. \textsuperscript{a}Model 5 was converted to 6 in 76\% isolated yield.

Following the oxidation of anisoin (5), the fragmentation of 4-4\textsuperscript{′}-dimethoxybenzil (6) was investigated. However, 6 showed little reactivity when subjected to the reaction conditions at 120 °C. This implies that 5 and 6 are not intermediates in the production of 1a.

Product 1a could result from of alkyl migration during Baeyer-Villiger Oxidation (BVO). Alkyl migration would result in the production of an ester which could then be hydrolyzed \textit{in situ}. To screen for evidence of BVO, 2-
adamantanone, which is known to be oxidized by BVO systems, was used as a probe molecule to determine if BVO was the pathway for oxidations using Ni-Cu-Al LDH. After 16 h at 120 °C 100 bar (6% O2/N2), the BVO product of 2-adamananone or the subsequent hydrolysis products were not observed, implying that oxidative fragmentation of β-O-4 and β-1 models proceeds through a different reaction pathway. Indeed, additional studies will need to be conducted to completely elucidate the reaction mechanism.

Surprisingly, when oxidations using Ni-Cu-Al LDH were run at elevated temperature and pressure, increased metal leaching was observed. Leaching, indicated by the green coloration of the reaction solution, is a consequence of deconstruction of the LDH structure. In the case of desoxyanisoin oxidation at 120 °C, the presence of metals in solution was confirmed by inductively coupled plasma (ICP) analysis (59 ppm Cu and 33 ppm Ni) after aqueous washes (2 mL, x3). Metal leaching is likely a result of the acidity of the benzoic acid produced. Furthermore, metal leaching was not observed in the oxidation of anisoin, which was directly converted to 6 (0% yield of 1a).

4.3.5. Oxidation of Indulin lignin

Based on the forgoing, the fragmentation of Indulin AT lignin was examined, the lignin first being oxidized according to a literature procedure.33 Previously, Westwood and co-workers33 found that 1,4-dioxane extracted birch lignin was selectivity oxidized using a homogeneous aerobic DDQ/β-BuONO
oxidation system. Given the success of this approach, the DDQ/t-BuONO system was applied to Indulin AT lignin. Fragmentation of the oxidized Indulin lignin was conducted in methanol over Ni-Cu-Al LDH under 6% O₂ (nitrogen as balance) atmosphere at 150 °C, the reaction being allowed to proceed for a longer time (48 h) than for the lignin model compounds in an effort to ensure complete reaction of the lignin (Scheme 39). After conclusion of the reaction, a gas fraction was collected and analyzed using a refinery gas analyzer (RGA). RGA results confirmed that nearly all of the oxygen had been consumed by the reaction (<0.5% O₂). The THF soluble portion of the reaction mixture was then analyzed via 2D-HSQC NMR spectroscopy, GC/MS, and GPC. Following filtration of the reaction mixture, it was found that 41% of the initial lignin mass was THF-soluble, the insoluble lignin remaining unrecovered as a solid mixture with the Ni-Cu-Al LDH.

Scheme 39. Fragmentation of DDQ oxidized Indulin lignin using Ni-Cu-Al LDH.

As shown in Fig. 27, the HSQC 2-D NMR spectrum of the linkage region of DDQ-oxidized lignin showed that the benzylic position of the β-O-4 linkages was indeed oxidized, as evidenced by the decreased intensity of the Aα cross-
peak at 5.0/70 ppm ($^1$H/$^{13}$C), and the $A_\beta$ peak at 4.4/84 ppm ($^1$H/$^{13}$C) which implies benzylic oxidation at the $\alpha$- and potentially the $\beta$-position. Furthermore, the presence of cross peaks at 5.7/82 ppm ($^1$H/$^{13}$C) and 3.9/64 ppm ($^1$H/$^{13}$C), corresponding to oxidized $\beta$-O-4 linkages ($A'_{\beta}$ and $A'_{\gamma}$, respectively), confirm oxidation. Additionally, cross-peaks corresponding to $\beta$-5 linkages, $B_\alpha$, at 5.5/88 ppm ($^1$H/$^{13}$C), and $B_\beta$, 3.2/52 ppm ($^1$H/$^{13}$C), and $\beta$-$\beta$ linkages, $C_\alpha$, 4.7/85 ppm ($^1$H/$^{13}$C), $C_\beta$, 3.0/52 ppm ($^1$H/$^{13}$C), and $C_\gamma$, 4.1/70 ppm and 3.7/70 ppm ($^1$H/$^{13}$C), also disappeared, presumably due to oxidation to give aromatic benzofuran rings in the case of $\beta$-5 linkages. The products of $\beta$-$\beta$ linkage oxidations have not been well characterized, but likely involve aromatization of one tetrahydrofuran ring and functionalization of the other. The oxidations of $\beta$ linkages are not well studied, likely due to its low natural abundance in lignin, and the difficult synthesis of realistic $\beta$-$\beta$ model compounds. The oxidation of $\beta$-5 and $\beta$-$\beta$ linkages has been previously reported in homogenous oxidation systems, including the report by Westwood and co-workers.\textsuperscript{30, 33} Although the $\alpha$-positions of many of the linkages were oxidized, the $\gamma$-alcohols for both the $\beta$-O-4 ($A_\gamma$, 3.5/60 ppm ($^1$H/$^{13}$C)) and $\beta$-5 ($B_\gamma$, 3.4/64 ppm ($^1$H/$^{13}$C)) linkages remained intact, suggesting that DDQ oxidation is selective for benzylic oxidation. Indeed, the 2D-HSQC NMR spectrum of oxidized Indulin lignin is consistent with the spectrum of oxidized 1,4-dioxane lignin reported by Westwood and co-workers.\textsuperscript{33}

After oxidative fragmentation over Ni-Cu-Al LDH, linkages oxidized during DDQ oxidation were no longer present. Cross-peaks such as $A_\gamma$, (3.5/60 ppm
(\(^1H/^{13}C\)) B\(_γ\), (3.4/64 ppm (\(^1H/^{13}C\))) A\(_β\), (5.7/82 ppm (\(^1H/^{13}C\))) and A\(_′\gamma\), (3.9/64 ppm (\(^1H/^{13}C\))) were also absent after Ni-Cu-Al LDH-mediated oxidation, implying that further oxidation occurred. Moreover, the oxidative fragmentation of DDQ-oxidized lignin over Ni-Cu-Al LDH did not result in resonances in HSQC NMR spectra that have been previously identified. It should also be noted that benzoic acids such as 1a (the primary product observed in the oxidation of models 1-4) do not appear in HSQC spectra, given that carboxylic acids do not contain C-H bonds that are polarized during HSQC spectroscopy.

Figure 27. 2D-HSQC NMR spectra of the linkage region for Indulin AT lignin (a), DDQ-oxidized Indulin AT lignin (b), and Ni-Cu-Al LDH oxidized Indulin AT lignin (c).

DDQ-mediated oxidation of Indulin AT lignin was further confirmed by analysis of the aromatic region (Fig. 28). First, it is important to note that the
Indulin lignin used in this work is isolated from softwood species, thus the lignin is absent of S-units. Oxidation of guaiacyl units was evident by the decrease in intensity of the G_2 (6.8/114 ppm (^{1}H/^{13}C)) and G_5/G_6 (6.8/122 ppm (^{1}H/^{13}C)) cross-peaks after DDQ oxidation. However, after oxidative fragmentation of DDQ-oxidized lignin over Ni-Cu-Al LDH, resonances corresponding to guaiacyl units G_2 (6.8/114 ppm (^{1}H/^{13}C)) and G_5/G_6 (6.8/122 ppm (^{1}H/^{13}C)) or oxidized guaiacyl units G'_2 (6.7/114 ppm (^{1}H/^{13}C)), G'_5 (7.0/116 ppm (^{1}H/^{13}C)), and G'_6 (7.6/122 ppm (^{1}H/^{13}C)) were no longer present in the HSQC NMR spectrum. Instead, small resonances at (6.9/119 ppm (^{1}H/^{13}C)) and (7.3/130 ppm (^{1}H/^{13}C)) were observed. These resonances have not been previously identified using HSQC NMR spectroscopy.
GPC showed a significant decrease in the average molecular weight of the THF-soluble portion of the oxidized lignin, the average molecular weight of the Indulin lignin decreasing from 5100 Da to ca. 1000 Da after DDQ oxidation and then to ca. 400 Da, which is similar to the molecular weight of lignin dimers, after treatment with Ni-Cu-Al LDH/O$_2$. Therefore, the THF-soluble lignin resulting from Ni-Cu-Al LDH-mediated oxidation was silylated and analyzed by GC/MS spectroscopy. Unfortunately, GC/MS analysis did not detect the presence of monomeric lignin-derived products.
4.4. Conclusions

Copper incorporation in the LDH structure proved to be an effective means for catalyzing the conversion of benzylic ketones directly to benzoic acids in β-O-4 lignin model compounds. The Ni-Cu-Al LDH-mediated oxidation of benzylic ketones in β-1 model compounds proved to be less effective, with lower yields of benzoic acids being obtained. The maximum yield of the benzoic acid product reached 59%, 53%, and 6% in the case of models 1, 2, and 3, respectively, whereas the oxidation of β-1 model 4 yielded a maximum of 27% 1a. Reaction conditions were compatible with polar protic and polar aprotic solvents, namely, methanol and DPE. The aerobic oxidation system used in this work resulted in poor phenol yields due to formation of unidentifiable products. Evidentially, a fine balance must be struck between providing sufficient energy to promote bond cleavage, while preventing oxygen reaction with unprotected phenols. Additionally, the average molecular weight of THF-soluble oxidized Indulin AT lignin was significantly decreased after fragmentation using the Ni-Cu-Al LDH/6% O₂/N₂ oxidation system. Although monomeric compounds were not detected, significant conversion of a technical lignin was inferred from GPC and HSQC 2-D NMR spectroscopy data. This contribution serves as one of the first examples of oxidative cleavage of a technical lignin using a copper-containing LDH. Future work will investigate the use of a Ni-Cu-Al LDH prepared by conventional methods.

Disclaimer: The work provided in this chapter is the result of collaboration with Justin Mobley, a post-doctoral scholar at the University of Wisconsin-Madison (Supervisor: John Ralph). Justin Mobley was responsible for collecting the heteronuclear single quantum coherence (HSQC) 2D-NMR spectra and gel permeation chromatograms (GPC) described in section 5.3.3 and 5.3.4.
5.1. Introduction

With the increasing demand for energy in all its forms, utilization of renewable resources is more important than ever. One of these resources is lignocellulosic biomass. While cellulose and hemicellulose can be industrially utilized for the production of ethanol, lignin remains largely under-utilized. However, when lignin is depolymerized it is of interest to multiple industries (e.g., fine chemicals, flavorings, bioplastics, etc.). Despite this, and the many attempts to depolymerize lignin involving thermal and reductive treatments that have been reported in the literature, to date thermal or reductive lignin depolymerization has not been successfully commercialized.

In opposition to the well-studied techniques mentioned above, several selective lignin depolymerization strategies have recently been introduced. One of the most successful was introduced by Stahl and co-workers. After initial benzylic oxidation using a TEMPO/O2 oxidation system, lignin was depolymerized using a HCOOH/HCOONa redox-neutral β-aryl ether cleavage reaction (Scheme 40). Although high yields of ethyl acetate-soluble low molecular weight products resulted from the reaction sequence, the feed used was not a commercial lignin. Rather, the lignin used by Stahl and co-workers was enzymatically purified by removal of carbohydrates after extraction. Furthermore, the reaction was conducted on a small (35 mg) scale.
In another report of selective benzylic oxidation, Westwood and co-workers\textsuperscript{33} described selective benzylic oxidation of lignin incorporating a catalytic DDQ/O\textsubscript{2} system. After subsequent zinc-based reductive cleavage (one-pot) lignin-derived phenols were recovered in 6\% yield. However, the authors used a non-commercial 1,4-dioxane-extracted lignin. Additionally, the reactions discussed above apply homogeneous catalysts, which are difficult to separate from product streams on an industrial scale.

While several genetically modified lignins have been introduced with the goal of producing a more easily depolymerized lignin,\textsuperscript{6} these modified lignins are years or even decades away from incorporation in an industrial setting. Although much progress has been made in this area, the importance of using existing technical lignins such as Kraft lignin cannot be over-emphasized. Technical lignins resulting from pulp milling have been extensively researched and are widely available. The abundance of Kraft lignin, in particular, would allow for faster incorporation into commercial processes. Therefore, utilization of lignins produced from current commercial processes such as paper and bioethanol production is a crucial step towards a sustainable biorefinery model.
In previous reports concerning the oxidation of Indulin lignin, catalytic molybdenum-based polyoxometalates (POMs)\textsuperscript{164} and non-catalytic alkaline oxidation of lower oligomers\textsuperscript{165} yielded vanillin in excellent yields (ca. 7%) compared to alkaline oxidation, which often yields a maximum of 4% vanillin. As reported by von Rohr and co-workers,\textsuperscript{164} in oxidations using POM catalysts, vanillin and methyl vanillate were each recovered in 3.5% yield. However, the POM catalyst was homogeneous in nature, making the catalyst difficult to recover. In a report by Rodrigues and co-workers,\textsuperscript{165} the efficiency of alkaline lignin depolymerization was investigated as a function of lignin molecular weight. The authors found that as lignin molecular weight was decreased, vanillin could be extracted in yields of up to 7.6%. While excellent yields of vanillin were obtained, oxidations using POMs resulted in vanillin solvent coupling, while alkaline oxidation used lignin of a lower molecular to increase its solubility and consequently the yield of vanillin.

In this work, a commercially produced technical lignin was oxidized using a step-wise heterogeneous catalytic system incorporating layered double hydroxides (LDHs). In a recent publication by Crocker and Mobley,\textsuperscript{81} LDHs were reviewed for their activity in aerobic oxidation reactions.\textsuperscript{81} Moreover, as previously reported by our group (Chapter 3) and others,\textsuperscript{79,82-83} LDHs are active catalysts for the oxidation of model compounds possessing lignin-like functionality.
Recently, our group identified several heterogeneous oxidation systems that are active for the oxidation of β-O-4 and β-1 model compounds to benzoic acids (Chapters 2-4). In this work, heterogeneous oxidative lignin depolymerization strategies are compared to select literature procedures for homogeneous lignin depolymerization using a technical lignin. According to a review by Mobley and Crocker, Mg-Al LDH or hydrotalcite supported gold nanoparticles (Au/HTC) was identified as an exceptionally active catalyst for the aerobic oxidation of benzylic alcohols. Therefore, a Au/HTC catalyst was chosen to investigate the aerobic oxidation of a technical lignin. Following Au/HTC-mediated oxidation, the Ni-Cu-Al LDH identified in chapter 4 was used to cleave lignin linkages by further oxidation. At the conclusion of the reactions, THF-soluble products were characterized by means of heteronuclear single quantum coherence (HSQC) 2D-NMR spectroscopy and gel permeation chromatography (GPC) molecular weight analysis.

5.2. Experimental

5.2.1. Catalyst Synthesis

5.2.1.1. Preparation of Mg-Al (3:1) LDH

Mg-Al LDH was prepared by previously reported coprecipitation methods. An aqueous solution of Mg(NO₃)₂•6H₂O (77 g, 0.3 mmol) and Al(NO₃)₃•9H₂O (38 g, 0.1 mol), and a solution of NaOH (120 g of 50 wt.%, 1.5 mol) and Na₂CO₃ (30 g, 0.280 mol), total volume (330 mL), were simultaneously added drop-wise in to
a vigorously stirred 5-necked flask (1 L) equipped with an overhead stirrer. The pH was maintained at ca. 9. The resulting slurry was aged overnight at 75 °C and was then washed by means of centrifuging, decanting, and suspending in water until the washings were neutral. The solid was then dried *in vacuo* at 60 °C.

5.2.1.2. Preparation of Au/Mg-Al (3:1) LDH

A solution of HAuCl₃•3H₂O (0.178 g, 0.5 mmol) in deionized water (225 mL) was stirred for 2 min before the slow addition of Mg-Al (3:1) LDH (4.5 g). After an additional 2 minutes of stirring, 10 wt.% NH₄OH (409 μL) was added, the pH reaching a value of ca. 9.8. The yellow suspension was stirred for 12 h. The catalyst was then washed by a series of centrifuging, decanting, and suspending in water until the decanted water was pH 7. The yellow solid was then dried *in vacuo* at 40 °C. The catalyst was then ground using a mortar and pestle and added to a solution of potassium borohydride (30 mg), methanol (10 mL), and tetrahydrofuran (10 mL). The suspension was stirred at room temperature for 1 h. The reduced catalyst was isolated by a series of cycles of centrifuging, decanting, and suspending in deionized water until the decanted water was neutral and dried in vacuo at 40 °C, affording 4.2 g of Au/Mg-Al (3:1) LDH (0.58 wt.% gold).
5.2.1.3. Synthesis of Ni-Cu-Al LDH

A solid mixture of Ni(NO$_3$)$_2$•6H$_2$O (17.5 g, 60 mmol), Cu(NO$_3$)$_2$•3H$_2$O (3.7 g, 15 mmol), and Al(NO$_3$)$_3$•9H$_2$O (9.4 g, 25 mmol) was dissolved in a 1:1 ethanol/water solution by volume (40 mL) and stirred for 24 h. The metal solution was then concentrated by rotary evaporation and dried *in vacuo* at 40 °C. A saturated aqueous solution of NaOH (3 g) and Na$_2$CO$_3$ (7.7 g) was added drop-wise to the dry metal salts. A NaOH solution (1 M) was used to adjust the pH to 7.8. The resulting suspension was stirred for 24 h, concentrated by rotary evaporation, and dried *in vacuo* at 40 °C. The resulting solid was treated with a series of cycles of centrifuging, decanting, and suspending in water until the washings were neutral, affording Ni-Cu-Al LDH (10.4 g).

5.2.2. Catalyst Characterization

Surface area, average pore diameter, and pore volume were determined using a Micromeritics Tristar 3000 porosity system using the Brunauer–Emmett–Teller (BET) method by N$_2$ adsorption at -196 °C or using a Micromeritics Gemini VII analyzer. Samples were outgassed under vacuum or nitrogen for at least 6 hours at 160 °C prior to measurement. Powder X-ray diffraction measurements were performed on a PANalytical X’Pert system using Cu K$_\alpha$ radiation ($\lambda = 1.5406$ Å) and a step size of 0.02°. Elemental analysis was performed on a Varian 720-ES inductively coupled plasma-optical emission spectrometer.
5.2.3. Evaluation of Lignin Solubility

30 mg of Indulin AT was added to 10 mL of phenyl ether, 1,4-dioxane, and acetonitrile in separate experiments. In each case, the resulting mixture was stirred for 48 h at 65 °C. The suspensions were then cooled and filtered with a syringe filter tip (2 micron pore size).

5.2.4. Procedure for Benzylic Oxidation of Indulin Lignin using DDQ

A solution of DDQ (0.25 g) and tert-butyl nitrite (0.25 g) in 2-ethoxyethanol (14 mL) and 1,2-dimethoxyethane (21 mL) was added to Indulin lignin (2.5 g). The reaction mixture was heated to 80 °C for 14 h under bubbling O₂. Oxidized lignin was precipitated with ether (450 mL), filtered, and washed with hexane (100 mL). The resulting lignin was dried in vacuo at 50 °C. Drying afforded oxidized lignin near quantitatively (2.5 g, >99% yield).

5.2.5. Procedure for Heterogeneous Benzylic Oxidation of Indulin Lignin using Au/Mg-Al LDH

Lignin (1.2 g), Au/Mg-Al LDH (1.0 g), and 1,4-dioxane (16 mL) were loaded into a Parr reactor (50 mL, Hastelloy C body) equipped with a magnetic stirrer. The reactor was then sealed and purged with 6% O₂ (N₂ as balance) three times (1450 psi). The reactor was then heated to 150 °C for 48 h. Next, the reactor was cooled, a gas fraction was collected in a Tedlar bag, and the reactor contents were washed with THF. The THF layer was then concentrated in vacuo.
to afford 525 mg of lignin (44% yield). The solids from filtration were washed with DMSO (30 mL x3) to afford 38 mg (3% yield) of DMSO-soluble lignin

5.2.6. Procedure for Depolymerization of DDQ-oxidized Lignin with HCOOH/HCOONa

DDQ-oxidized lignin (210 mg), HCOONa (77 mg) and HCOOH (15 mL) were added to a stirred thick-walled 50 mL round-bottomed flask. The flask was sealed with a Teflon cap and subsequently heated to 110 °C for 24 h. The resulting solution was neutralized with NaHCO₃ and extracted with EtOAc (75 mL, x2) and THF (3 mL). The organic layers were then concentrated in vacuo yielding soluble lignin (77 mg, 36% yield). The solids recovered after washing with water were dried in vacuo to afford insoluble lignin (105 mg, 50% yield).

5.2.7. Procedure for Depolymerization of Au/HTC-oxidized Lignin with HCOOH/HCOONa

Au/HTC-oxidized lignin (70 mg), HCOONa (25 mg), and HCOOH (5 mL) were added into a stirred thick-walled 50 mL round-bottomed flask. The flask was then sealed with a Teflon cap and subsequently heated to 110 °C for 24 h. The resulting solution was concentrated in vacuo. The solid lignin was then extracted with ethyl acetate (2 mL, x3) and THF (1 mL). The combined organic layers were then concentrated in vacuo to afford soluble lignin (5 mg, 7% yield). The solids
recovered after washing with water were dried in vacuo to afford insoluble lignin (49 mg, 70% yield).

5.2.8. Procedure for Depolymerization of DDQ-oxidized Lignin using Ni-Cu-Al LDH

Ni-Cu-Al LDH (400 mg), DDQ oxidized lignin (400 mg), and methanol (16 mL) were loaded into a Parr reactor (50 mL, Hastelloy C body) equipped with a magnetic stirrer. The reactor was then sealed and purged with 6% O₂ (N₂ as balance) (1450 psi, x3). The reactor was heated to 150 °C for 48 h. The reactor was then cooled, a gas fraction was collected in a Tedlar bag, and the reactor contents were washed with THF. The THF layer was concentrated in vacuo to afford 165 mg of lignin (41% yield of soluble material).

5.2.9. Procedure for Depolymerization of Au/HTC-oxidized lignin using Ni-Cu-Al LDH

Ni-Cu-Al LDH (400 mg), Au/HTC oxidized lignin (400 mg), and methanol (16 mL) were loaded into a Parr reactor (50 mL, Hastelloy C body) equipped with a magnetic stirrer. The reactor was then sealed and purged with 6% O₂ (N₂ as balance) (1450 psi, x3). The reactor was heated to 150 °C for 48 h. The reactor was then cooled, a gas fraction was collected in a Tedlar bag, and the reactor contents were washed with THF. The THF layer was concentrated in vacuo to afford 195 mg of lignin (50% yield of soluble material).
5.2.10. Procedure for Lignin Molecular Weight Determination

Molecular weights of lignins were determined by size exclusion chromatography utilizing a Shimadzu LC20-AD LC pump equipped with a Shimadzu SPD-M20A UV-Vis detector set at 280 nm and a Polymer Standard Services GPC column and guard column (PSS PolarSil 8 mm ID x 5 cm, 5 μm \(\Rightarrow\) PSS PolarSil 8 mm ID x 30 cm, 5 μm, 100 angstrom porosity). The samples and column compartment were held at 40 °C during analysis. The mobile phase for SEC analysis was DMF with 0.1 M lithium bromide. A conventional calibration curve using a ReadyCal Kit from Sigma-Aldrich (Aldrich # 76552, M(p) 250-70000) and Wyatt ASTRA 7 software were used to determine the molecular weight distribution for each sample.

5.2.11. Procedure for Collection of HSQC Spectra

The lignins were placed directly in NMR tubes (ca. 20 mg for each sample) and dissolved using DMSO-d6/pyridine-d5 (4:1) NMR spectra were acquired on a Bruker Biospin (Billerica, MA) Avance 700 MHz spectrometer equipped with a 5-mm quadruple-resonance \(^1\)H/\(^{31}\)P/\(^{13}\)C/\(^{15}\)N QCI gradient cryoprobe with inverse geometry (proton coils closest to the sample). The central DMSO solvent peak was used as an internal reference (\(\delta^C\) 39.5, \(\delta^H\) 2.5 ppm). The \(^1\)H–\(^{13}\)C correlation experiment was an adiabatic HSQC experiment (Bruker standard pulse sequence 'hsqcetgpsi2p2.2'; phase-sensitive gradient-edited-2D HSQC using adiabatic pulses for inversion and refocusing). HSQC experiments were carried out using the following parameters: acquired from 11.5
to -0.5 ppm in F2 ($^1$H) with 3366 data points (acquisition time 200 ms), 215 to -5 ppm in F1 ($^{13}$C) with 620 increments (F1 acquisition time 8 ms) of 16 scans with a 1 s interscan delay; the $d_{24}$ delay was set to 0.86 ms (1/8J, J = 145 Hz). The total acquisition time for a sample was 3 h. Processing used typical matched Gaussian apodization (GB = 0.001, LB = -0.1) in F2 and squared cosine-bell and one level of linear prediction (32 coefficients) in F1. HSQC plots were generated using Bruker’s TopSpin 3.5pl5 (Mac version) software and used spectra reprocessed without linear prediction.

5.3. Results and Discussion

5.3.1. Catalyst Characterization

As shown in Table 25, the surface area of Au/HTC was fairly typical of an LDH (61.6 m$^2$g$^{-1}$). On the other hand, Ni-Cu-Al LDH displayed low surface area (1.5 m$^2$g$^{-1}$); as previously discussed, the low surface area is likely due to the incorporation of copper in the metal precursor solution. However, the presence of copper had no affect on the platelet morphology (confirmed by SEM) or the formation of brucite-like layers (confirmed by XRD), as discussed in Chapter 4. Regardless, both catalysts used in this work have large enough pores to allow lignin to diffuse through the pore network (i.e., 22.1 and 14.6 nm average pore diameter). Additionally, elemental analysis of the Au/HTC revealed the gold loading to be 0.58 wt.%, which is less than the amount of gold used in the synthesis solution (ca. 2 wt.%).
5.3.2. Solvent Selection

Using solvents previously reported to be capable of partial lignin dissolution, a qualitative solvent screening experiment was conducted. Three solvents were screened for their ability to dissolve Indulin AT lignin; diphenyl ether (DPE), 1,4-dioxane, and acetonitrile. After heating for 48 h at 65 °C, 1,4-dioxane was found to form the darkest Indulin lignin/solvent mixture, followed by acetonitrile and lastly DPE, which was virtually colorless after removal of lignin via filtration. Therefore, 1,4-dioxane was selected as the solvent for heterogeneous benzylic oxidation using Au/HTC. The exact mass of the dissolved lignin was not determined due to the small sample size.

Given that 1,4-dioxane is capable of peroxide formation, safety precautions were taken. Lignin oxidation was performed below the limiting oxygen concentration of common organic solvents. The advantage of using 6% O₂/N₂ gas mixture is two-fold: first, there is not a large excess of oxygen so over-oxidation reactions are suppressed. Second, extensive dioxane-based peroxide formation is avoided. Moreover, the solvent is stabilized with butylated
hydroxytoulene (1-5 ppm) as a radical scavenger. For the above reasons 1,4-dioxane was determined to be a suitable solvent for the oxidation of Indulin lignin.

5.3.3. Benzylic Oxidation of Indulin AT lignin

5.3.3.1. DDQ-mediated Oxidation of Indulin AT Lignin

As a reference, Indulin lignin was oxidized using an oxidation system reported by Westwood and co-workers (Fig. 29). This system was selected due to its high conversion, selectivity, and scalability. As previously reported, DDQ-oxidized lignin was recovered near quantitatively from the reaction solvent by precipitation with ether. As discussed in Chapter 4, the DDQ oxidation system used in this work has been previously identified as a selective benzylic oxidation system.

![Figure 29. Catalytic oxidation of Indulin lignin using a previously reported DDQ/O2 oxidation system.](image)

Catalytic oxidation of Indulin lignin was confirmed by HSQC NMR spectroscopy, as shown in Fig. 30 (spectrum (b)). As previously discussed in Chapter 4, cross-peaks corresponding to β-O-4 linkages (Aα, 5.0/70 ppm (1H/13C), Aβ, 4.4/84 ppm (1H/13C)) were completely absent after DDQ oxidation. In addition, cross-peaks corresponding to the β-5 (Bα, 5.5/88 ppm (1H/13C), and Bβ, 3.2/52 ppm (1H/13C)) and β-β linkages (Cα, 4.7/85 ppm (1H/13C), Cβ, 3.0/52 ppm (1H/13C)) were also absent.
ppm ($^1$H/$^{13}$C), and Cγ, 4.1/70 ppm ($^1$H/$^{13}$C) and 3.7/70 ppm ($^1$H/$^{13}$C)) were also absent after oxidation. Although the oxidized lignin was precipitated out of the reaction solution by adjusting the polarity of the solvent using ether, some solvent derived (2-ethoxyethanol and 1,2-dimethoxyethane) cross-peaks were observed in the HSQC spectrum (Fig. 30 spectrum (b), 3.2/72 ppm, 3.2/66 ppm, and 3.2/58 ppm ($^1$H/$^{13}$C)).

As previously reported by Meier and co-workers, the reversibility of the DDQ oxidation reaction can be investigated by HSQC NMR spectroscopy following sodium borohydride reduction. In this work, DDQ oxidation of β-O-4 linkages in Indulin lignin was shown to be reversible after sodium borohydride reduction by analyzing the linkage region of the HSQC spectrum (Fig 30. spectrum (c)). While the oxidation of the β-O-4 linkage was found to be reversible (evidenced by the resonances at $A_\alpha$, 5.0/70 ppm ($^1$H/$^{13}$C), and $A_\beta$, 4.4/84 ppm ($^1$H/$^{13}$C)) resonances corresponding to the α- and β-positions in β-5 and the α, β, and γ-positions in β-β linkages were not present after NaBH₄ reduction (Fig. 30, spectrum (c)). β-5 and β-β linkages are a few degrees of unsaturation removed from aromaticity; hence, these linkages commonly aromatize under acidic or basic conditions (specific chemical shifts for β-5 and β-β linkages are discussed in Chapter 4). The absence of resonances corresponding to these linkages is commonly observed, although rarely addressed in the literature. Indeed, β-5 models are often converted to their corresponding benzofurans. While β-β linkages cannot be aromatized to two furans, some increase in the degree of
unsaturation or oxidation is evident. The conversion of β-β linkages is confirmed by the absence of corresponding resonances in the HSQC spectra. The oxidation products of β-β linkages are not commonly studied due to the low natural abundance of β-β linkages as well as the difficulty of synthesizing models of this type.

![HSQC spectra of the linkage region of Indulin lignin (a), DDQ-oxidized lignin (b), and sodium borohydride reduced lignin after DDQ oxidation (c). The reduction highlights the reversibility of benzylic oxidation.](image)

In addition to the linkage region, the aromatic region of the HSQC NMR spectrum was also analyzed. As previously discussed in Chapter 4, the Indulin AT lignin in this work had no apparent S-unit content via HSQC NMR spectroscopy. DDQ oxidation was confirmed by the decreased intensity of resonances corresponding to the G_2 (6.8/114 ppm (¹H/¹³C)) and G_5/G_6 (6.8/122 ppm (¹H/¹³C)).
ppm ($^{1}H^{13}C$)) protons (these protons being indistinguishable prior to oxidation) present on guaiacyl rings and the increased resonances corresponding to oxidized guaiacyl units $G'_2$ (6.7/114 ppm ($^{1}H^{13}C$)), $G'_5$ (7.0/116 ppm ($^{1}H^{13}C$)), and $G'_6$ (7.6/122 ppm ($^{1}H^{13}C$), Fig. 31, spectrum (e)). The aromatic region confirmed that DDQ-oxidized lignin was reduced by sodium borohydride (Fig. 31, spectrum (f)). In fact, more oxidized $\beta$-O-4 linkages were present in Indulin lignin prior to DDQ oxidation as compared to after borohydride reduction, shown by the resonances assigned to $G'_2$, $G'_5$, and $G'_6$ present in Fig. 31, spectrum (d).

Figure 31. HSQC spectra of the aromatic region of Indulin lignin (d), DDQ-oxidized lignin (e), and sodium borohydride reduced lignin after DDQ oxidation (f). The reduction highlights the complete reversibility of benzylic oxidation.

In addition to HSQC NMR spectroscopy, the average molecular weight of each THF-soluble lignin sample was determined by GPC (referenced to
polystyrene standards). After DDQ oxidation, the average molecular weight of lignin was reduced from 5100 Da to 1000 Da. Considering the selectivity of DDQ oxidation, as evidenced by HSQC spectroscopy, the reduction in molecular weight is likely due to the removal of hydrogen bond donors; hence, lignin agglomerates are dissociated, resulting in a decrease in the observed molecular weight.

5.3.3.2. Oxidation of Lignin over Au/HTC

Previously, it has been reported that supported gold nanoparticles are capable of oxidizing a range of alcohols using O\textsubscript{2} as the oxidant.\textsuperscript{81} With this in mind, the oxidation of a technical lignin using hydrotalcite-supported gold nanoparticles was investigated (Fig. 32). Au/HTC oxidation was conducted at 150 °C under 100 bar (6% O\textsubscript{2}/N\textsubscript{2} gas mixture) for 48 h. Following filtration, 44% of the initial lignin mass was recovered as THF-soluble lignin. Due to the heterogeneous nature of the catalytic system, lignin that was not THF-soluble was not isolated and was separated during filtration as a mixture with the catalyst. Furthermore, when the catalyst was further washed with DMSO (ca. 90 mL) a minimal amount of soluble lignin was recovered (38 mg, 3% mass recovery).
At the conclusion of the reaction, the gas mixture was analyzed by a refinery gas analyzer (RGA). It was found that the gas mixture contained 0.1% oxygen, implying that all of the benzylic alcohols should have reacted. Additionally, infrared spectra were collected for Indulin lignin (as a reference), DDQ-oxidized lignin as a literature comparison, and Au/HTC-oxidized lignin (Fig. 33). The presence of a maximum at 1686 cm\(^{-1}\) in Au/HTC-oxidized lignin is likely due to the oxidation of benzylic alcohol groups to ketones, similar results being observed for DDQ-oxidized lignin. Additionally, the absorbance corresponding to O-H bond stretching (ca. 3400 cm\(^{-1}\)) was notably decreased after Au/HTC and DDQ oxidizations. Moreover, wavenumbers commonly observed for aromatic moieties (ca. 1596 cm\(^{-1}\) and 1514 cm\(^{-1}\)) were largely unchanged after DDQ and Au/HTC oxidations, implying that the oxidation process did not destroy the lignin aromaticity.
To provide additional information, HSQC NMR spectroscopy was employed to characterize the Au/HTC oxidized lignin. According to HSQC NMR spectra (Fig. 34, spectra (b)), significant Au/HTC-mediated lignin oxidation was observed. Indeed, the cross-peaks corresponding to the benzylic position in the β-O-4 linkage were significantly smaller ($A_\alpha$, 5.0/70 ppm ($^1$H/$^{13}$C)), while the β-carbon resonance of the β-O-4 linkages ($A_\beta$, 4.4/84 ppm ($^1$H/$^{13}$C)) was not observed. Similar to the results obtained from DDQ oxidation, resonances assigned to the α- and β-positions of β-5 linkages ($B_\alpha$ and $B_\beta$) were absent after oxidation using Au/HTC/O$_2$, implying that β-5 linkages may have been oxidized to their corresponding benzo furans. Surprisingly, some β-β linkages were still present after Au/HTC-mediated oxidation ($C_\alpha$, 4.6/84 ppm ($^1$H/$^{13}$C), and $C_\gamma$, 4.2/70 ppm ($^1$H/$^{13}$C)). Although the resonances corresponding to β-β linkages were less intense, they were still observed in contrast to the DDQ oxidation system.
Following oxidation, the reversibility of the Au/HTC-mediated oxidation was investigated via sodium borohydride reduction. Contrary to DDQ oxidation, Au/HTC/O₂ oxidation was determined to be only partially reversible (Fig. 34 spectrum (c)). Following reduction, the Aα cross-peak centered at 4.8 ppm (¹H) and 70 ppm (¹³C) corresponding to β-O-4 benzylic alcohols, showed no change in intensity. The presence of these peaks after reduction is likely a consequence of dehydration, which forms enol ethers as discussed in Chapter 3.

Figure 34. HSQC spectra of the linkage region of Indulin lignin (a), Au/HTC-oxidized lignin (b), and sodium borohydride reduced lignin after Au/HTC oxidation (c). The reduction highlights the partial reversibility of benzylic oxidation.
The aromatic region of the HSQC NMR spectra also showed evidence of 
Au/HTC-mediated oxidation as confirmed by the increase in intensity of peaks 
corresponding to oxidized guaiacyl units G’2, G’5, and G’6 (Fig. 35, spectrum (e)).
Following sodium borohydride reduction (Fig. 35, spectrum (f)), the intensity of 
resonances assigned to oxidized guaiacyl units G’2, G’5, and G’6 decreased,
further supporting the conclusion that Au/HTC-mediated oxidation of Indulin AT 
lignin is partially reversible.

![HSQC spectra](image)

Figure 35. HSQC spectra of the aromatic region of Indulin lignin (d), Au/HTC oxidized lignin (e), and sodium borohydride reduced lignin after Au/HTC oxidation (f). The reduction highlights the partial reversibility of benzylic oxidation.

A significant reduction in the average molecular weight of the THF-soluble 
lignin was also observed after oxidation using Au/HTC. Indeed, the molecular 
weight was reduced from 5100 Da to 800 Da. The observed decrease in
molecular weight as compared to DDQ oxidized lignin (1000 Da) suggests that some linkages may have been cleaved during Au/HTC-mediated oxidation, in addition to the dissociation of lignin agglomerates.

5.3.4. Fragmentation of Lignin Linkages

5.3.4.1. Formic Acid Induced Depolymerization of Oxidized Lignin

Following oxidation with DDQ and Au/HTC, the oxidized lignin was treated with HCOOH/HCOONa according to a literature procedure reported by Stahl and co-workers.\textsuperscript{31} Contrary to the literature, after the treatment a significant portion of the lignin was no longer soluble. Indeed, after extraction with an EtOAc/THF mixture, only 20% and 5% of the initial (oxidized) lignin was soluble, corresponding to the DDQ oxidized lignin and Au/HTC oxidized lignin, respectively. In addition, a significant increase in the average molecular weight (\textit{i.e.}, 3500 Da for DDQ-oxidized lignin and 1900 Da for Au/HTC-oxidized lignin) was observed by GPC analysis. The differing results from the initial literature report\textsuperscript{31} are likely due to the use of a more degraded, while industrially relevant, lignin.

5.3.4.2. Ni-Cu-Al LDH Depolymerization of Oxidized Lignin

Following Au/HTC oxidation, oxidative depolymerization was explored using Ni-Cu-Al LDH. Ni-Cu-Al LDH-mediated fragmentation of DDQ-oxidized lignin was discussed in Chapter 4 and will not be further discussed in this chapter. As previously discussed, reactions involving Ni-Cu-Al LDH were found to be compatible with methanol. The use of a polar protic solvent greatly
increases lignin solubility. Ni-Cu-Al LDH oxidation of the THF-soluble portion of the Au/HTC-oxidized lignin was conducted at 150 °C under 100 bar (6% O2/N2 gas mixture) for 48 h (Fig. 36). RGA results revealed that most of the primary oxidant was consumed during the reaction (ca. 0.6% O2 remaining). After filtration, 50% of the initial lignin mass was THF-soluble, the balance remaining as an insoluble lignin/catalyst mixture.

![Diagram of catalytic oxidative fragmentation of Au/HTC oxidized Indulin lignin using Ni-Cu-Al LDH.](image)

Figure 36. Proposed catalytic oxidative fragmentation of Au/HTC oxidized Indulin lignin using Ni-Cu-Al LDH.

Surprisingly, after oxidative fragmentation with Ni-Cu-Al LDH, no HSQC NMR cross-peaks previously assigned to lignin structures were observed (Fig. 37, spectrum (c)). In fact, the only resonances that could be assigned were the methoxyl units (3.8/55 ppm (1H/13C)). Furthermore, after oxidation using Ni-Cu-Al LDH, a large resonance was present at ca. 3.5/40 ppm (1H/13C). Crocker and co-workers53 reported a similar resonance following Swern oxidation. While the source of this resonance is still unknown, it is possible that it is derived from base-promoted esterification of carboxylic acids by the methanol solvent. In esterified models such as methyl p-anisate, transfer of magnetization from the protons to carbon should result in a methyl ester resonance at ca. 3.8 ppm166
(1H) and 51 ppm167 (13C), which is in accordance with the large upfield peak present in Fig. 37 spectrum (c).

Figure 37. HSQC spectra of the linkage region of Indulin lignin (a), Au/HTC oxidized lignin (b), and product of Ni-Cu-Al LDH-catalyzed oxidative fragmentation of Au/HTC oxidized lignin (c).

Similar to the linkage region of the spectrum, the aromatic region did not show intense resonances previously assigned to lignin-derived aromatic protons (Fig. 38 spectrum (f)). Rather, a few weak resonances in the range of 7.4-6.8 ppm (1H) and 138-118 ppm (13C) were the only signals present. The absence of aromatic resonances is possibly due to over-oxidation, which destroys the aromatic character of lignin. Over-oxidation to dicarboxylic acids has been reported in strongly oxidizing reactions such as ozonolysis54 and methyltrioxorhenium/hydrogen peroxide,168 but is not commonly reported in other oxidation systems. Alternatively, it is possible that the reaction solvent
functionalized some aromatic positions. Resonances resulting from lignin methoxylation would be at a similar chemical shift as methoxy groups present in guaiacyl units.

![Diagram](image)

Figure 38. HSQC spectra of the aromatic region of Indulin lignin (d), Au/HTC oxidized lignin (e), and product of Ni-Cu-Al LDH-catalyzed oxidative fragmentation of Au/HTC oxidized lignin (f).

GPC molecular weight analysis revealed that the average molecular weight of the THF-soluble fraction was reduced from 800 Da (Au/HTC-oxidized lignin) to 400 Da. An average molecular weight of 400 Da falls between the dimer and trimer region (where lignin monomers are estimated to possess a molecular weight of ca. 180 Da). From the established reactivity trends discussed in Chapter 4, it is hypothesized that benzoic acids are likely present after oxidation,
so a small portion of the THF-soluble lignin was dried and derivatized with BSTFA. However, following silylation, no small molecules were observed.

5.4. Conclusions

In this study, the extent of Au/HTC-mediated Indulin lignin oxidation was monitored by IR and HSQC NMR spectroscopies, and compared to a previously reported DDQ oxidation system. Similar C=O absorbances centered at ca. 1686 cm\(^{-1}\) were observed in DDQ- and Au/HTC-oxidized lignins. HSQC spectroscopy indicated near complete benzylic oxidation of \(\beta\text{-O-4}, \beta\text{-5}, \text{ and } \beta\text{-\beta}\) linkages using the homogeneous DDQ oxidation system. However, oxidation over Au/HTC did not result in complete oxidation of \(\beta\text{-O-4}\) or \(\beta\text{-\beta}\) linkages, as evidenced by the presence of \(\alpha\)- and \(\gamma\)-protons after oxidation. While DDQ-oxidation was reversible after sodium borohydride reduction, Au/HTC oxidized lignin was only partially reversible, leaving some oxidized guaiacyl units remaining. Although not all \(\beta\text{-O-4}\) linkages were oxidized, Au/HTC oxidation resulted in a significant decrease in the average molecular weight observed via GPC analysis (\textit{i.e.}, 5100 Da to 800 Da compared to 1000 Da for DDQ-oxidized lignin). Furthermore, after Ni-Cu-Al LDH-mediated oxidation, the molecular weight was further decreased into a range approaching that of lignin model dimers (ca. 400 Da). Although GPC molecular weight analysis showed a significant reduction in molecular weight, GC/MS analysis did not detect oxidized lignin-derived compounds. In addition, the chemical shifts obtained by 2-D HSQC NMR spectroscopy were inconclusive and did not align with previous literature reports. While the nature of the
complicated product mixture has not been fully elucidated, this serves as a promising means for the production of significantly reduced molecular weight lignins. Future work will focus on identification of the low molecular weight compounds formed using advanced NMR spectroscopy, infrared, and MS techniques.
Chapter 6. Concluding Remarks
Due to its inherent properties such as heterogeneity and hydrophobicity, lignin represents a challenging feedstock. It has been the focus of academic researches for more than a century. However, a large disconnect between academic interest and industrial reality is very evident with respect to lignin. Performing lignin depolymerization on the benchtop or in an autoclave can yield monomeric products in yields of up to ca. 15% in some of the most successful reports of lignin depolymerization. While this represents progress, a yield of 15% monomers as a complex mixture is not promising with respect to development of a profitable biorefinery model. Therefore, not only should academic research focus on production of monomeric compounds, it should also focus on the properties of modified lignin as a renewable material (e.g., possessing increased solubility and lower glass transition temperature).

Although reports of reductive lignin utilization are commonplace in the academic community, these reports do not represent feasible means for lignin valorization. In the case of hydrodeoxygenation (HDO), the high-temperatures and pressures required, along with the expense of the H\textsubscript{2} reductant, render this approach prohibitively expensive for commercial application. Moreover, the molecules desired for jet fuel (i.e., benzene, toluene, and xylene) are not commonly formed. Ring hydrogenation is facile compared to cleavage of the aryl-oxygen bond, and results in conversion of higher value aromatics to cyclohexane and cyclohexanols, eliminating the primary characteristic of lignin as a source of aromatics. Those lignin HDO processes that do not afford ring hydrogenation
products usually produce phenols. The latter represent relatively low value bulk chemicals compared to fine chemicals such as vanillin produced by oxidative lignin depolymerization.

In this contribution, several lignin model compounds and a technical lignin were successfully oxidized using heterogeneous catalysts (i.e., a post-synthetically modified tin-β zeolite and several layered double hydroxides (LDHs)). While the conversion of models was high, yields of monomers were modest due to side reactions such as phenolic radical coupling and ring hydroxylation. During step-wise oxidation of Indulin AT lignin using Au/HTC, followed by Ni-Cu-Al LDH, a significant amount (ca. 40%-50%) of the resulting oxidized lignin was THF-soluble after each step. Moreover, a significant reduction in molecular weight was observed (i.e., 5100 Da to 400 Da after Ni-Cu-Al LDH-mediated oxidation) and generally resonances corresponding to β-O-4, β-5, and β-β linkages were absent after oxidation using both Au/HTC and Ni-Cu-Al LDH. Furthermore, lignin oxidation reactions were found to be compatible with polar solvents such as 1,4-dioxane and methanol. The use of such polar solvents is highly desirable due to their ability to dissolve lignin.

Notably, reactions were conducted in a non-flammable oxidation system. The advantage to having a non-flammable gas mixture is two-fold: first, the reaction conditions are applicable on an industrial scale. Second, near-
stoichiometric amounts of oxygen suppress over-oxidation of aromatic compounds to diacids.

Although this contribution demonstrates progress toward lignin utilization, more work is needed to make lignin oxidation feasible from a commercial standpoint. Some of the issues encountered in this work are a consequence of the reactor mode (batch). If the reaction conditions were modified to conditions suitable for a continuous process, small molecules could be removed from the catalyst bed in real time (i.e., a shorter residence time). Removal of small molecules upon formation may prevent undesired reactions such as direct hydroxylation and phenolic radical coupling. Higher yields of lignin oxidation products may be achievable by limiting conversion, either by lowering the temperature or decreasing the residence time, which in theory will result in higher selectivity to oxidized small molecules. The insoluble lignin could then be separated by filtration and subsequently recycled through the catalyst bed.

Additionally, by using a lignin more similar to native lignin, monomer yields would likely be increased. In this contribution, lignin precipitated from black liquor resulting from the Kraft process was used as a well-characterized feedstock. It is believed that the $\beta$-O-4 linkages in Kraft-derived lignins are largely degraded during pulp processing. Therefore, the yields of monomers would likely increase if a lignin extracted under milder conditions were incorporated into the LDH
oxidation systems in this work. Most current lignin oxidation studies are highly dependent on using a high-quality lignin feedstock.

Furthermore, at high conversions in reactions using LDH catalysts, leaching of metals was experienced in polar protic solvents, presumptively due to the acidity of the benzoic acid product formed from the model compounds employed. Metal leaching could potentially be avoided by the incorporation of a catalyst support that was less sensitive to acidic environments (\textit{e.g.}, mesoporous copper exchanged zeolites). Additionally, zeolite supports would allow for removal of coke via calcination without the rehydration step requisite for LDH regeneration.

As discussed throughout this contribution redox-neutral reactions, such as the one demonstrated by Stahl and co-workers,\textsuperscript{31} resulted in excellent yields of phenols following oxidation. In this context, redox neutral means that the moiety of interest is oxidized (β-O-4 linkages) while another sacrificial moiety is reduced. Although we found that HCOOH/HCOONa was not effective for fragmentation of Indulin AT lignin, other heterogeneously catalyzed redox-neutral reactions (\textit{e.g.}, MPV reductions/Oppenauer oxidation) have been published, and proceed through two-electron processes. In theory, lignin could be oxidized in acetone (a solvent capable of lignin dissolution) over a Lewis acid catalyst (\textit{e.g.}, tin-β zeolite), yielding oxidized lignin and isopropanol.
While selective lignin oxidation is still in its infancy, future contributions from the academic community will need to focus on application of oxidation systems (i.e., non-flammable gas mixtures, heterogeneous catalysts resistant to metal leaching, and scalable reaction conditions). In this dissertation, efforts toward development of commercially scalable reaction conditions using a commercially produced lignin and lignin model compounds were discussed. However, much work is still needed to increase the yield of usable lignin-derived material, whether it is oxidized lower oligomers for dispersants, resin production, or monomeric compounds for fine chemicals.
Appendices
Appendix I. Supplementary Information for Regioselective Baeyer-Villiger Oxidation of Lignin Model Compounds with Tin Beta Zeolite Catalyst and Hydrogen Peroxide
Synthesis of Lignin Model Compounds

Synthesis of 2-(4-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (6)

A suspension of 4-methoxyphenol (16 g, 129 mmol), potassium carbonate (20 g, 144 mmol) and acetone (100 mL) was cooled to 0 °C and 2-bromo-4′-methoxyacetophenone (25 g, 110 mmol) was added slowly. After the addition, the reaction mixture was heated to reflux and held overnight. The reaction mixture was then allowed to cool, and was filtered through a pad of Celite® and was then concentrated in vacuo. The resulting solid was dissolved in chloroform (100 mL), washed with 1 M sodium hydroxide (50 mL x 3) followed by brine (100 mL x 2), and was dried over sodium sulfate. After filtration, the product was concentrated in vacuo, resulting in a red-brown solid. The solid was purified by recrystallization in water and acetone, resulting in a white solid (29.7 g, 94% yield). GCMS: m/z 272.1 (24%), 135.1 (100%), 77.1 (15%) and 1H-NMR (400 MHz, CDCl3) δ: 8.02-7.96 (m, 2H), 6.98-6.82 (m, 6H), 5.28 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H). The 1H-NMR spectrum is consistent with the spectrum previously reported by Lee et al.103

Synthesis of 2-(2-methoxyphenoxy)-1-(4-methoxyphenyl)-ethanone (7)

A suspension of guaiacol (16.56 g, 138 mmol), potassium carbonate (21.1 g, 153 mmol) and acetone (140 mL) was cooled to 0 °C and 2-bromo-4′-methoxyacetophenone (24.3 g, 106 mmol) was added slowly. After the addition, the reaction was heated to reflux and held overnight. The mixture was then
allowed to cool, and was filtered through a pad of Celite® and was then concentrated in vacuo. The resulting solid was dissolved in ethyl acetate (200 mL), washed with 1 M sodium hydroxide (75 mL x 3) followed by brine (100 mL x 2), and was dried over anhydrous sodium sulfate. After filtration, the product was concentrated in vacuo. The resulting solid was recrystallized from acetone, resulting in a white solid (20.3 g, 71% yield). GCMS: m/z 272.1 (20%), 135.1 (100%), 121.1 (7%) and 1H-NMR (400 MHz, CDCl₃) δ: 8.04-7.98 (m, 2H), 6.98-6.94 (m, 2H), 6.92-6.78 (m, 4H), 5.15 (s, 2H), 3.36 (s, 3H), 3.17 (s, 3H). The 1H-NMR spectrum is consistent with spectra previously reported by Dawange et al. 169

Models 6a170 and 8a171 have been previously reported but were not completely characterized. NMR spectra provided below contain minor impurities corresponding to unreacted starting material. Spectra of contaminants have previously been reported.103-104, 169 Resonances resulting from unreacted starting material are indicated with an asterisk.
Figure S1. Diffuse Reflectance UV-vis spectra of tin-beta zeolite and tin dioxide. Spectra were normalized and the zeolite background was subtracted.
NMR Spectra of BVO Products of Lignin Model Compound Oxidation
Figure S2. 1H-NMR spectrum of compound 6a in CDCl₃.
Figure S3. $^{13}$C-NMR spectrum of compound 6a in CDCl$_3$. 
Figure S4. 1H-NMR spectrum of compound 7a in CDCl3.
Figure S5. $^13$C-NMR spectrum of compound 7a in CDCl$_3$. 

![NMR Spectrum](image-url)
Figure S6. 1H-NMR spectrum of compound 8a in CDCl₃.
Figure S7. $^{13}$C-NMR spectrum of compound 8a in CDCl$_3$. 
Crystallographic Tables

Table 26 Crystal data and structure refinement for molecule 6a.

Table 27 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule 6a.

Table 28 Bond lengths [Å] and angles [deg] for molecule 6a.

Table 29 Anisotropic displacement parameters (A^2 x 10^3) for molecule 6a.

Table 30 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for molecule 6a.

Table 31 Torsion angles [deg] for molecule 6a.

Table 32 Crystal data and structure refinement for molecule 7a.

Table 33 Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule 7a.

Table 34 Bond lengths [Å] and angles [deg] for molecule 7a.

Table 35 Anisotropic displacement parameters (A^2 x 10^3) for molecule 7a.

Table 36 Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for molecule 7a.

Table 37 Torsion angles [deg] for molecule 7a.
Table 26. Crystal data and structure refinement for molecule 6a

<table>
<thead>
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<tr>
<td>Empirical formula</td>
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<td>288.29</td>
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<tr>
<td>Temperature</td>
<td>90.0 (2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54178 Å</td>
</tr>
<tr>
<td>Crystal system space group</td>
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</tr>
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<td>Unit cell dimensions</td>
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<tr>
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</tr>
<tr>
<td>Calculated density</td>
<td>4, 1.393 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.864 mm⁻¹</td>
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<tr>
<td>F(000)</td>
<td>608</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.340 x 0.250 x 0.170 mm</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>4.801 to 68.365 deg</td>
</tr>
<tr>
<td>Limiting indices</td>
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</tr>
<tr>
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<tr>
<td>Completeness to theta = 67.679</td>
<td>99.7 %</td>
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<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
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<tr>
<td>Max. and min. transmission</td>
<td>0.929 and 0.762</td>
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<td>Full-matrix least-squares on F²</td>
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<tr>
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<td>Extinction coefficient</td>
<td>n/a</td>
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<tr>
<td>x</td>
<td>y</td>
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<tr>
<td>-------</td>
<td>-------</td>
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<td>2724(1)</td>
<td>2964(1)</td>
</tr>
<tr>
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</tr>
<tr>
<td>O(1)</td>
<td>13923(1)</td>
</tr>
<tr>
<td>C(2)</td>
<td>4714(1)</td>
</tr>
<tr>
<td>C(3)</td>
<td>5241(1)</td>
</tr>
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<td>C(4)</td>
<td>4698(1)</td>
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<td>C(5)</td>
<td>12815(1)</td>
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<td>C(6)</td>
<td>8781(2)</td>
</tr>
<tr>
<td>C(7)</td>
<td>10543(2)</td>
</tr>
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**Table 28. Bond lengths [Å] and angles [deg] for molecule 6a**

<table>
<thead>
<tr>
<th>Bond Lengths</th>
<th>Angle Degrees</th>
</tr>
</thead>
<tbody>
<tr>
<td>O (1) - C (7)</td>
<td>118.05(9)</td>
</tr>
<tr>
<td>O (2) - C (8)</td>
<td>116.15(9)</td>
</tr>
<tr>
<td>O (2) - C (1)</td>
<td>121.46(11)</td>
</tr>
<tr>
<td>O (2) - C (3)</td>
<td>119.04(11)</td>
</tr>
<tr>
<td>O (2) - C (4)</td>
<td>119.22(11)</td>
</tr>
<tr>
<td>O (2) - C (6)</td>
<td>119.29(11)</td>
</tr>
<tr>
<td>O (3) - C (8)</td>
<td>115.46(10)</td>
</tr>
<tr>
<td>O (5) - C (10)</td>
<td>120.02(11)</td>
</tr>
</tbody>
</table>

Additional bond and angle data for molecule 6a:
\begin{align*}
\text{C (6)} & - \text{C (5)} - \text{C (4)} & 119.37(11) \\
\text{C (6)} & - \text{C (5)} - \text{H 5A} & 120.3 \\
\text{C (4)} & - \text{C (5)} - \text{H 5A} & 120.3 \\
\text{C (1)} & - \text{C (6)} - \text{C (5)} & 119.74(11) \\
\text{C (1)} & - \text{C (6)} - \text{H (6A)} & 120.1 \\
\text{C (5)} & - \text{C (6)} - \text{H (6A)} & 120.1 \\
\text{Q (1)} & - \text{C (7)} - \text{H 7A} & 109.5 \\
\text{Q (1)} & - \text{C (7)} - \text{H 7B} & 109.5 \\
\text{H 7A} & - \text{C (7)} - \text{H 7B} & 109.5 \\
\text{Q (1)} & - \text{C (7)} - \text{H 7C} & 109.5 \\
\text{H 7B} & - \text{C (7)} - \text{H 7C} & 109.5 \\
\text{O (3)} & - \text{C (8)} - \text{O (2)} & 125.59(11) \\
\text{O (3)} & - \text{C (8)} - \text{C (9)} & 127.07(11) \\
\text{O (2)} & - \text{C (8)} - \text{C (9)} & 107.33(10) \\
\text{O (4)} & - \text{C (9)} - \text{H 9A} & 110.0 \\
\text{O (4)} & - \text{C (9)} - \text{H 9B} & 110.0 \\
\text{O (4)} & - \text{C (9)} - \text{H 9B} & 110.0 \\
\text{H 9A} & - \text{C (9)} - \text{H 9B} & 108.3 \\
\text{Q (4)} & - \text{C (10)} - \text{C (15)} & 124.78(11) \\
\text{Q (4)} & - \text{C (10)} - \text{C (11)} & 115.68(11) \\
\text{C (15)} & - \text{C (10)} - \text{C (11)} & 119.54(11) \\
\text{C (12)} & - \text{C (11)} - \text{C (10)} & 120.19(11) \\
\text{C (12)} & - \text{C (11)} - \text{H 11A} & 119.9 \\
\text{C (10)} & - \text{C (11)} - \text{H 11A} & 119.9 \\
\text{C (11)} & - \text{C (12)} - \text{C (13)} & 120.45(11) \\
\text{C (11)} & - \text{C (12)} - \text{H 12A} & 119.8 \\
\text{C (13)} & - \text{C (12)} - \text{H 12A} & 119.8 \\
\text{Q (5)} & - \text{C (13)} - \text{C (14)} & 124.96(11) \\
\text{Q (5)} & - \text{C (13)} - \text{C (12)} & 115.56(11) \\
\text{Q (14)} & - \text{C (13)} - \text{C (12)} & 119.48(11) \\
\text{Q (13)} & - \text{C (14)} - \text{C (15)} & 120.03(11) \\
\text{C (13)} & - \text{C (14)} - \text{H 14A} & 120.0 \\
\text{C (15)} & - \text{C (14)} - \text{H 14A} & 120.0 \\
\text{C (10)} & - \text{C (15)} - \text{C (14)} & 120.31(11) \\
\text{C (10)} & - \text{C (15)} - \text{H 15A} & 119.8 \\
\text{C (14)} & - \text{C (15)} - \text{H 15A} & 119.8 \\
\text{Q (5)} & - \text{C (16)} - \text{H 16a} & 109.5 \\
\text{Q (5)} & - \text{C (16)} - \text{H 16B} & 109.5 \\
\text{H 16a} & - \text{C (16)} - \text{H 16B} & 109.5 \\
\text{Q (5)} & - \text{C (16)} - \text{H 16C} & 109.5 \\
\text{H 16a} & - \text{C (16)} - \text{H 16C} & 109.5 \\
\text{H 16B} & - \text{C (16)} - \text{H 16C} & 109.5 \\
\end{align*}

Symmetry transformations used to generate equivalent atoms:
Table 29. Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for molecule 6a. The anisotropic displacement factor exponent takes the form

$$-2\pi^2 \{h^2 \text{a}^*^2 U_{11} + ... + 2hk \text{a}^* \text{b}^* U_{12}\}$$

<table>
<thead>
<tr>
<th></th>
<th>U12</th>
<th>U3</th>
<th>U23</th>
<th>U13</th>
<th>U12</th>
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</thead>
<tbody>
<tr>
<td>24(1)</td>
<td>17(1)</td>
<td>-2(1)</td>
<td>2(1)</td>
<td>-4(1)</td>
<td>Q(2)</td>
</tr>
<tr>
<td>19(1)</td>
<td>18(1)</td>
<td>33(1)</td>
<td>-2(1)</td>
<td>-1(1)</td>
<td>1(1)</td>
</tr>
<tr>
<td>19(1)</td>
<td>18(1)</td>
<td>Q(5)</td>
<td>18(1)</td>
<td>26(1)</td>
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<tr>
<td>15(1)</td>
<td>18(1)</td>
<td>24(1)</td>
<td>3(1)</td>
<td>5(1)</td>
<td>I(1)</td>
</tr>
<tr>
<td>14(1)</td>
<td>13(1)</td>
<td>14(1)</td>
<td>14(1)</td>
<td>13(1)</td>
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<td>2(1)</td>
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<td>16(1)</td>
<td>17(1)</td>
<td>18(1)</td>
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<td>1(1)</td>
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<td>20(1)</td>
<td>17(1)</td>
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</tr>
<tr>
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<td>0(1)</td>
<td>O(7)</td>
<td>15(1)</td>
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<tr>
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<td>16(1)</td>
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<td>3(1)</td>
<td>1(1)</td>
<td>Q(9)</td>
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<tr>
<td>1(1)</td>
<td>Q(10)</td>
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<td>-2(1)</td>
</tr>
<tr>
<td>4(1)</td>
<td>I(1)</td>
<td>Q(12)</td>
<td>15(1)</td>
<td>20(1)</td>
<td>19(1)</td>
</tr>
<tr>
<td>16(1)</td>
<td>-1(1)</td>
<td>3(1)</td>
<td>0(1)</td>
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<tr>
<td>16(1)</td>
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<td>22(1)</td>
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<td>9(1)</td>
<td>1(1)</td>
<td>1(1)</td>
<td>4(1)</td>
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Table 30. Hydrogen coordinates ($10^4$) and isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for molecule 6a.

<table>
<thead>
<tr>
<th>x</th>
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<th>z</th>
<th>U(eq)</th>
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<td>23</td>
<td>H3A</td>
</tr>
<tr>
<td>3239</td>
<td>5937</td>
<td>22</td>
<td>H6a</td>
</tr>
<tr>
<td>2188</td>
<td>3342</td>
<td>30</td>
<td>H7B</td>
</tr>
<tr>
<td>2201</td>
<td>4870</td>
<td>30</td>
<td>H9A</td>
</tr>
<tr>
<td>5029</td>
<td>7219</td>
<td>21</td>
<td>H11A</td>
</tr>
<tr>
<td>4707</td>
<td>10311</td>
<td>21</td>
<td>H14A</td>
</tr>
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<td>7294</td>
<td>23</td>
<td>H16a</td>
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<tr>
<td>7079</td>
<td>11009</td>
<td>34</td>
<td>H16C</td>
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<th>z</th>
<th>U(eq)</th>
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</thead>
<tbody>
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<td></td>
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<td>H5A</td>
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</tr>
<tr>
<td>H7A</td>
<td>-505</td>
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<td></td>
</tr>
<tr>
<td>H7C</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>H9B</td>
<td>7990</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H12A</td>
<td>13719</td>
<td></td>
<td></td>
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<tr>
<td>H15A</td>
<td>9799</td>
<td></td>
<td></td>
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<tr>
<td>H16B</td>
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Table 31. Torsion angles [deg] for molecule 6a

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<th>C(8) - C(2) - C(1) - C(2)</th>
<th>C(8) - C(2) - C(1) - C(1)</th>
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</thead>
<tbody>
<tr>
<td>C(6)</td>
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<td>-1.21(18)</td>
<td>-90.58(13)</td>
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<tr>
<td>C(1)</td>
<td>175.02(10)</td>
<td>0.22(18)</td>
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<tr>
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<tr>
<td>C(3)</td>
<td>-179.5(1)</td>
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<td>C(4)-C(5)-C(6)</td>
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<tr>
<td>C(4)</td>
<td>179.31(11)</td>
<td>-1.24(18)</td>
<td>C(2)-C(1)-C(6)-C(5)</td>
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<tr>
<td>C(5)</td>
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<td>174.79(10)</td>
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</tr>
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<td>0.99(17)</td>
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<td>-179.09(10)</td>
<td>-168.50(9)</td>
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<tr>
<td>C(8)</td>
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<td>176.13(9)</td>
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</tr>
<tr>
<td>C(9)</td>
<td>-10.15(16)</td>
<td>170.22(10)</td>
<td>C(11)-C(10)-C(11)-C(12)</td>
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<tr>
<td>C(10)</td>
<td>179.81(10)</td>
<td>0.17(17)</td>
<td>C(10)-C(11)-C(12)-C(13)</td>
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<tr>
<td>C(11)</td>
<td>0.40(17)</td>
<td>-0.17(16)</td>
<td>C(16)-C(13)-C(13)-C(12)</td>
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<tr>
<td>C(12)</td>
<td>178.8(1)</td>
<td>-179.72(10)</td>
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</tr>
<tr>
<td>C(13)</td>
<td>-0.68(17)</td>
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<td>C(12)-C(13)-C(14)-C(15)</td>
</tr>
<tr>
<td>C(14)</td>
<td>0.40(17)</td>
<td>179.94(11)</td>
<td>C(11)-C(10)-C(15)-C(14)</td>
</tr>
<tr>
<td>C(15)</td>
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<td>0.16(18)</td>
<td>C(11)-C(10)-C(15)-C(14)</td>
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</table>

Symmetry transformations used to generate equivalent atoms:
Table 32: Crystal data and structure refinement for molecule 7a

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<tbody>
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<td>Identification code</td>
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<tr>
<td>Empirical formula</td>
<td>C₁₆ H₁₆ O₅</td>
</tr>
<tr>
<td>Formula weight</td>
<td>288.29</td>
</tr>
<tr>
<td>Temperature</td>
<td>90.0(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.54178 Å</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Triclinic, P-1</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>( a = 5.8859(5) ) Å</td>
<td>( \alpha = 87.423(4) ) deg.</td>
</tr>
<tr>
<td>( b = 12.7775(10) ) Å</td>
<td>( \beta = 89.813(5) ) deg.</td>
</tr>
<tr>
<td>( c = 19.1219(14) ) Å</td>
<td>( \gamma = 77.523(5) ) deg.</td>
</tr>
<tr>
<td>Volume</td>
<td>1402.69(19) Å³</td>
</tr>
<tr>
<td>Z, Calculated density</td>
<td>4, 1.365 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.847 mm⁻¹</td>
</tr>
<tr>
<td>( F(000) )</td>
<td>608</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.200 x 0.140 x 0.120 mm</td>
</tr>
<tr>
<td>Theta range for data collection</td>
<td>2.313 to 68.429 deg.</td>
</tr>
<tr>
<td>Limiting indices</td>
<td>-7 ( \leq h \leq 7, ) -15 ( \leq k \leq 15, ) -21 ( \leq l \leq 23 )</td>
</tr>
<tr>
<td>Reflections collected/unique</td>
<td>24835/24835 [( R_{int} = ? ) ]</td>
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<tr>
<td>Completeness to theta</td>
<td>67.679/98.5 %</td>
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<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
</tr>
<tr>
<td>Min. and max. transmission</td>
<td>0.893 and 0.610</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on ( F^2 )</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>24835/0/385</td>
</tr>
<tr>
<td>Goodness-of-fit on ( F^2 )</td>
<td>1.104</td>
</tr>
<tr>
<td>Final ( R ) indices ( [I&gt;2\sigma(I)] )</td>
<td>( R_I = 0.0684, ) ( wR_2 = 0.2084 )</td>
</tr>
<tr>
<td>( R ) indices (all data)</td>
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</tr>
<tr>
<td>Extinction coefficient</td>
<td>0.0022(7)</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.389 and -0.347 e. Å⁻³</td>
</tr>
</tbody>
</table>
Table 33. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for molecule 7a.

U(eq) is defined as one third of the trace of the orthogonalized U_ij tensor.

<table>
<thead>
<tr>
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<th>y</th>
<th>z</th>
<th>U(eq)</th>
</tr>
</thead>
<tbody>
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<td>7404(2)</td>
<td>6646(1)</td>
<td>34(1)</td>
</tr>
<tr>
<td>34(1)</td>
<td>Q 5 A</td>
<td>14437(5)</td>
<td>9738(2)</td>
</tr>
<tr>
<td>6617(2)</td>
<td>28(1)</td>
<td>Q 2 A</td>
<td>1354(7)</td>
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<td>6852(2)</td>
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C(14B) - H(14B) 0.9500
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C(16B) - H(16E) 0.9800
C(16B) - H(16F) 0.9800
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C(6A) - O(2A) - C(8A) 116.4(3)
C(9A) - O(4A) - C(10A) 115.5(3)
C(13A) - O(5A) - C(16A) 117.2(3)
C(1A) - C(1A) - C(2A) 125.7(3)
C(1A) - C(1A) - C(6A) 115.5(3)
C(2A) - C(1A) - C(6A) 118.9(4)
C(3A) - C(2A) - C(1A) 120.4(4)
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C(3A) - C(2A) - H(2A) 119.8
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C(5A) - C(6A) - O(2A) 124.6(3)
C(5A) - C(6A) - C(1A) 120.4(3)
C(2A) - C(6A) - C(1A) 115.0(4)
C(1A) - C(7A) - H(7A1) 109.5
C(1A) - C(7A) - H(7A2) 109.5
H(7A1) - C(7A) - H(7A2) 109.5
C(1A) - C(7A) - H(7A3) 109.5
H(7A1) - C(7A) - H(7A3) 109.5
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C(2A) - C(8A) - H(8A1) 110.4
C(9A) - C(8A) - H(8A1) 110.4
C(2A) - C(8A) - H(8A2) 110.4
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O (3A) - C (9A) - C (8A)  127.9(4)
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H (16A) - C (16A) - H (16B)  109.5
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H (16A) - C (16A) - H (16C)  109.5
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C (9B) - C (4B) - C (10B)  116.7(3)
C (13B) - C (5B) - C (16B)  117.5(3)
O (1B) - C (1B) - C (2B)  124.9(4)
O (1B) - C (1B) - C (6B)  116.0(3)
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C (3B) - C (4B) - H (4B)  120.4
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C (6B) - C (5B) - C (4B)  120.3(4)
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C (4B) - C (5B) - H (5B)  119.8
C (5B) - C (6B) - C (2B)  125.2(3)
C (5B) - C (6B) - C (1B)  120.5(4)
C (2B) - C (6B) - C (1B)  114.2(3)
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H (7B1) - C (7B) - H (7B2)  109.5
O (1B) - C (7B) - H (7B3)  109.5
H (7B1) - C (7B) - H (7B3)  109.5
H (7B2) - C (7B) - H (7B3)  109.5
O (2B) - C (8B) - C (9B)  106.4(3)
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Symmetry transformations used to generate equivalent atoms:
Table 35. Anisotropic displacement parameters (Å² x 10^3) for molecule 7a. 

The anisotropic displacement factor exponent takes the form:

\[-2π^2 h^2 a^*^2 U_{11} + ... + 2hk a^* b^* U_{12} \]

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**Symmetry transformations used to generate equivalent atoms:**
Appendix II. Supplementary information for Oxidation of Lignin Model Compounds with Layered Double Hydroxide catalysts
Catalyst preparation

Ni-Cu-Cr-LDH

The metal solution contained Cu(NO$_3$)$_2$•3H$_2$O (30.92 g, 0.128 mol), Ni(NO$_3$)$_2$•6H$_2$O (38.71 g, 0.133 mol), and Cr(NO$_3$)$_3$•9H$_2$O (53.24 g, 0.133 mol) in 212 mL of deionized water.

Ni-Cr-LDH

The metal solution contained Ni(NO$_3$)$_2$•6H$_2$O (38.74 g, 0.133 mol) and Cr(NO$_3$)$_3$•9H$_2$O (26.67 g, 0.067 mol) in 210 mL of deionized water. Also, the base solution had a lower concentration of NaOH (1.42 M). The pH was maintained between 9 and 10.
Mg-Al-LDH-1

Mg-Al-LDH-1 was prepared for Ni-Cr-LDH. The metal solution contained Mg(NO$_3$)$_2$$\cdot$6H$_2$O (38.47 g, 0.150 mol) and Al(NO$_3$)$_3$$\cdot$9H$_2$O (18.76 g, 0.05 mol) in 210 mL of deionized water. The base solution contained NaOH (1.45 M) and Na$_2$CO$_3$ (0.60 M).

Mg-Al-LDH-2

Mg-Al-LDH-2 was prepared as for Ni-Cr-LDH. The metal solution contained Mg(NO$_3$)$_2$$\cdot$6H$_2$O (41.02 g, 0.160 mol) and Al(NO$_3$)$_3$$\cdot$9H$_2$O (15.01 g, 0.04 mol) in 210 mL of deionized water. The base solution contained NaOH (1.46 M) and Na$_2$CO$_3$ (0.60 M).

Ni-Al-LDH-1

Ni-Al-LDH-1 was prepared as for Ni-Cr-LDH. The metal solution contained NaOH Ni(NO$_3$)$_2$$\cdot$6H$_2$O (38.98 g, 0.134 mol) and Al(NO$_3$)$_3$$\cdot$9H$_2$O (24.71 g, 0.066 mol) in 210 mL of deionized water. The base solution contained NaOH (1.41 M) and Na$_2$CO$_3$ (0.60 M).

Ni-Al-LDH-2

Ni-Al-LDH-2 was prepared as for Ni-Cr-LDH. The metal solution contained Ni(NO$_3$)$_2$$\cdot$6H$_2$O (43.61 g, 0.150 mol) and Al(NO$_3$)$_3$$\cdot$9H$_2$O (18.72 g, 0.05 mol) in
210 mL of deionized water. The base solution contained NaOH (1.41 M) and Na$_2$CO$_3$ (0.60 M).

Catalyst leaching study

1-phenyl ethanol (2 mmol), phenyl ether (10 mL) and Ni-Cr (2:1) LDH (0.5 g) were added to a 3-necked flask equipped with an oxygen bubbler, a reflux condenser, and a glass stopper. The reaction was stirred at 150 °C for 1 h and then hot filtered to remove the catalyst. A sample of the filtrate was taken for GC-FID analysis and the remainder was added to a fresh 3-neck flask equipped with an oxygen bubbler, a reflux condenser, and a glass stopper. The reaction mixture was stirred at 150 °C for an additional 23 h. Conversion, selectivity, and yield were determined via the GC-FID method below. The amount of metal leached was determined by ICP-OES.

Catalyst reusability

The study was carried out using the same proportions of catalyst, solvent, and starting material as in the general procedure. Before each use the catalyst Ni-Al-LDH-1 was thermally pretreated at 175 °C for 3 h. The reaction mixture was stirred at 150 °C, sample aliquots (0.1 mL) being taken at 0.5 h, 1 h, 2 h and added to 0.9 mL of toluene. Each sample was filtered with a PTFE membrane syringe filter. After the reaction was finished the reaction was quenched in an ice bath and THF (10-15 mL) was added to the reaction mixture. The contents were then filtered through a PTFE membrane and the catalyst was washed with THF.
and hexanes. The catalyst was then placed in a vacuum oven overnight at 50 °C to dry. Conversion, selectivity, and yield were determined using the GC-FID method below. After the third cycle 0.2 g of the catalyst was washed with 50 g of 10% Na₂CO₃ in deionized water. The mixture was allowed to stir overnight. The mixture was then centrifuged and washed (cyclically) with DI water until the supernatant was of neutral pH. After drying overnight in a vacuum oven the catalyst Ni-Al-LDH-1 was thermally pretreated at 175 °C for 3 hours and then added to the reaction mixture in the same proportions as noted in the general procedure.

Synthesis of lignin model compounds

Synthesis of compounds 4d and 5d

A suspension of guaiacol (16.56 g, 138 mmol), potassium carbonate (21.1 g, 153 mmol) and acetone (140 mL) was cooled to 0 °C and 2-bromo-4′-methoxyacetophenone (24.3 g, 106 mmol) was added slowly. After the addition, the reaction was heated to reflux and held overnight. The mixture was then allowed to cool, and was filtered through a pad of Celite® and was then concentrated in vacuo. The resulting solid was dissolved in ethyl acetate (200 mL), was washed with 1 M sodium hydroxide (75 mL x 3), followed by brine (100 mL x 2), and was dried over anhydrous sodium sulfate. After filtration, the product was concentrated in vacuo. The resulting red-brown solid was recrystallized using acetone resulting in a white solid (20.3 g, 71% yield). GCMS:
Compound 5 was synthesized in an analogous manner to compound 4. The synthesis of compound 5 resulted in a white powder (29.7 g, 94% yield): GCMS: m/z 272.1 (24%), 135.1 (100%), 77.1 (15%) and 1H-NMR (400 MHz, CDCl$_3$) δ: 8.02-7.96 (m, 2H), 6.98-6.82 (m, 6H), 5.28 (s, 2H), 3.88 (s, 3H), 3.87 (s, 3H). The 1H-NMR spectrum is consistent with the spectrum previously reported by Lee et al.$^{103}$

**Synthesis of compounds 4 and 5**

Following isolation of 4d, a solution of tetrahydrofuran (150 mL), methanol (300 mL), and 4d (8 g, 29 mmol) were cooled to 0 °C and sodium borohydride (1 g, 26 mmol) was added. After the addition, the reaction mixture was allowed to stir at room temperature overnight. The reaction was then concentrated *in vacuo* and extracted with ethyl acetate (100 mL, x2). The resulting organic layer was then extracted with brine (50, mL x3) and dried over anhydrous magnesium sulfate. Volatile material was then removed *in vacuo* to afford a white solid with a low melting point (ca. 40 °C) (8.1 g, 99% yield). 1H-NMR (400 MHz, CDCl$_3$) δ: 7.37-7.7.35 (d, 2H), 7.01-6.89 (m, 6H), 5.08-5.02 (d, 1H), 4.17-4.12 (d, 1H), 4.0-3.92 (dd, 1H), 3.89 (s, 3H), 3.81 (s, 3H). The 1H-NMR spectrum is consistent with spectra previously reported by Dawange et al.$^{169}$ Compound 5, previously reported by Ren et al.$^{173}$ was synthesized in an analogous manner to compound
4. $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 7.40-7.35 (d, 2H), 6.94-6.80 (m, 6H), 5.08-5.02 (dd, 1H), 4.04-3.90 (m, 2H), 3.82 (s, 3H), 3.77 (s, 3H).

Synthesis of compound 6

Compound 4d (3.5 g, 12.8 mmol) was added to a suspension of formaldehyde 37% (1.6 g, 19.2 mmol), potassium carbonate (2.3 g, 15.4 mmol), and ethanol (205 mL). The suspension was stirred at room temperature for approximately 2 h (monitored by TLC) before the addition of sodium borohydride (1.7 g, 44.8 mmol). The reaction mixture was then stirred at room temperature for 1 h. After filtration, the reaction mixture was concentrated in vacuo, quenched by slowly adding a saturated ammonium chloride solution (20 mL), and filtered. The resulting oil was purified by gradient column chromatography (50% to 100% ethyl acetate in hexanes). After chromatography the product was concentrated in vacuo, resulting in a pale yellow oil (1.8 g, 46% yield). $^1$H-NMR (400 MHz, CDCl$_3$) $\delta$: 7.40-7.34 (m, 2H), 7.34-7.29 (m, 2H), 7.15-6.86 (m, 12H), 5.02-4.98 (m, 2H), 4.18-4.00 (m, 2H), 3.92 (s, 3H), 3.89 (s, 3H), 3.80, (d, 6H), 3.68-3.58 (m, 2H), 3.50-3.40 (m, 2H), 2.74 (br. s., 2 H). The $^1$H-NMR spectrum is consistent with spectra previously reported by Dawange et al.$^{169}$

GC analysis

Gas chromatography analysis was carried out on an HP 6890A GC equipped with a J&W Scientific DB-Wax Column (30 m x 0.53 mm x 0.50 µm). A 1 µL sample was injected and the inlet was run in split mode (Split Ratio
Helium was used as the carrier gas and the column was held under constant pressure at 20 psi. The Flame Ionization Detector was held at 240 °C. Method A, used for analysis of the oxidation product of 1, employed an isothermal inlet temperature of 220 °C. The initial oven temperature was 50 °C and was immediately increased to 150 °C at a rate of 5 °C/min and held isothermally for 2 min resulting in a total run time of 22 min. Method B, used for analysis of the oxidation products of 2, was similar to Method A with the following changes: The initial oven temperature was 50 °C and was immediately increased to 230 °C at a rate of 10 °C/min and held isothermally for 6 min resulting in a total run time of 24 min. The inlet temperature was also lowered to 180 °C. Method B was slightly altered by raising the inlet temperature to 220 °C to create Method C, which was used for the analysis of the oxidation products of 3. All products from the reactions of 1 and 2 were quantified using response factors generated from an external calibration curve created by the use of authentic standards and an internal standard of anisole or guaiacol. When 3 was used as a starting material, 1,4-dimethoxybenzene was used as an internal standard in the reaction mixture and yields were determined from response factors generated from an external calibration curve.

Organosolv lignin solubility in diphenyl ether

Organosolv lignin (10.333 g) obtained from American Science and Technology (Wausau, WI) was added to a round bottom flask containing phenyl ether (ca. 100 mL). The contents were then heated at 90 °C for 20.5 h then at 190 °C for
6.5 h and finally at 90 °C for another 18.5 h. The contents of the flask were then vacuum filtered through a coarse fritted funnel. 7.540 g of lignin was recovered from the frit.

Catalyst characterization

Scanning electron microscopy (SEM) of select catalysts

Figure S1. Scanning electron micrograph of Ni-Al-LDH-1
Figure S2. Scanning electron micrograph of Ni-Cr-LDH.
Ammonia temperature programmed desorption (NH$_3$-TPD) of select catalysts

**Ni-Al-LDH-1**

![Graph](image1)

**Ni-Al-LDH-2**

![Graph](image2)

Figure S3. NH$_3$-TPD of Ni-Al-LDH-1

Figure S4. NH$_3$-TPD of Ni-Al-LDH-2
Figure S5. \( \text{NH}_3 \)-TPD of Mg-Al-LDH-1

Figure S6. \( \text{NH}_3 \)-TPD of Ni-Cr-LDH-1
Figure S7. NH$_3$-TPD of Ni-Cu-Cr-LDH

Infrared (IR) spectra of select catalysts

Figure S8. FT-IR analysis of LDH catalysts
Powder x-ray diffraction (XRD) of recycled catalysts

Figure S9. X-ray diffractogram of Ni-Cr-LDH after 3 cycles of use.
Figure S10. X-ray diffractogram of Ni-Al-LDH-1 after 2 cycles of use.

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Vita

John Adam Jennings

Education

Western Kentucky University, Bowling Green, KY
B.S. in General Chemistry, Minor in Mathematics (Honors College)
2011, GPA: 3.5 (Cum Laude)

Publications And Presentations


Honors

- Center for Nanophase Materials Sciences User Project Grant Number: CNMS2016-024 “Diffuse reflectance UV-vis spectroscopic analysis of Sn-grafted beta zeolite” John Jennings, Mark Crocker
- Max Steckler Fellowship
- Arts and Sciences Certificate for Outstanding Teaching
- Competitive Travel Award Grant Number: NSF-1604019
- Western Kentucky University Honors College Pass with Distinction
- Harvey T. Skaggs Scholarship
- The Scott’s Chemistry Scholarship
- “Best Undergraduate Paper” in the Natural Sciences, Session 8 at the 41st Annual WKU Student Research Conference