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Knocking on Wood: Base Metal Complexes as Catalysts for Selective Oxidation of Lignin Models and Extracts

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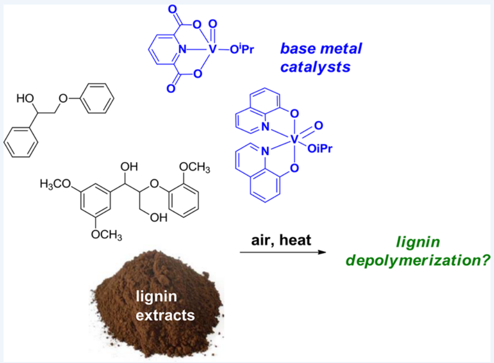

CONSPECTUS: This work began as part of a biomass conversion catalysis project with UC Santa Barbara funded by the first NSF Chemical Bonding Center, CATSB. Recognizing that catalytic aerobic oxidation of diol C−C bonds could potentially be used to break down lignocellulose, we began to synthesize oxovanadium complexes and explore their fundamental reactivity. Of course there were theories regarding the oxidation mechanism, but our mechanistic studies soon revealed a number of surprises of the type that keep all chemists coming back to the bench! We realized that these reactions were also exciting in that they actually used the oxygen-on-every-carbon property of biomass-derived molecules to control the selectivity of the oxidation. When we found that these oxovanadium complexes tended to convert sugars predominantly to formic acid and carbon dioxide, we replaced one of the OH groups with an ether and entered the dark world of lignin chemistry. In this Account, we summarize results from our collaboration and from our individual labs. In particular, we show that oxidation selectivity (C−C vs C−O bond cleavage) of lignin models using air and vanadium complexes depends on the ancillary ligands, the reaction solvent, and the substrate structure (i.e., phenolic vs non-phenolic). Selected vanadium complexes in the presence of added base serve as effective alcohol oxidation catalysts via a novel base-assisted dehydrogenation pathway. In contrast, copper catalysts effect direct C−C bond cleavage of these lignin models, presumably through a radical pathway. The most active vanadium catalyst exhibits unique activity for the depolymerization of organosolv lignin. After Weckhuysen's excellent 2010 review on lignin valorization, the number of catalysis studies and approaches on both lignin models and extracts has expanded rapidly. Today we are seeing new start-ups and lignin production facilities sprouting up across the globe as we all work to prove wrong the old pulp and paper chemist's adage: you can make anything from lignin except money!

1. INTRODUCTION

Because of concerns over the environmental impact of fossil fuel use and the limited long-term supply of petroleum, several countries have initiated research programs aiming to better utilize renewable carbon resources like biomass. The development of new catalytic methods to convert nonfood biomass (lignocellulose) to chemicals and fuels has thus become an area of recent research focus.[1−5]

Nonfood biomass is composed primarily of three polymers: cellulose (∼40−80%), a crystalline linear polymer of glucose; hemicellulose (15−30%), an amorphous polymer of xylose and other sugars; and lignin (15−30%), an irregular polymer composed of methoxy-substituted phenolic subunits.[6,7] Despite the natural abundance of lignin, converting this polymer to more useful chemicals has proven to be a major challenge. Lignin is held together by a number of different chemical linkages, and this inherent complexity makes achieving selectivity in chemical transformations difficult. Additional difficulties are posed by the limited solubility of lignocellulose and its resistance to chemical breakdown.

In lignin, three different monomer units (sinapyl alcohol, coniferyl alcohol, and *p*-coumaryl alcohol) combine to make a polymer with a branched structure that varies depending on plant type and growing conditions.[8] The monomeric units of lignin are connected through more than six different types of linkages with examples shown in Figure 1.[9] The linkages feature a combination of carbon−oxygen (ether) and carbon−carbon bonds. A few of the most commonly occurring linkages are the *β*-O-4 linkage (30−50%), the 5−5′ linkage (10−25%), and the *β*-1 linkage (6−10%).

Both reduction and oxidation have been explored in detail as strategies to produce more valuable chemicals from lignin. The hydrogenation of lignin has been investigated as a potential approach to produce phenols, cyclohexane, other alkane derivatives, and simple aromatic compounds (e.g., xylene).[10,11] The oxidation of lignin also has promise to yield valuable chemicals, particularly aromatic and highly functionalized

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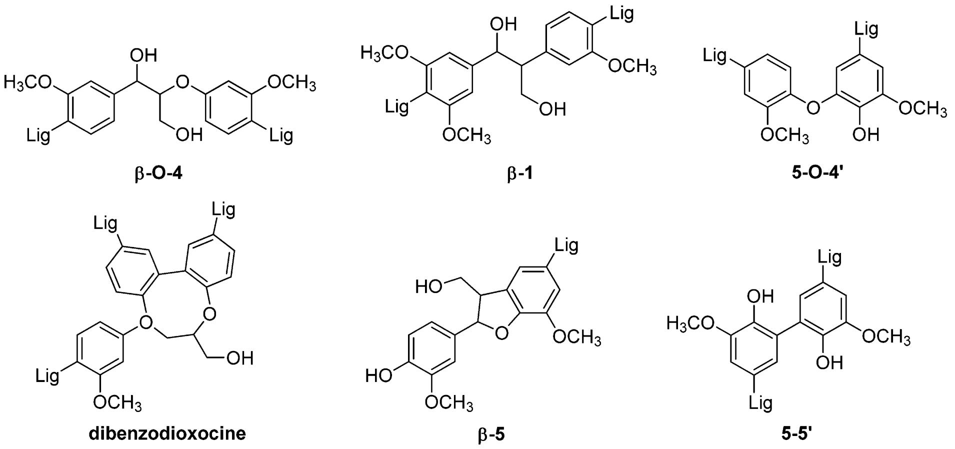


Figure 1. Common lignin linkages.

compounds.[1,9,12] A number of studies have focused on the oxidative depolymerization of lignin using hydrogen peroxide or other strong chemical oxidants with metal catalysts.[2,9,13−16]

Aerobic oxidation of lignin using a base metal catalyst would be an attractive alternative approach to obtain more valuable chemicals from lignin.[17] Toward this end, Drago, Bozell, and others have demonstrated that homogeneous cobalt salen complexes are effective catalysts for the aerobic oxidation of lignin, converting organosolv lignin partly to quinones and other monomeric units.[18−26] Studies of the oxidation of lignin model compounds suggest that the cobalt salen catalyst breaks C−C bonds in phenolic linkages via a cobalt superoxo intermediate that abstracts a hydrogen atom from the substrate, generating a phenoxy radical.[20,25−27]

When we began our work, homogeneous copper and vanadium complexes were known to be effective catalysts for aerobic oxidation reactions, but less was known about their reactivity with lignin. Both metals had previously been reported to catalyze the aerobic oxidation of diols with concomitant C−C bond cleavage, suggesting their promise as catalysts for the depolymerization of lignin.[28,29]

2. OXIDATION OF SIMPLE LIGNIN MODEL COMPOUNDS

Simple lignin model compounds, including 2-phenoxyethanol (**A**), 1-phenyl-2-phenoxyethanol (**B**), and 1,2-diphenyl-2-methoxyethanol (**C**) (Figure 2), were studied to better understand the reactivity and selectivity of vanadium and copper complexes. Our goal was to understand how different types of functional groups and increasing complexity of the substrate would impact the oxidation reactions.

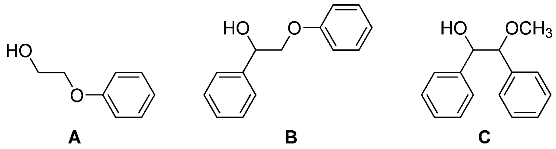


Figure 2. Simple lignin model compounds.

2.1. Reactions with Vanadium

We began by exploring the stoichiometric reactivity of the vanadium complex (dipic)V^V(O)(O^{i}Pr) (**1**) (dipic = dipicolinate) as a test of the ability of **1** to mediate oxidative C−C bond cleavage reactions. In acetonitrile solution, **1** rapidly underwent alkoxide exchange in the presence of excess pinacol, generating the vanadium(V) pinacolate complex (dipic)V^V(O)(pin) (**2**) (Figure 3).[30] Complex **2** reacted in pyridine solution at room temperature, cleaving the C−C bond of the bound pinacol to afford acetone (0.5 equiv) and the vanadium(IV) complex (dipic)V^{IV}(O)$(pyr)_2$ (**3**). Upon heating under inert atmosphere, further reaction with pinacol occurred, forming an additional 0.5 equiv of acetone, water, and the dark purple vanadium(III) dimer $[(dipic)V^{III}(pyr)_2]_2(\mu\text{-}O)$ (**4**) (Figure 3).[30]

1,2-Hydroxyether compounds also bound to the vanadium center in a chelating fashion (Figure 3, complexes **5** and **6**). Oxidative carbon−carbon bond cleavage was observed when pinacol monomethyl ether complex **5** was heated, affording acetone (0.5 equiv), 2-methoxypropene (0.5 equiv), and vanadium(IV) complex **3** (Scheme 1).[31] In contrast, compounds with C−H bonds on the coordinated alcohol moiety underwent oxidative C−H bond cleavage in pyridine solvent. For example, complex **6** reacted upon thermolysis, affording 2-phenoxyacetaldehyde (0.5 equiv) and vanadium(IV) complex **3** (Scheme 1). These and related reactions indicated that vanadium(V) could oxidatively cleave both C−C and C−H bonds.[31]

A series of experiments was then carried out to evaluate the ability of the dipic vanadium complexes to catalyze oxidative C−C bond cleavage. It was found that complex **1** (10 mol %) catalyzed the aerobic oxidation of pinacol upon heating with 20 turnovers observed after 48 h.[30]

Vanadium complex **1** also proved to be a competent catalyst for the aerobic oxidation of simple lignin model compounds (Figure 2). In general, substrates with backbone phenyl substituents were oxidized more readily with the order of reactivity increasing **A** < **B** < **C**.[31] When heated under air with **1** (10 mol %), 1-phenyl-2-phenoxyethanol afforded a mixture of benzoic acid, formic acid, phenol, and 2-methoxyacetophenone. The ketone 2-methoxyacetophenone is likely formed initially and then undergoes oxidative C−C bond cleavage to afford phenol, formic acid, and benzoic acid.[31]

For the related substrate, 1,2-diphenyl-2-methoxyethanol (**C**), the product distribution depended on the solvent (Scheme 2).[31] The oxidation occurred rapidly with catalyst **1** in DMSO solvent, generating predominantly benzaldehyde and methanol. When the same reaction was carried out in pyridine solvent, a different product distribution was observed. The oxidation of **C** in pyridine solvent using catalyst **1** afforded benzoic acid and

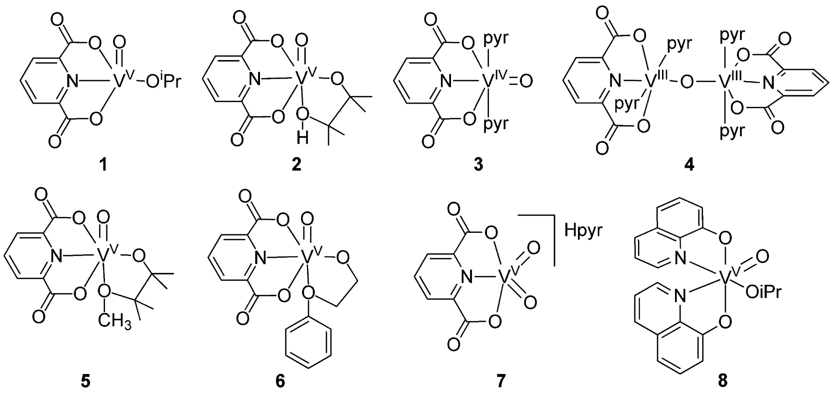
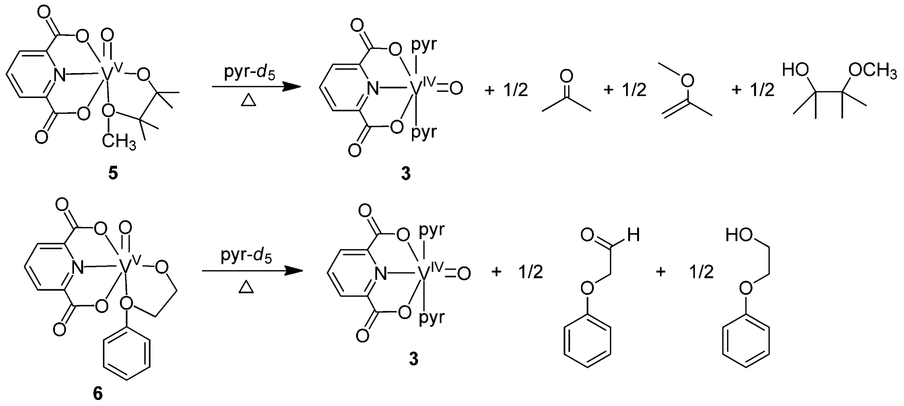
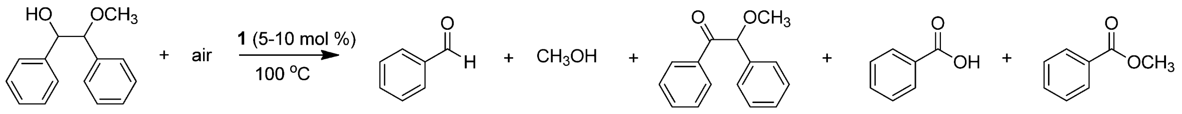


Figure 3. Vanadium complexes **1**–**8**.

Scheme 1. Stoichiometric Reactions of Vanadium(V) Complexes[31]



Scheme 2. Catalytic Aerobic Oxidation of 1,2-Diphenyl-2-methoxyethanol[31]



solvent	% yield				
DMSO	73	69	13	5	5
pyridine	9	6	9	85	84

methyl benzoate as the major products. The ketone benzoin methyl ether is an intermediate in this reaction, being detected initially as the major product in the reaction mixture and then oxidized further to benzoic acid and methyl benzoate.[31]

The pyridine base appeared to have a significant impact on the reactivity and selectivity of the vanadium catalyst.[32] Although the exact role of the base was not yet clear (vide infra), we screened a number of different vanadium complexes and bases for the aerobic oxidation of 4-methoxybenzyl alcohol in an attempt to develop more active vanadium catalysts.[33] Several of the vanadium complexes shown in Figure 4 showed good catalytic activity (using triethylamine as a base promoter) with high yields of 4-methoxybenzaldehyde observed after 24 h. The most effective catalyst was the bis(quinolinate) vanadium(V) complex $(HQ)_2V(O)(O^iPr)$ (**8**).[33] In an effort to increase the activity of the catalyst, a vanadium complex with a similar bis(phenolate) structure and an additional open site at the metal center (**9**) was synthesized (Figure 4).[34] Unfortunately, complex **9** was a less effective catalyst than **8**, although it did display increased solubility and activity in nonpolar solvents.[34]

Oxidation of the simple lignin model compounds was then evaluated using the most active catalyst (**8**). 2-Phenoxyethanol, which was oxidized poorly by **1** (~20% conversion after heating for 1 week), was oxidized somewhat more effectively using catalyst **8** (~70% conversion after 48 h). The reaction afforded a mixture of formic acid, phenol, and the formylated substrate 2-phenoxyethylformate.

Overall, although the exact reactivity depended on the substrate and reaction conditions, the vanadium catalysts with added base tended to operate by initial cleavage of a C−H bond of an alcohol carbon on the lignin model compound, affording a ketone or aldehyde intermediate. The intermediate ketone or aldehyde species was then subject to further oxidation, resulting in C−C bond cleavage and fragmentation of the lignin model compound.

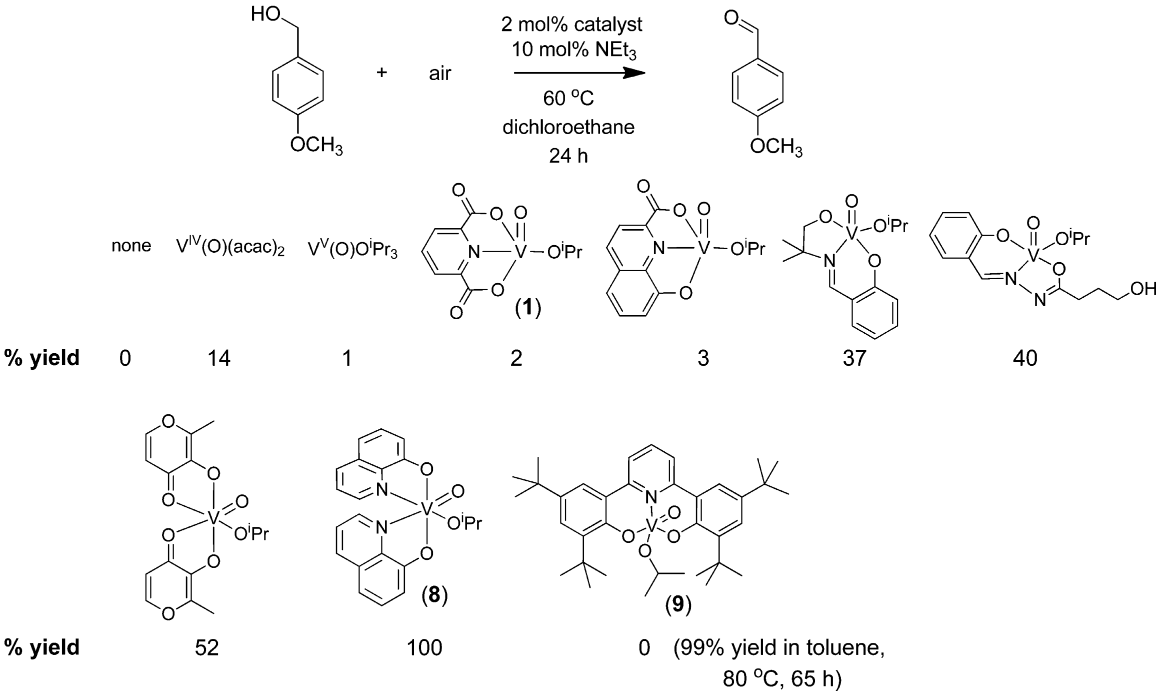


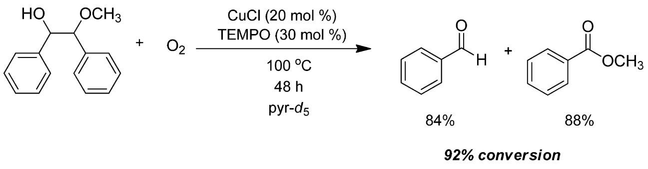
Figure 4. Vanadium complexes screened as catalysts for aerobic oxidation.[33,34]

2.2. Reactions with Copper

Copper catalysts were also evaluated for the aerobic oxidation of simple lignin model compounds. Highly effective copper catalytic systems for the aerobic oxidation of alcohols reported by Markó and Sheldon require a mixture of components, including a strong base (potassium *tert*-butoxide or other alkoxide bases).[35−38] Initial control experiments with these systems and lignin model compounds revealed that the alkoxide base mediated decomposition or other side reactions of the substrate. To avoid these complications, we turned to a copper catalytic system composed of copper(I) chloride, TEMPO, and pyridine. Rossi and co-workers had previously shown that a similar copper system (composed of CuCl and pyridine) catalyzed the aerobic oxidation of diols,[28,29] highlighting the potential of CuCl to catalyze C−C bond cleavage.

The CuCl/TEMPO/pyridine mixture proved effective for the oxidation of simple lignin model compounds. For example, 1,2-diphenyl-2-methoxyethanol (**C**) was oxidized under O_2 using CuCl (20 mol %) and TEMPO (30 mol %) (pyridine solvent, 100 °C, 48 h), affording a mixture of benzaldehyde (84%) and methyl benzoate (88%) (Scheme 3).[39] Here, oxidative C−C bond cleavage is thought to occur directly without intermediacy of the ketone. Control reactions with TEMPO alone in pyridine under O_2 showed no reaction, demonstrating a key role for the copper center in the catalytic activity. Although these results indicated that the copper catalytic system successfully mediated the aerobic oxidative cleavage of C−C bonds, the active copper catalytic species was not stable under the reaction conditions, and in some cases, multiple additions of CuCl were required.[39]

Scheme 3. Catalytic Oxidation of 1,2-Diphenyl-2-methoxyethanol Using CuCl/TEMPO[39]



Subsequently, a more effective copper catalyst mixture was developed. A number of different nitrogen ligands were screened in combination with various copper salts for the aerobic oxidation of an aryl glycerol *β*-aryl ether lignin model compound (**G**, vide infra), and the reactivity of the resulting copper catalysts was compared. The best results were obtained for the combination of CuCl, TEMPO, and 2,6-lutidine in toluene solvent.

The more active copper catalyst mixture (composed of CuCl, TEMPO, and 2,6-lutidine) showed interesting reactivity in the aerobic oxidation of simple lignin model compounds. For example, aerobic oxidation of 1-phenyl-2-phenoxyethanol using CuCl/TEMPO (20 mol % each) and 2,6-lutidine (10 equiv) proceeded with 67% conversion, affording formylated and unusual TEMPO adducts of the starting material, along with minor amounts of phenol and benzoic acid (Scheme 4). Additional experiments indicated that phenolic groups may inhibit the copper catalyst by binding to the metal center, potentially contributing to the low conversion and incomplete mass balance observed for the oxidation of **B**.

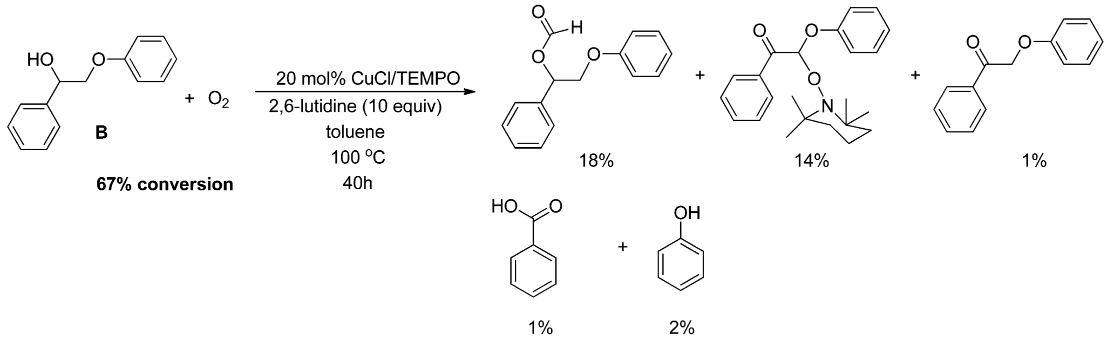
Overall, unlike the vanadium systems, the copper-catalyzed reactions were generally characterized by direct C−C bond cleavage of the lignin model compound without ketone or aldehyde intermediates.

3. MECHANISTIC CONSIDERATIONS

3.1. Vanadium

Our experiments indicated that base played an important role in the vanadium-mediated oxidation reactions. To better understand this effect, we studied a simple reaction where the base was crucial: the oxidation of the isopropoxide ligand of the vanadium(V) complex (dipic)$V^V(O)(O^iPr)$ (**1**).[40] Complex **1** reacted with pyridine to afford acetone (0.5 equiv), isopropanol

Scheme 4. Aerobic Oxidation of 1-Phenyl-2-phenoxyethanol Using CuCl/TEMPO/2,6-Lutidine

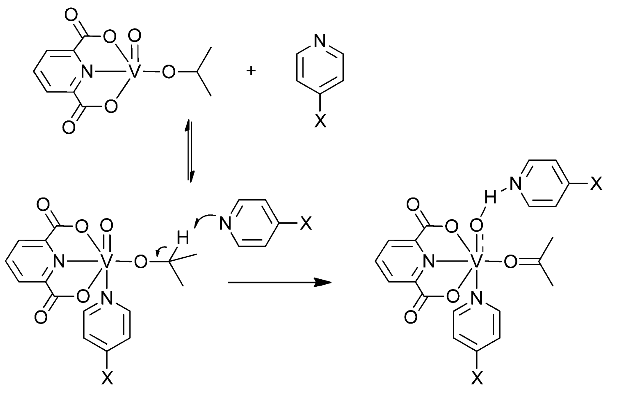


(0.5 equiv), and vanadium(IV) complex **3**. NMR experiments indicated that equilibrium binding of pyridine to the five-coordinate vanadium center of **1** occurs. Kinetic studies were performed and revealed that the reaction is first-order in vanadium and zero-order in isopropanol. A complex dependence on the concentration of pyridine was observed, suggesting an additional role for the base in the reaction. Activation parameters for the reaction were consistent with a highly ordered transition state, and more basic pyridines accelerated the reaction.[40] Ultimately, a mechanism was proposed wherein pyridine coordinates to the vanadium center and participates in a second, bimolecular step involving attack on the C−H bond of the isopropoxide ligand (Scheme 5a). A second competing pathway involves attack of pyridine directly on the C−H bond of the isopropoxide ligand of 5-coordinate complex **1** without prior pyridine coordination.[40]

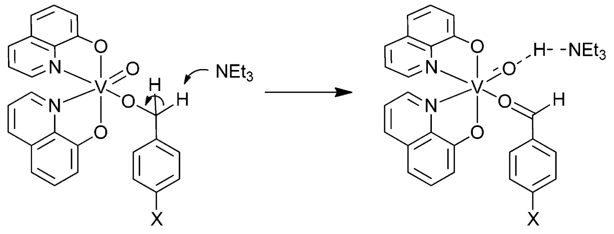
As a further probe of the reaction mechanism, the reaction of the vanadium(V) cyclobutanoxide complex (dipic)V^V(O)-(OC_4H_7) (**10**) with pyridine was studied.[40] The products of this reaction were cyclobutanone (0.5 equiv, 93% yield), cyclobutanol (0.5 equiv), and vanadium(IV) complex **3**, suggesting a two-electron pathway involving a vanadium(III) intermediate (whereas one-electron oxidation of cyclobutanol typically affords ring-opened products).[41] A fast conproportionation of vanadium(III) and vanadium(V) likely yields the vanadium(IV) product.[42]

Scheme 5. Proposed Oxidation Mechanisms for Vanadium Complexes 1 and 11[43]

(a) pyridine-assisted alcohol dehydrogenation pathway



(b) NEt_3-assisted alcohol dehydrogenation pathway



The more active vanadium catalyst $(HQ)_2V(O)(O^iPr)$ (**8**) also experienced base promotion, showing behavior similar to **1**. To gain further insight into the base promotion, we studied the reaction of the vanadium(V) benzyl alcoholate complex $(HQ)_2V(O)(OCH_2C_6H_5)$ (**11**) with triethylamine.[43] The products of this reaction were benzaldehyde (0.5 equiv), benzyl alcohol (0.5 equiv), and vanadium(IV) complex $(HQ)_2V^{IV}(O)$ (**12**). Kinetic studies were performed, and the reaction was found to be first order in both vanadium and triethylamine with activation parameters ($\Delta H^\ddagger = 28 \pm 4$ kJ/mol and $\Delta S^\ddagger = -169 \pm 4$ J/mol·K) consistent with a bimolecular reaction.[43] A large primary kinetic isotope effect (10.2 ± 0.6) was determined, indicating that C−H bond breaking occurs at or before the rate-limiting step. Finally, a Hammett study performed using a series of vanadium complexes with *para*-substituted benzyl alcoholate ligands suggested that negative charge develops on the benzylic carbon atom in the transition state.[43] Together, these results were consistent with a pathway for oxidation that involved deprotonation of the C−H bond of the benzyl alcoholate ligand by the base (NEt_3) in concert with 2e-reduction of the vanadium center (Scheme 5b).[43] Computational studies successfully located this novel base-assisted dehydrogenation pathway and were able to independently replicate the experimentally observed electronic trends. In addition, these studies suggested that the base shuttles a proton from the benzylic C−H to the vanadium-oxo, generating the vanadium(III) hydroxide intermediate $[(HQ)_2V^{III}(OH)(O{=}CHPh)]$.[43]

The mechanism of alcohol oxidation by the vanadium catalysts has major implications for the reaction selectivity. For instance, a preference of the vanadium center to react via a two-electron pathway (rather than a one-electron pathway) could significantly impact the product distribution in the oxidation of lignin model compounds. In the oxidation of lignin model compounds, the ketone products likely result from a two-electron, base-assisted dehydrogenation pathway similar to that proposed for the simple alkoxide ligands.

3.2. Copper

Multiple different pathways have been proposed for copper-mediated oxidation reactions. For instance, recent mechanistic studies of copper/nitroxyl radical catalyst systems suggest that the alcohol oxidation proceeds by concerted hydrogen transfer from a copper(II)-alkoxide to an η^1 coordinated nitroxyl ligand.[44,45] Alternatively, Rogić and co-workers have proposed a single electron transfer step in the aerobic oxidation of catechols using catalytic CuCl/pyridine.[46,47] Hydrogen atom abstraction has also been invoked as a pathway in the oxidation of alcohols by several copper complexes that model the enzyme galactose oxidase.[48,49]

In the aerobic oxidation of the simple lignin model compounds, the copper catalytic system exhibits quite different selectivity from the vanadium one. In general, the copper catalyst mediated C−C bond cleavage directly.[39] A similar selectivity was observed when the stoichiometric oxidation of the lignin model compounds was carried out by cerium ammonium nitrate (CAN), a well-known one-electron oxidant.[39] The similarities in product distribution between CAN and the copper system suggested that copper may mediate the oxidation by an electron transfer pathway.[50] However, more recently, Stahl and co-workers have reported oxidative C−C bond cleavage in aryl glycerol β-aryl ether lignin model compounds catalyzed by CuCl/NMI/TEMPO (NMI = *N*-methyl-imidazole).[51] The group proposed a pathway involving oxidation of the primary alcohol on the lignin model compound followed by a retro-aldol reaction.

Overall, the precise mechanism of the oxidation reactions mediated by CuCl/TEMPO/pyridine is still somewhat uncertain. Although the details of the copper system are not completely understood at this time, the selectivity clearly differs from that of the vanadium system. As discussed below, we found that the differences in selectivity observed between copper and vanadium catalysts extended to the oxidations of more complex lignin model compounds.

4. OXIDATION OF COMPLEX LIGNIN MODEL COMPOUNDS

Although the simple lignin model compounds described above provided a useful indication of the reactivity of the vanadium and copper catalysts, complex lignin models, such as aryl glycerol β-aryl ethers (Figure 5), are more realistic representations of the β-O-4 structures actually found in lignin. In particular, the additional γ-OH group on the lignin model compound can significantly impact the reactivity of the linkage. The presence of phenolic groups, generally prevalent in native and processed lignins, can also affect the selectivity of the oxidation reaction. To better understand these factors, we studied the aerobic oxidation of aryl glycerol β-aryl ether lignin model compounds with both vanadium and copper catalysts.

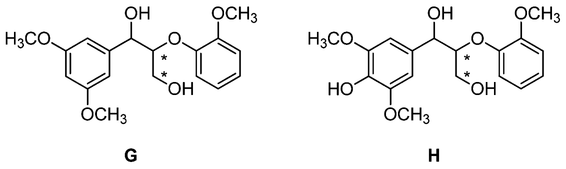


Figure 5. Aryl glycerol β-aryl ether models of the β-O-4 linkage of lignin.

4.1. Aryl Glycerol β-Aryl Ether Models of the β-O-4 Linkage

As we began our studies on the reactivity of aryl glycerol β-aryl ether lignin model compounds, our attention was drawn by a report of a transformation of lignin model compound **D** using a vanadium catalyst (Scheme 6).[52] Toste and co-workers demonstrated that vanadium−salen complex **13** (10 mol %) mediated an unusual type of C−O bond cleavage, affording 2-methoxyphenol and alkene derivative **F** as products.[52] The overall transformation is proposed to proceed through a pathway involving hydrogen atom abstraction of the benzylic C−H bond of **D** by the vanadium(V) center.[52]

We synthesized the new lignin model compounds **G** and **H** (Figure 5), where ^{13}C labels were introduced to facilitate product identification and quantification.[39] Lignin model compound **G** was oxidized under air by dipic vanadium catalyst **1** (10 mol %). C−H, C−O, and C−C bonds were broken in the products (Scheme 7).[39] Additional experiments suggested that ketone **I** formed initially and was further oxidized or dehydrated under the reaction conditions (Scheme 8).[39] The vanadium bis(quinolinate) catalyst with added NEt_3 also was effective for the oxidation of **G**, exhibiting a much higher selectivity for the ketone under milder conditions. Aerobic oxidation of compound **G** using **8** proceeded with 70% conversion, affording ketones **I** (55%) and **J** (10%).

Using a combination of CuCl, TEMPO, and pyridine, lignin model compound **G** underwent oxidative C−C bond cleavage. The use of a stoichiometric amount of CuCl and TEMPO was necessary due to the limited catalyst lifetime and deactivation by phenolic products. After being heated under an atmosphere of O_2, **G** was observed to undergo 89% conversion, affording 3,5-dimethoxybenzaldehyde (43%), 3,5-dimethoxybenzoic acid (13%), and phenol (7%) as the major products.[39] The copper system exhibited a markedly different selectivity from the vanadium system with 3,5-dimethoxybenzaldehyde (arising from cleavage of the C_α−C_β bond) being formed as the major product. Ketone **I** is not an intermediate in this reaction, and the C−C bond cleavage reaction likely occurs directly from **G**.[39]

Phenolic lignin model compound **H** was also oxidized by the vanadium catalysts.[53] Using vanadium catalyst **8**, a different reaction was observed in which the C−C bond between the aryl ring and the adjacent alcohol group was broken. The products of this aerobic oxidation reaction were 2,6-dimethoxybenzoquinone and acrolein derivative **L** (Scheme 9).[53] In contrast, the catalyst reported by Toste's group (**13**; Scheme 6) oxidized **H** with a different selectivity, cleaving the C−O bond to afford alkene **M** and 2-methoxyphenol as major products. Remarkably, the difference in oxidation selectivity depended on the vanadium catalyst in this case and not the substrate or reaction conditions.[53]

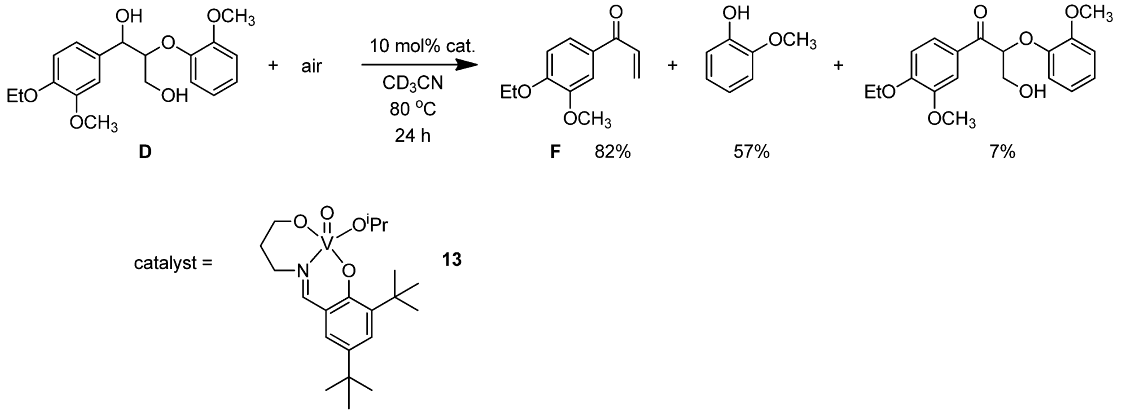
In general, the oxidation reactions of aryl glycerol β-aryl ether lignin model compounds were complex with the product distribution varying depending on the metal catalyst, ligand set, and substrate structure. Multiple reaction pathways were accessible for vanadium and copper, highlighting the potential of first-row transition metal catalysts and the challenges of controlling selectivity in the aerobic oxidation of lignin.

4.2. Models of the β-1 Linkage

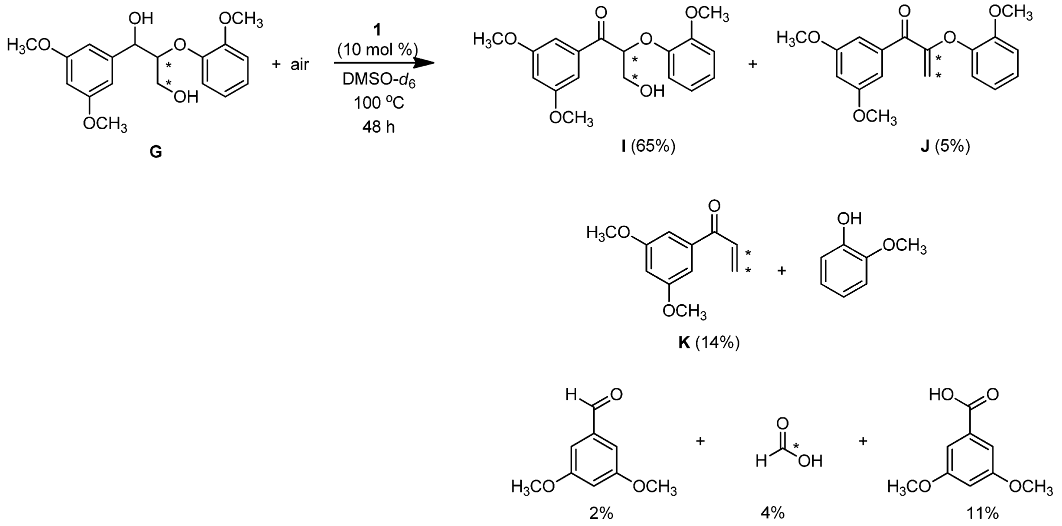
The β-1 linkage is thought to be a significant component of wood structure (for example, 7−9% of spruce lignins).[54] The β-1 linkage differs from β-O-4 in structure, being linked by C−C bonds and having a C-bound aryl group in place of the O-bound phenoxy group. The reactivity of the vanadium and copper catalysts with the β-1 lignin model compounds **N** and **O** was compared (Scheme 10).

When β-1 lignin model compound **N** was heated under air with vanadium catalyst **8** in pyridine solvent, aerobic oxidation

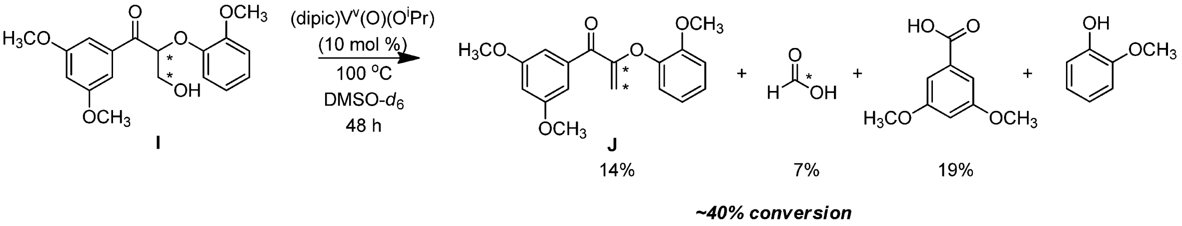
Scheme 6. Vanadium-Catalyzed C–O Bond Cleavage Reaction Reported by Son and Toste[52]



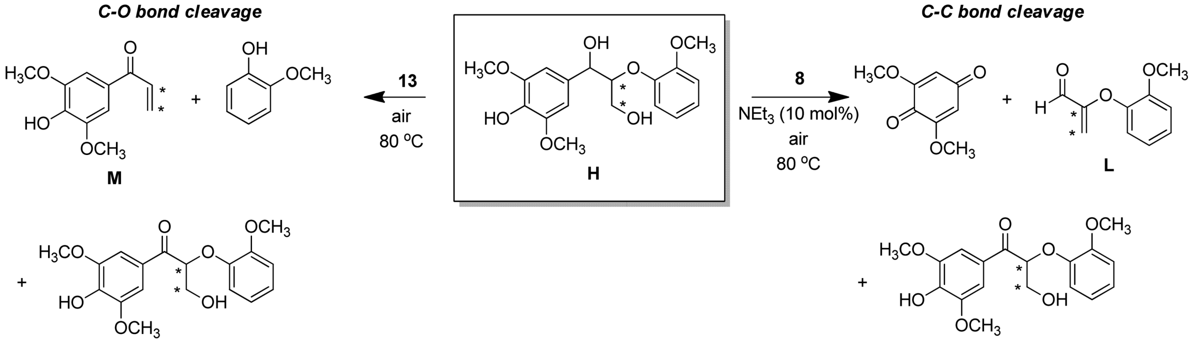
Scheme 7. Oxidation of Lignin Model Compound G Using Vanadium Catalyst 1[39]



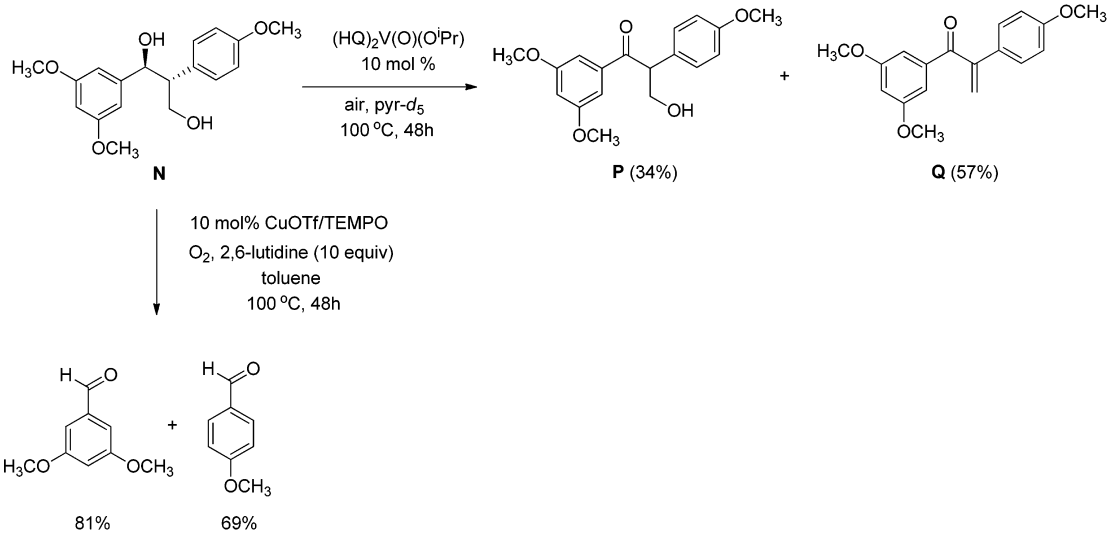
Scheme 8. Aerobic Oxidation of Ketone I Proceeds with C–C Bond Cleavage[39]



Scheme 9. Different Selectivity Observed in the Aerobic Oxidation of Phenolic Lignin Model Compound H with Vanadium Catalysts 8 and 13[53]

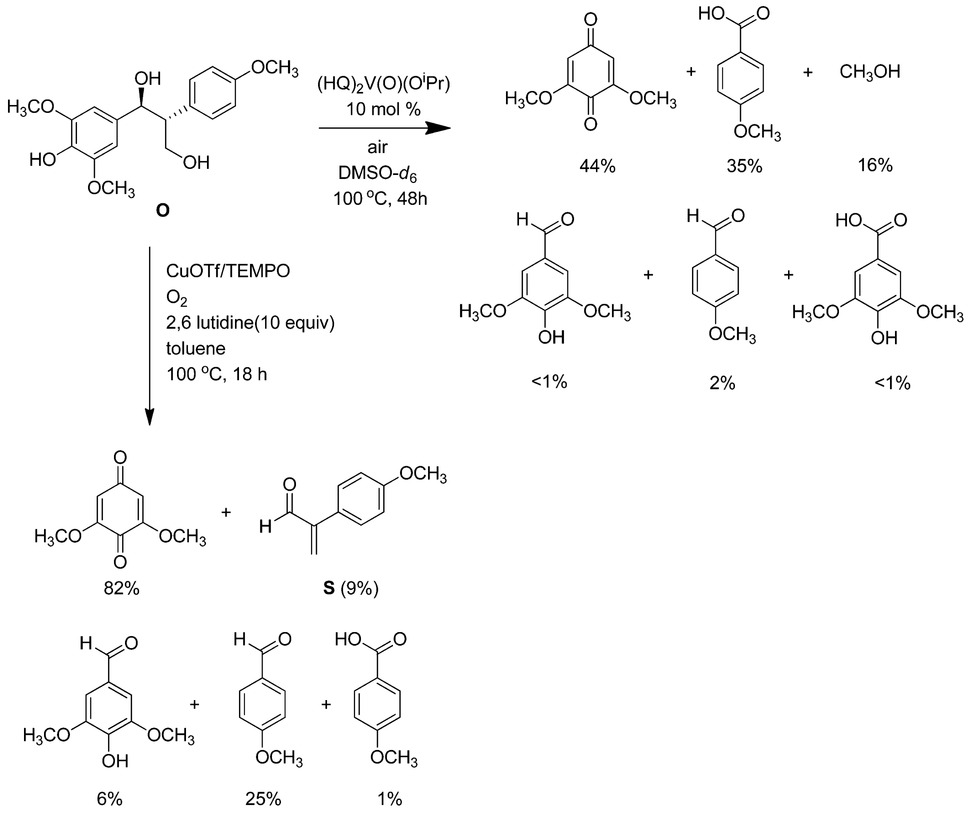


Scheme 10. Comparison of Vanadium and Copper Catalysts for the Aerobic Oxidation of *β*-1 Lignin Model Compound N[a]



[a] Additional minor products (not shown here) were observed in <5% yield with both catalysts, including 3,5-dimethoxybenzoic acid and 4-methoxybenzoic acid.[54]

Scheme 11. Aerobic Oxidation of Phenol *β*-1 Lignin Model Compound O Proceeds with C−C Bond Cleavage[54]



occurred, affording ketone **P** and dehydrated ketone **Q** as the major products.[54]

For the aerobic oxidation of **N**, the copper catalyst system once again operated with a different selectivity from that of the vanadium catalysts. The combination of CuCl, TEMPO, and 2,6-lutidine mediated C−C bond cleavage in lignin model **N**, affording 3,5-dimethoxybenzaldehyde and 4-methoxybenzaldehyde as the major products.[54]

Introducing a phenolic group onto the *β*-1 lignin model compound was found to have a dramatic impact on the selectivity of both vanadium and copper catalysts.[54] Aerobic oxidation of phenolic lignin model compound **O** proceeded with vanadium catalyst **8**, affording C−C bond cleavage products (Scheme 11).[54] An incomplete mass balance was observed in this reaction, arising presumably from polymerization or other reactions of radical intermediates.[50]

Oxidation of **O** with stoichiometric CuCl/TEMPO/2,6-lutidine (due to deactivation of the copper catalyst by phenolic functionalities) also proceeded with cleavage of the C_α−C_{aryl} bond as the dominant pathway (Scheme 11).[54] For both copper and vanadium catalysts, the cleavage of the C_α−C_{aryl} bond in the phenolic substrate is reminiscent of the reactivity of cobalt salen catalysts previously studied by Drago, Bozell, and others.[18−24,27] The cobalt salen complexes were found to mediate C_α−C_{aryl} bond breaking reactions in a variety of phenolic β-O-4, β-1, and β-5 lignin model compounds, as well as organosolv lignin.

In the end, the selectivity of the aerobic oxidation of β-1 lignin model compounds depended on both the catalyst and substrate. In the absence of phenolic groups, vanadium catalyst **8** operated with high selectivity for C−H bond cleavage (affording ketone products), whereas the copper catalyst system operated by C−C bond cleavage (affording aldehyde products). The introduction of a phenolic functional group in the substrate enabled cleavage of the C_α−C_{aryl} bond, which was observed with both vanadium and copper catalysts.

5. OXIDATION OF LIGNIN EXTRACTS

The aerobic oxidation of lignin extracts was evaluated using the different vanadium and copper catalysts. Commercial organosolv lignin (Lignol Corporation)[55] was obtained by extraction of mixed hardwoods with a mixture of ethanol and water.

The catalysts shown in Figure 6 were evaluated for the oxidation of organosolv lignin, and the extent of depolymerization was assessed using gel permeation chromatography (GPC), quantitative HSQC, and ^{31}P NMR spectroscopy after derivatization to phosphite esters. The results with the different catalysts were compared to control reactions containing no catalyst, base only, TEMPO only, and 4-acetamido-TEMPO.[56]

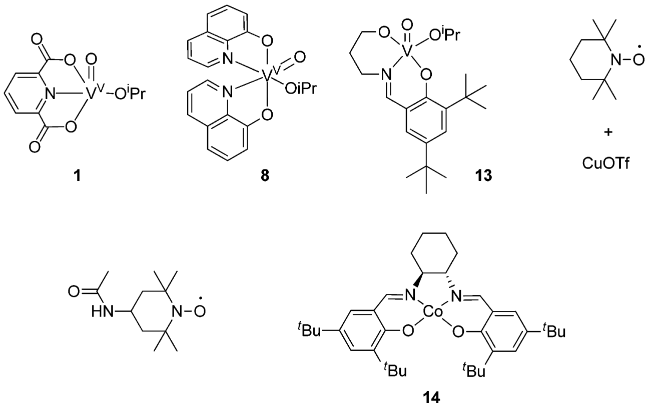


Figure 6. Catalysts tested for the aerobic oxidation of organosolv lignin extracts.

The GPC experiments revealed that, under the reaction conditions tested, vanadium catalyst **8** was most effective for the depolymerization of lignin (Figure 7). A large shift in average molecular weight and a major increase in the lower molecular weight components was observed. For the copper catalyst CuOTf/TEMPO/2,6-lutidine in DMF, only a modest shift to lower molecular weights was observed. Moreover, nearly identical results were obtained when only TEMPO and 2,6-lutidine were present (i.e., without CuOTf), suggesting that radical processes not mediated by the metal are contributing to the depolymerization process. Using either 4-acetamido-TEMPO or cobalt complex **14** showed no difference in the retention times between the catalytic and control experiments with no catalyst.[56]

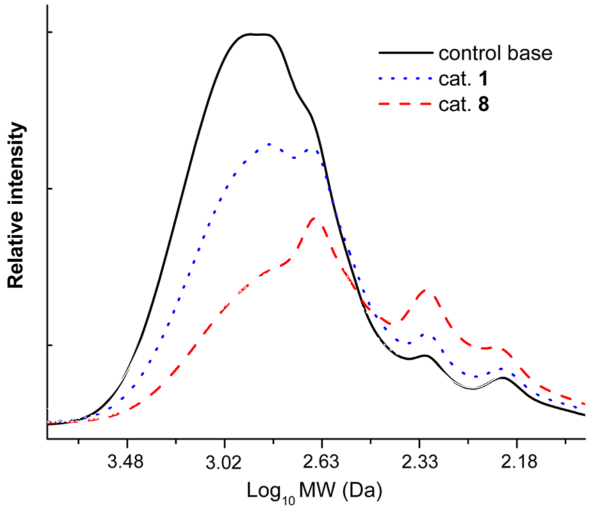


Figure 7. GPC data for the catalytic oxidation of organosolv lignin using **1** (10 wt % **1** and 10 wt % Et_3N) and **8** (10 wt % **8** and 10 wt % Et_3N) compared with the control experiment (10 wt % Et_3N). Molecular weights are compared to polystyrene standards. For all runs: solvent = EtOAc; temperature = 100 °C; pressure of synthetic air = 8.2 atm; and reaction time = 18 h.[56]

HSQC NMR analyses and phosphitylation experiments were also performed on the reaction mixtures resulting from the organosolv lignin oxidations. With vanadium catalyst **8,** decreases in the concentrations of aliphatic and phenolic O−H units of the organosolv lignin were observed.[56]

Some reactivity and decrease in the molecular weight of the organosolv lignin were observed under nearly all of the conditions tested. However, vanadium catalyst **8** was significantly more effective at inducing the depolymerization of the organosolv lignin than any of the other catalysts or control experiments with base alone. These experiments suggest that it is important to evaluate the impact of both metal catalyst and additives (i.e., base) on the depolymerization of lignin. For some catalysts, the lignin may be oxidized without significant overall reduction in the molecular weight.[56]

VI. CONCLUSIONS AND OUTLOOK

This Account has highlighted some of the unique properties offered by molecular oxovanadium complexes for the aerobic oxidation of lignin models and extracts. The importance of base promotion in the initial oxidation step suggests that refined ligand designs with appended bases could promote this intermolecular step, thus increasing reaction rates and perhaps allowing for lower catalyst loading. In addition to the novel base-assisted dehydrogenation pathway that affords ketones from nonphenolic β-O-4 and β-1 linkages, these catalysts are uniquely effective at cleaving the C−C bond of these ketone oxidation products (cf. Scheme 8). Preliminary mechanistic studies of this novel transformation reveal faster reaction rates in the presence of added base, suggesting that the enol tautomer may interact with the vanadium catalyst. The detailed role played by oxygen in this transformation is currently the subject of further experimental and computational investigations in our laboratories.

Practical applications of selective molecular catalysts to obtain aromatic chemicals from lignin faces a number of additional challenges. The heterogeneity of lignin coming from different species of trees or plants, such as sugar cane or corn waste products, is compounded by the variety of processing techniques. As biorefineries evolve, we will see less production of Kraft lignin tied to pulp and paper production and more utilization of native lignin that has not been treated with strong acids or bases. Green solvents and reactive product separations will likely be needed to develop practical processes to families of lignin-derived aromatic chemicals. As exciting results on tandem redox[4,5] and biocat-chemcat[3] approaches to lignin valorization are being disclosed, a selective and productive homogeneous oxidation catalyst could be a key component of these new processes.

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The authors declare no competing financial interest.

Biographies

Susan Hanson grew up in Rochester, NY. In 2003, she graduated from Dartmouth College with a B.A. in Chemistry. She then moved to Seattle, WA, where she completed Ph.D. studies at the University of Washington in 2007 with Karen Goldberg and Mike Heinekey. Her dissertation work involved the study of platinum, rhodium, and iridium complexes for the activation and functionalization of C−H bonds. In 2008, Susan began working at Los Alamos National Laboratory as part of a joint UCSB-LANL collaboration between Peter Ford, Susannah Scott, Tom Baker, and Dave Thorn. She joined LANL as a Director's Funded postdoc in 2009 and became a staff scientist in 2010. Her work at LANL has focused on the development of earth-abundant metal catalysts as well as other national security-related applications of inorganic chemistry.

Tom Baker hails from Tsawwassen, British Columbia, and obtained his B.Sc. (Honours) in Chemistry (1975) from UBC in Canada and Ph.D. in Inorganic Chemistry (1980) from UCLA with Fred Hawthorne. After a postdoctoral stint with Philip Skell at Penn State working on metal atom chemistry and EPR spectroscopy, Tom spent 15 years at DuPont CR&D developing applications of homogeneous catalysis to fluorochemicals, titanium dioxide, and nylon intermediates. In 1996, he joined the Chemistry division at Los Alamos National Laboratory, where he led projects on bifunctional and multiphasic catalysis approaches for alkane functionalization and chemical hydrogen storage and production. In 2008, Baker joined the Chemistry Department at uOttawa as Tier 1 Canada Research Chair in Catalysis Science for Energy Applications and Director of the Centre for Catalysis Research and Innovation. He is a founding member of the US NSF-funded Center for Enabling New Technology through Catalysis (CENTC) and the Catalytic Processing theme leader of Canada's *Lignoworks* Biomaterials and Chemicals research network.

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