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Efficient Cobalt-Catalyzed Oxidative Conversion of Lignin Models to Benzoquinones

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ABSTRACT

Phenolic lignin model monomers and dimers representing the primary substructural units of lignin were successfully oxidized to benzoquinones in high yield with molecular oxygen using new Co-Schiff base catalysts bearing a bulky heterocyclic nitrogen base as a substituent. This is the first example of a catalytic system able to convert both S and G lignin model phenols in high yield, a process necessary for effective use of lignin as a chemical feedstock.

The recognition that biomass is a viable raw material for chemicals and fuels[1] has brought increased recent attention to lignin.[2] Lignin comprises as much as 25 wt % of lignocellulosic biomass, making it the second most abundant source of renewable carbon in nature, and a potentially rich source of biobased aromatics. However, lignin conversion presents a significant challenge as lignin's biosynthesis from syringyl (S), guaiacyl (G), and *p*-hydroxyphenyl (H) subunits **1**, **2**, and **3** (Figure 1)[3] leads to structural heterogeneity that frustrates its utility as a chemical feedstock. Recent reports describe systems that deconstruct lignin models, using reductive processes catalyzed by Ru,[4] Ni,[5] or Pd,[6] or both oxidative and nonoxidative processes catalyzed by Co[7] or V.[8] These studies focus on the cleavage of β-aryl ethers, representative of lignin's β-O-4 linkage, which can account for 50–65% of the interunit bonding present in native lignin.[9]

Native lignin, however, does not retain its original substructural profile when it is isolated from a lignocellulosic matrix. Biorefining processes designed for the pretreatment or fractionation of biomass into its individual components (lignin, cellulose, and hemicellulose)[10] introduce significant changes to the native lignin structure. For example, solvent fractionation, acid hydrolysis, or catalyzed steam explosion of biomass can nearly eliminate β-aryl ethers.[11]

Moreover, as these units are cleaved, the number of free (i.e., nonetherified) phenolic –OH groups present in both

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[1] (a) Bozell, J. J.; Petersen, G. R. *Green Chem.* **2010**, *12*, 539–554. (b) Bozell, J. J. *Clean-Soil Air Water* **2008**, *36*, 641–647.

[2] (a) Zakzeski, J.; Bruijnincx, P. C. A.; Jongerius, A. L.; Weckhuysen, B. M. *Chem. Rev.* **2010**, *110*, 3552–3599. (b) Sannigrahi, P.; Pu, Y. Q.; Ragauskas, A. *Curr. Opin. Environ. Sus.* **2010**, *2*, 383–393.

[3] Boerjan, W.; Ralph, J.; Baucher, M. *Ann. Rev. Plant Biol.* **2003**, *54*, 519–546.

[4] (a) Wu, A.; Patrick, B. O.; Chung, E.; James, B. R. *Dalton Trans.* **2012**, *41*, 11093–11106. (b) Nichols, J. M.; Bishop, L. M.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2010**, *132*, 12554–12555.

[5] (a) Sergeev, A. G.; Hartwig, J. F. *Science* **2011**, *332*, 439–443. (b) He, J. Y.; Zhao, C.; Lercher, J. A. *J. Am. Chem. Soc.* **2012**, *134*, 20768–20775.

[6] Parsell, T. H.; Owen, B. C.; Klein, I.; Jarrell, T. M.; Marcum, C. L.; Haupert, L. J.; Amundson, L. M.; Kenttamaa, H. I.; Ribeiro, F.; Miller, J. T.; Abu-Omar, M. M. *Chem. Sci.* **2013**, *4*, 806–813.

[7] Zakzeski, J.; Bruijnincx, P. C. A.; Weckhuysen, B. M. *Green Chem.* **2011**, *13*, 671–680.

[8] (a) Hanson, S. K.; Wu, R.; Silks, L. A. P. *Angew. Chem., Int. Ed.* **2012**, *51*, 3410–3413. (b) Son, S.; Toste, F. D. *Angew. Chem., Int. Ed.* **2010**, *49*, 3791–3794.

[9] Lin, S. Y.; Dence, C. W. *Methods in Lignin Chemistry*; Springer-Verlag: Berlin, 1992.

[10] Mosier, N.; Wyman, C.; Dale, B.; Elander, R.; Lee, Y. Y.; Holtzapple, M.; Ladisch, M. *Bioresour. Technol.* **2005**, *96*, 673–686.

[11] (a) Bozell, J. J.; O'Lenick, C. J.; Warwick, S. *J. Agric. Food. Chem.* **2011**, *59*, 9232–9242. (b) Li, J. B.; Gellerstedt, G.; Toven, K. *Bioresour. Technol.* **2009**, *100*, 2556–2561. (c) Samuel, R.; Pu, Y. Q.; Raman, B.; Ragauskas, A. J. *Appl. Biochem. Biotechnol.* **2010**, *162*, 62–74.

10.1021/ol401065r

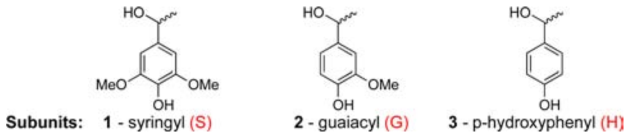

Figure 1. Primary monomeric subunits of lignin.

dissolved lignin and fragments bearing residual β-O-4 linkages increases dramatically. Aromatic units in native lignin contain 7–13% phenolic –OH depending on the source,[12] but as lignin transitions from the growing plant to a biorefinery feedstock, its dissolution and removal from the matrix can increase this amount to over 70%.[13] Even residual lignin in woody biomass after fractionation exhibits as much as 25% free phenols.[14] Accordingly, catalyst development focusing on selective transformation of substituted phenols would more accurately model the structure of lignin as an isolated source of renewable carbon.

Co-Schiff base complexes catalyze the aerobic oxidation of phenols under mild conditions via formation of an intermediate Co-superoxo complex that abstracts a phenolic hydrogen and affords a reactive phenoxy radical (Figure 2).[15] Using Co(salen) (**4**) and related complexes, we demonstrated one of the first examples of selective catalytic oxidation of *para*-substituted phenolic lignin models and its utility in the synthesis of benzoquinones.[16]

We now report the synthesis of a new series of unsymmetrical Co-Schiff base oxidation catalysts[17] that exploits phenolic functionality in both G and S lignin models to afford methoxybenzoquinone (MBQ, **5**) and 2,6-dimethoxybenzoquinone (DMBQ, **6**) as primary oxidation products. Phenolic β-O-4 model dimers are converted to quinones not *via* β-aryl ether cleavage, but through a unique cleavage of the C–C bond between the aromatic ring and the α-carbon of the lignin model side chain to afford the quinone products and fragment **7**. This is the first example of a catalytic system able to convert both S and G lignin model phenols in high yield, a process necessary for effective lignin conversion.

Previous studies from our laboratory showed that 10 mol % Co(salen) in the presence of an axial ligand (pyridine or imidazole) and molecular O_2 (50–60 psi) converted several S models to **6** in high yield.[16a] Although yields for S oxidation ranged above 70%, oxidation of the less reactive G models afforded ≤20% **5** under the same conditions because of the reduced ability of G models to form an intermediate phenoxy radical.[18] However, the yield of MBQ was increased to 51% upon addition of a stoichiometric amount of a sterically hindered aliphatic nitrogen base. The additional base likely deprotonates the phenol substrate to give a more easily oxidized phenoxide anion.[16b] Based on these results, we designed a new family of Co-Schiff base catalysts **8** and **9** incorporating a sterically hindered base within their structure (Table 1).

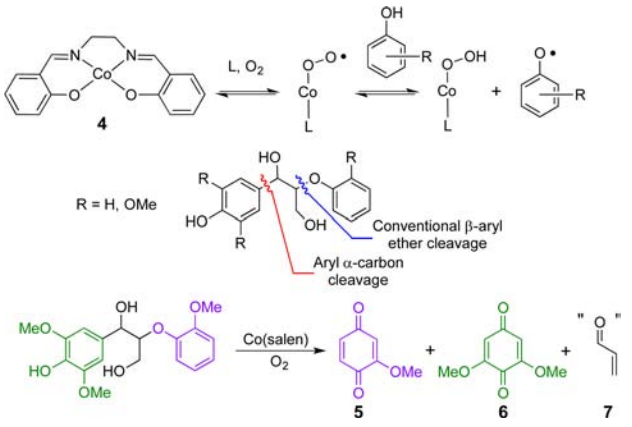

Figure 2. Co-Schiff base catalyzed cleavage of lignin models.

Catalyst **8a** symmetrically substituted with *t*-Bu groups provides DMBQ with yields and rates comparable to those for oxidations catalyzed by **4** (entries 2–4), but catalyst **8b** bearing symmetric bulky piperazine groups on the Co ligand afforded lower selectivity and much higher levels of syringaldehyde **12** (entry 5). In contrast, several unsymmetric catalysts **9** bearing a single functionalized substituent provided **6** in good yield. Using catalyst **9a** under conditions optimized for **4** gave a 67% yield of **6**. However, **9a** also exhibits significantly higher reactivity than **4**, as reducing the catalyst level to 5% and the reaction time to 5 h gave nearly the same yield of **6** (entries 6 and 7). Further reduction in catalyst level and reaction time led to poorer DMBQ yields (entry 8). Interestingly, oxidation with catalysts **9** does not require the addition of an external axial ligand for Co, and indeed, the addition of pyridine to the oxidation led to low yields of **6** and recovery of much of the starting material (entry 9). *N*-Methyl catalyst **9b** exhibited a lower yield and reactivity (entry 10). Conversely, *N*-benzyl catalyst **9c** showed the highest reactivity, affording **6** in 74% yield after only 1 h (entry 11), and comparable yields of **6** after 16 h using as little as 2% catalyst (entry 12). Because oxidations with complex **4** generally require the presence of an axial pyridine ligand, **9f** was synthesized and oxidized **10** to **6** in moderate yields but at a lower rate (entry 14), possibly reflecting an effect similar to that of adding pyridine to the oxidation catalyzed by **9a**.

Upon identifying **9c** as a lead catalyst, several monomeric and dimeric lignin models representing G and S

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(12) Lai, Y. Z.; Guo, X. P. *Wood Sci. Technol.* **1991**, *25*, 467–472.

(13) Robert, D. R.; Bardet, M.; Gellerstedt, G.; Lindfors, E. L. *J. Wood Chem. Technol.* **1984**, *4*, 239–263.

(14) Gellerstedt, G.; Lindfors, E. *Svensk Papperstidn.* **1984**, *87*, R115–R118.

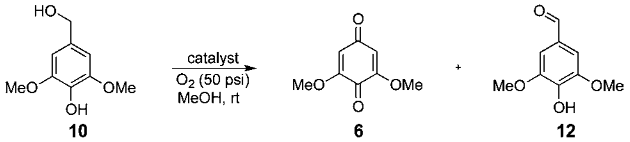
(15) Zombeck, A.; Drago, R. S.; Corden, B. B.; Gaul, J. H. *J. Am. Chem. Soc.* **1981**, *103*, 7580–7585.

(16) (a) Bozell, J. J.; Hames, B. R.; Dimmel, D. R. *J. Org. Chem.* **1995**, *60*, 2398–2404. (b) Cedeno, D.; Bozell, J. J. *Tetrahedron Lett.* **2012**, *53*, 2380–2383.

(17) Kleij, A. W. *Eur. J. Inorg. Chem.* **2009**, 193–205.

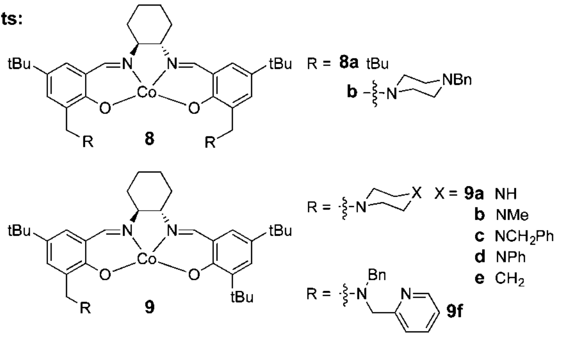
(18) Mulder, P.; Saastad, O. W.; Griller, D. *J. Am. Chem. Soc.* **1988**, *110*, 4090–4092.

Table 1. Catalyst Screening for the Oxidation of Syringyl Alcohol **10** into DMBQ **6** and Syringaldehyde **12**



10 **6** **12**

Catalysts:

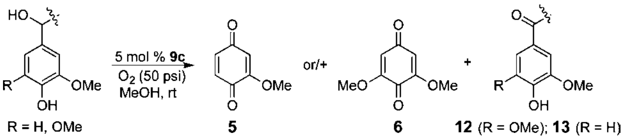


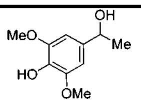
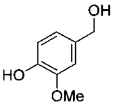
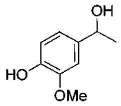
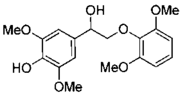
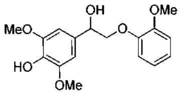
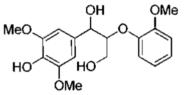
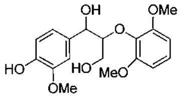
8 **9**

entry	catalyst (mol %)	additive (mol %)[c]	*t* (h)	**6** (%)[a]	**12** (%)	**10** (%)
1[b]	–	–	16	0	7	93
2	**4**(10)	pyr (100)	16	82	<5	0
3	**8a** (10)	DBZP (15)	16	50	5	28
4	**8a** (10)	pyr (100)	16	79	10	traces
5	**8b** (5)	–	16	39	32	6
6	**9a** (10)	–	16	67	20	traces
7	**9a** (5)	–	5	61	25	traces
8[b]	**9a** (2)	–	3	34	31	35
9[b]	**9a** (10)	pyr (100)	16	11	29	60
10	**9b** (5)	–	16	54	0	40
11	**9c** (5)	–	1	74	19	0
12	**9c** (2)	–	16	69	30	0
13	**9d** (5)	–	2	65	22	traces
14	**9e** (5)	–	16	75	19	0
15	**9f** (5)	–	16	46	0	44

[a] Yields are given for isolated material unless otherwise specified. [b] Yields determined by ^{1}H NMR analysis. [c] Mol % based on substrate; pyr = pyridine, DBZP = dibenzylpiperazine.

Table 2. Co-Catalyzed Oxidation of Lignin Models



entry	substrate	*t*(h)	**5** (%)[a]	**6** (%)	**12/13** (%)
1	 **14**	16	-	72	11
2	 **15**	16	83	-	-
3[b]	 **16**	24	51	-	22
4[c]	 **17**	16	-	81	traces
5	 **18**	16	17	86	traces
6[b]	 **19**	48	21	64	traces
7[b]	 **20**	48	0[d]	10	0[e]

[a] Yields are given for isolated material. [b] 10 mol % of catalyst used. [c] Yields relative to 2 equiv of product formed. [d] 14% 2,5-DMBQ isolated.[19] [e] 30% aldehydes.[20]

subunits and bearing a phenolic OH were treated under the optimized conditions (Table 2). Oxidation of substituted benzyl alcohol **14** proceeded smoothly, and DMBQ was obtained in high yields using 5 mol % catalyst, although increased substitution at the benzylic position slowed the reaction (entry 1). Importantly, the increased effectiveness of **9c** as a catalyst was demonstrated by the oxidation of vanillyl alcohol **15** to MBQ **5** in high yield and selectivity (entry 2) and the oxidation of the more substituted **16** to MBQ in moderate yield (entry 3).

G models have been subject to extensive investigation due to either their slow oxidation to **5** by Co-Schiff base catalysts[16b,21] or their dimerization *via* a radical shift to the *ortho*[22] or *para*[23] position of the intermediate phenoxy radical. The effect of the pendant base on the oxidation is under investigation, but we suspect that its proximity to the catalyst center may promote rapid oxidation of an intermediate phenolate anion to the corresponding phenoxy radical.

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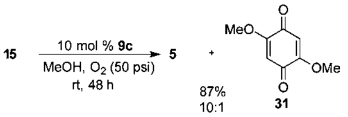
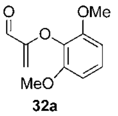
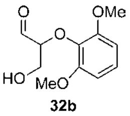
(19) Prolonged reaction in MeOH converts MBQ **5** to **31**:



(20) Inseparable mixture of aldehydes **32a** and **32b**:



32a



32b

(21) (a) Pratt, D. V.; Ruan, F. Q.; Hopkins, P. B. *J. Org. Chem.* **1987**, *52*, 5053–5055. (b) Saa, J. M.; Llobera, A.; Garciaraso, A.; Costa, A.; Deya, P. M. *J. Org. Chem.* **1988**, *53*, 4263–4273.

(22) Kadla, J. F.; Kubo, S. *Macromolecules* **2003**, *36*, 7803–7811.

(23) Singh, S. N.; Bhattacharjee, M.; Mahanti, M. K. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1855–1856.

Several phenolic lignin dimers modeling both S and G subunits linked through a β-aryl ether bond are also converted to the corresponding benzoquinones. Compound **17** was converted to 2 equiv of **6** in excellent yield (entry 4). Gratifyingly, compounds **18**, **19**, and **20** incorporating both S and G subunits and representing residual potential β-O-4 linkages remaining after lignin isolation were also oxidized to high yields of **6**. More moderate yields of **5** were observed for these dimers as a result of possible rapid dimerization of the intermediate phenoxy radical to biphenols or diphenoquinones.[20,21] Models **18** and **19** gave **5** and **6** in similar yields although longer reaction times and higher catalyst loadings were required to accommodate the increased level of benzylic substitution. Only traces of ketone **12** or **13** are detected in these reactions.

We suggest that the mechanism in Figure 3 may be operative. Based on mechanistic studies for simpler complexes, we propose that starting Co-Schiff base/ligand complex **21** is converted to superoxo complex **22** upon reaction with O_2.[24] Reaction of **22** with a lignin model (e.g., **19**) first generates phenoxy radical **23**,[25] which is transformed to intermediate **24** through addition of a second equivalent of **22**. Compound **24** undergoes cleavage of the α-aryl carbon to form **6** and concomitant formation of enol **25**, Co intermediate **27**, and phenoxy radical **28**[8b] which can dimerize to **29a**[20] or **29b**.[21] Intermediate **28** can also be trapped as **30**[26] through radical coupling with **22** in the *para* position of the phenoxy radical, followed by elimination of water and regeneration of the catalyst to give **5**.

Preliminary experiments examining the direct oxidative cleavage of lignin have been carried out. Lignin isolated by organosolv fractionation of tulip poplar under conditions[11a] that retain (by NMR) a significant amount of nonphenolic β-O-4 units, and thus a lower amount of free phenolic OH, was treated with catalyst **9c** and O_2 for 72 h at rt in a MeOH/DMSO mixture.

The product mixture revealed the presence of DMBQ **6** as well as benzaldehydes **12** and **13** (Scheme 1). The low absolute yields of monomeric aromatic compounds from this lignin sample likely result from the relatively low amount of free –OH groups. Given the strong impact of lignin isolation conditions on the concentration of phenolic OH groups,[13] we expect that lignins isolated under more severe conditions will lead to higher levels of aromatics.

In conclusion, we report the oxidative cleavage of monomeric and dimeric lignin models catalyzed by a new family of Co-Schiff base catalysts bearing bulky cyclic nitrogen bases as substituents. Catalyst **9c** efficiently converts S and G subunit models in good yield and also gives access to benzoquinones from lignin model dimers. The promising results from this work suggest that ongoing catalyst design will lead to selective oxidation systems able to navigate multiple substructural units present in lignin.

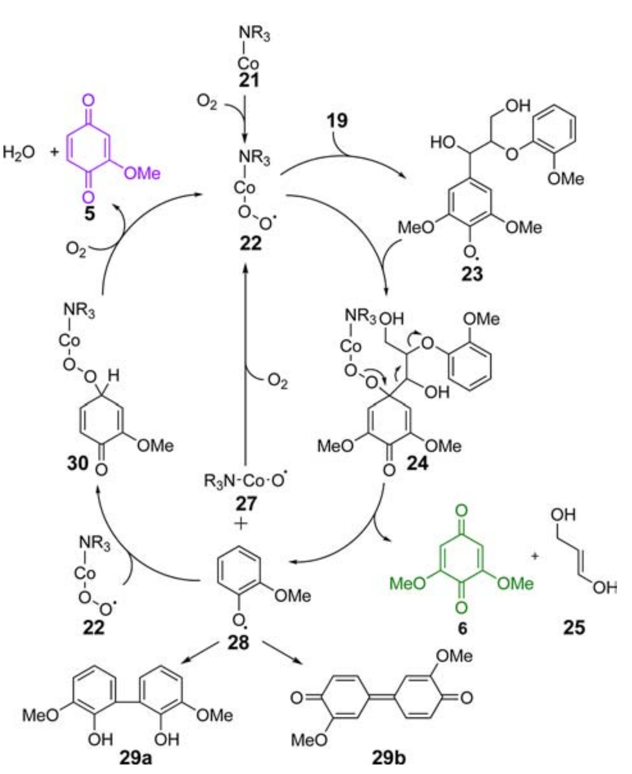
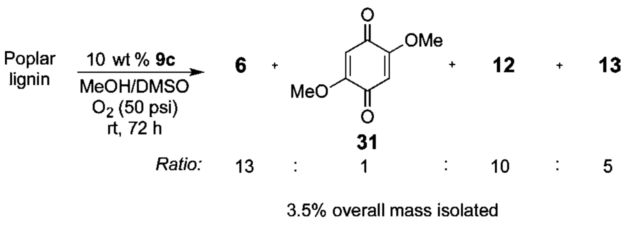


Figure 3. Proposed mechanism for the formation of **5** and **6** from **19**.

Scheme 1. Direct Oxidative Cleavage of Poplar Lignin



The impact of lignin structure and isolation methods on oxidation yields and the design of new catalysts are under active investigation.

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Supporting Information Available. Experimental procedures and spectroscopy analysis for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(24) Cozzi, P. G. *Chem. Soc. Rev.* **2004**, *33*, 410–421.

(25) Hwang, S.; Lee, C. H.; Ahn, I. S. *J. Ind. Eng. Chem.* **2008**, *14*, 487–492.

(26) Gaudemer, A.; Nguyenvanduong, K.; Shahkarami, N.; Achi, S. S.; Frostinrio, M.; Pujol, D. *Tetrahedron* **1985**, *41*, 4095–4106.
