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Oxidation of Lignin and Lignin β-O-4 Model Compounds *via* Activated Dimethyl Sulfoxide

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Abstract

Lignin oxidation reactions are increasingly being utilized in the field of lignin valorization. This is primarily due to the prospect of obtaining high-value aromatic products from cleavage of the C_α-C_β bond in lignin's β-O-4 linkages. In this work activated dimethyl sulfoxide reactions, namely Swern and Parikh-Doering oxidations, were performed both on lignin and on compounds modeling the β-O-4 linkage. When phenolic moieties were present in the model compounds, enol ethers were formed rather than the ketone expected from oxidation of the β-O-4 alcohol moiety. Conversely, in the absence of phenolic moieties, the β-O-4 alcohol was oxidized to a ketone. These results are interpreted in terms of enol ether formation from a quinone methide intermediate formed *via* deprotonation of the phenolic –OH in the initial sulfur ylide species. When applied to Kraft lignin, alcohol oxidation was observed at both the α and γ positions in lignin under both Swern and Parikh-Doering conditions, although analytical data were unable to shed light on the relative importance of enol ether versus 1,3-diketone formation (or its tautomer). These results emphasize the importance of working with realistic lignin model compounds in order to understand and develop lignin chemistry.

Keywords: lignin, Swern oxidation, Parikh-Doering oxidation, β-O-4 alcohol, enol ether, HSQC

1. Introduction

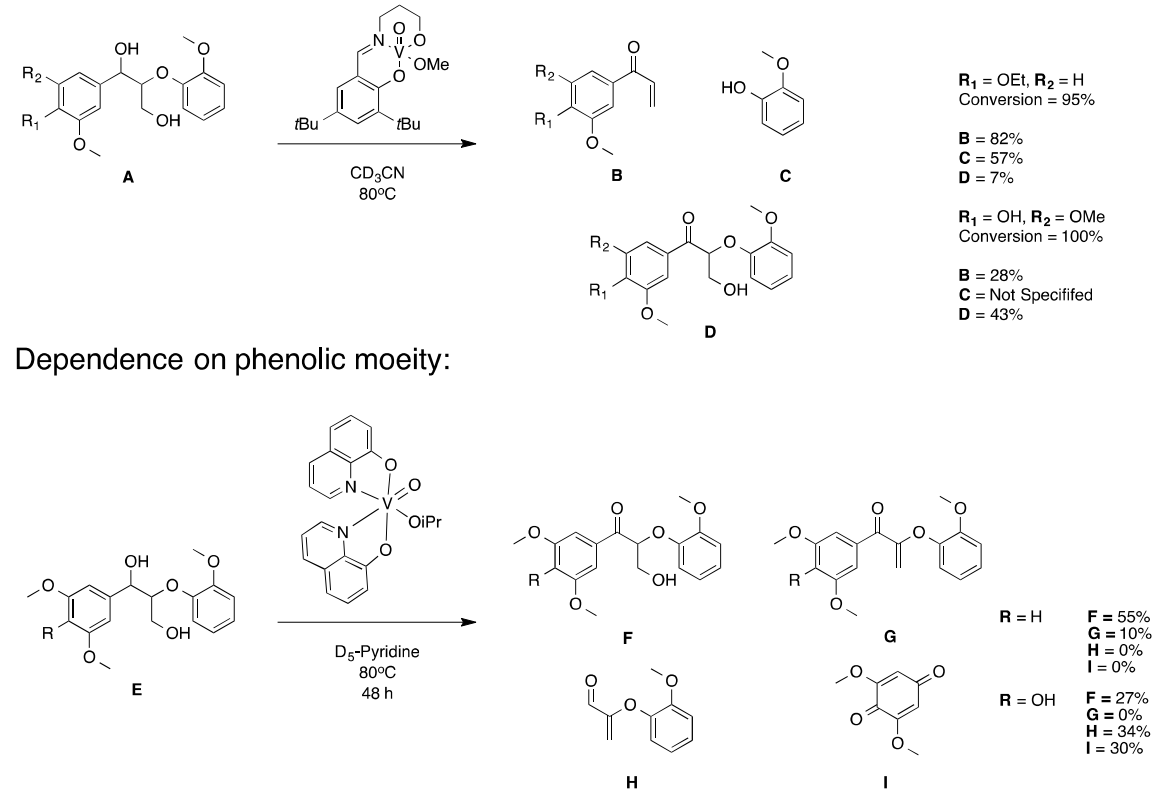
Given the finite nature of crude petroleum reserves, attention is shifting towards the utilization of renewable resources for the production of fuels and chemicals. One such resource is lignin, which could play a key role in supplying these commodities.[1-3] Lignin is the second most abundant biopolymer on earth[4] and currently has limited commercial use, serving mainly as a low-grade fuel[5, 6]. A significant amount of research has been directed at lignin conversion and valorization *via* pathways involving alkaline oxidation, hydrotreating, and pyrolysis.[7] While these processes convert lignin to value-added products, they are made impractical by the necessity of high temperatures and pressures, expensive and/or caustic reagents and catalysts, as well as low conversions. In this respect, new methods are needed which convert or modify lignin to valuable products.

Lignin contains an assortment of well-defined linkages, arranged randomly, of which certain linkages can be targeted for selective cleavage. Due to the abundance of the β-O-4 linkage (*ca.* 50 % of linkages in hardwood and softwood lignin[3]), and the potential reactivity of its characteristic benzylic alcohol moiety, it is commonly selected as the focal point for depolymerization. Indeed, many groups have recently enjoyed success in the application of selective oxidation protocols for the cleavage of lignin model compounds by specifically targeting this functionality. Rahimi and Stahl, who screened a series of traditional stoichiometric oxidants as well as organic catalysts for lignin oxidation, have pioneered much of this work. They found that acetamido-TEMPO and oxygen efficiently convert benzylic alcohol groups to ketones.[8] Likewise, Dawange and Samec have recently succeeded in the selective dehydrogenation of benzylic alcohols in lignin model dimers using Pd/C.[9] Using glucose as a metal stabilizer, they were able to obtain a 60-93% yield of the benzylic ketone in a lignin model dimer.[9]

Other groups have focused on the use of DDQ for the selective oxidation of benzylic alcohols in the β-O-4 linkage. Westwood and co-workers utilized a DDQ/*t*BuONO/O_2 system to oxidize benzylic alcohols followed by reductive cleavage of the newly generated acyloin moiety with zinc to cleave the β-O-4 linkage.[10] Recent work in our group has also focused on the use of homogeneous catalysts such as DDQ, TEMPO, and an iron-porphyrin complex for benzylic oxidation. This step was followed by Baeyer-Villiger oxidation of the benzylic ketone utilizing a formic acid/hydrogen peroxide system to achieve conversion to an ester.[11] In this manner, we were able to achieve complete cleavage of a substituted lignin model dimer.

Also noteworthy is the use of homogeneous organometallic and metal catalysts for lignin oxidations. Hanson and Baker achieved oxidation of lignin model compounds using (dipic)V^{V}(O)O^{i}Pr catalyst at 100^{o}C in air.[12] Likewise, Son and Toste were able to obtain monomeric ketones *via* a redox neutral C-O bond cleavage of β-O-4 models through a 1-electron reaction using an

organometallic vanadium catalyst. The reaction is initiated by hydrogen abstraction, followed by an elimination of the aryloxy radical and subsequent hydroxyl elimination to form an enone. Unique to this approach is the tunability of the catalyst selectivity *via* variation of the tridentate Schiff base ligand bite angle.[13] In a follow up to Toste's work[13], Hanson[14] utilized the same vanadium catalyst with an analogous phenolic model compound. When Toste's catalyst was used with the phenolic model, similar results were seen as with the non-phenolic analogue (Scheme 1, top). However, with Hanson's catalyst the non-phenolic model exhibited benzylic oxidation while the phenolic model underwent C(alkyl)-C(phenyl) bond cleavage (Scheme 1, bottom), which suggests that phenols may play a vital role in the understanding of lignin chemistry.[14] Similarly, Biannic and Bozell found that Co-Schiff base catalysts were able to cleave phenolic model dimers in good yields under oxidative conditions. When applied to lignin, small products were obtained although yields were low due to the low phenolic content of organosolv lignin.[15] Recently, Corma and co-workers reported the oxidative cleavage of lignin using copper and vanadium containing hydrotalcite catalysts with O_2 as the terminal oxidant.[16] Their catalyst was able to depolymerize lignin to small molecular weight oligomers (*ca.* 300 Da), however, the catalyst suffered from significant metal leaching. Ma *et al.* also reported that a vanadium catalyst coupled with acetic acid was able to cleave carbon-carbon bonds in lignin phenethyl ether linkages.[17]



Scheme 1: (Top) Oxidation of lignin model compound A according to Hanson and Toste. [13, 14] (Bottom) Oxidation of model compound E according to Hanson.[14]

The purpose of the current work is two-fold. First, we introduce an alternative pathway for the oxidation of lignin and lignin model compounds based on the use of activated DMSO. Second, we emphasize the limitations of certain compounds as models for the β-O-4 linkage in lignin, given differences in the reactivity of phenolic and non-phenolic models. With regard to the first point, it should be noted that the Swern reaction has been applied to lignin model compounds by Rahimi and Stahl,[8] although they saw only minor success in selective benzylic oxidation, obtaining *ca.* 20% conversion at the benzylic position and even less at the gamma alcohol. It is important to note that the model compounds used did not contain unprotected phenolic moieties, which we believe play a significant role in reactivity under oxidative conditions.

Addressing the second point, we would like to draw attention to the formation of enol ethers which is made possible through the phenolic groups that are highly prevalent in native[18] and industrial lignins[19]. We propose that quinone methide chemistry occurs as a result of unprotected phenolic groups, which has been well detailed for lignin isolation procedures such as alkaline

pulping.[19] Indeed, we have found that when phenolic models were subjected to Swern conditions, enol-ethers were formed rather than the expected aliphatic ketones. In theory these enol-ethers can be cleaved to produce small aromatic products from lignin *via* simple acid catalysed hydrolysis[20]; similar enol-ether hydrolysis of model compounds has recently been demonstrated by Stahl and Rahimi.[21]

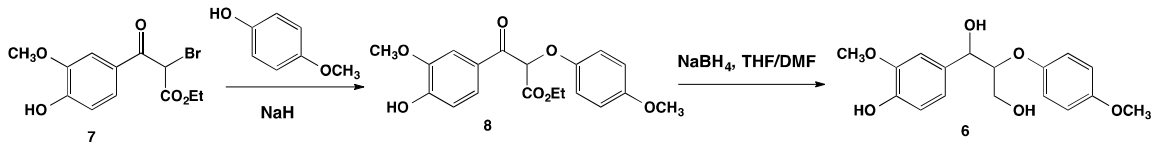
Experimental

2.1 General Considerations

Kraft (Indulin AT) lignin was obtained from MeadWestvaco. Solvents were dried over freshly activated 3 Å molecular sieves (20% mass/volume) for 48 h according to a procedure by Williams[22] or procured from Sigma Aldrich and used without further purification.

2.2 Preparation of the Lignin Model Dimers

Model dimers **1**-**5** (Figure 1) were prepared using the procedures recently reported by our group[11], while **6** was prepared according to Scheme 2. The procedure for the synthesis of **6** is the same as that for **5**, except that a different phenol was used, producing ketone **10**, which was then reduced to produce **6**.



Scheme 2: Preparation of 6.

2.2.1 Preparation of 8.

NaH (60% dispersion in mineral oil, 1.12 g, 28.12 mmol), **7** (4.95 g, 15.62 mmol)[11] and 4-methoxyphenol (3.96 g, 31.24 mmol) were placed in 3 individual one-neck round bottom flasks. The flasks were purged with N_2 for 15 min after which 9.8 mL THF and 3.5 mL DMF were added to each flask. The solution of NaH in THF/DMF was cooled to 0° C and the solution of 4-methoxyphenol was added. The mixture was stirred at room temperature for 1 h and then cooled to 0° C again. The solution of **7** was added, and the resulting mixture was stirred at room temperature for 8 h. The mixture was then poured onto ice-water (100 mL) and the resulting aqueous layer was extracted with EtOAc (3x50 mL). The EtOAc extract was washed with water (100 mL), dried with $MgSO_4$, and concentrated under vacuum. The residue was subjected to column chromatography on silica gel (EtOAc:hexane 3:7) to yield **8** (1.0 g, 2.8 mmol, 18%). ^{1}H NMR (400 MHz, CDCl3): δ 7.76 (dd, J=8.4,

2.27, 1H), δ 7.63 (d, J=1.9, 1H), δ 6.94 (d, J=8.5, 1H), δ 6.93 – 6.87 (m, 2H), δ 6.83 – 6.75 (m, 2H), δ 5.62 (s, 1H), δ 4.28 (q, J+7.3, 2H), δ 3.92 (s, 3H), δ 3.74 (s, 3H), δ 1.24 (t, J=7, 3H). ^{13}C NMR (100 MHz, CDCl3): δ 189.98, 167.1, 155.03, 151.43, 151.03, 146.64, 126.67, 125.43, 116.77, 114.76, 114.13, 111.21, 82.17, 62.27, 56.1, 55.6, 14.0. GC-MS m/z (relative intensity): 360 (M^+, 10), 288(1), 259 (1), 207 (1), 163(1), 151(100), 135(4), 123(10), 109(4), 92(3), 77(3), 65(2), 52(1).

2.2.2 Preparation of Lignin Model Dimer 6 (Scheme 2).[11]

A solution of **8** (1.0 g, 2.78 mmol) in THF (33 mL) and H_2O (3.3 mL) was stirred at room temperature. Sodium borohydride (1.06 g, 27.8 mmol) was added over 3 h and the solution was further stirred for 24 h at room temperature. The reaction mixture was treated with a saturated solution of ammonium chloride, after which the volatile materials were removed under vacuum. The residue was diluted with water (100 mL) and extracted with dichloromethane (3 × 50 mL). After evaporation of the solvent, the residue was subjected to column chromatography on silica gel (EtOAc:hexane 1:1) to produce **6** (0.683 g, 2.13 mmol, 77%). ^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereomers): δ 7.0 - 6.76 (m, 7H), δ 4.99 - 4.92 (m, 1H), δ 4.25 – 4.18 (m, 1H), δ 3.87, 3.86 (s, 3H), δ 3.77, 3.75 (s, 3H), δ 3.96 - 3.48 (m, 2H). ^{13}C NMR (400 MHz, $CDCl_3$, mixture of diastereomers): δ 154.7, 154.6, 152.1, 151.7, 146.7, 146.6, 145.5, 145.2, 132.5, 131.8, 119.9, 119.3, 118.3, 118.1, 114.8, 114.7, 114.4, 114.4, 109.5, 109.0, 84.4, 83.5, 73.8, 73.8, 61.4, 61.0, 55.9, 55.7. GC-MS m/z (relative intensity): 302 (M+ -18, 0.4), 272(100), 255 (0.8), 243(2.8), 211 (1.3), 183(1.7), 149(1.3), 133(1.5), 124(1.6), 109(1.5), 89(1.0), 77(1.4), 63(0.6), 51(0.6). HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{17}H_{20}O_6Na$ 343.1152, found 343.1152.

2.3 Swern Oxidation of Lignin Model Dimers

2.3.1 Oxidation of 1.

A solution of DMSO (717 μL, 10 mmol) in CH_2Cl_2 (0.25 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (438 μL, 5 mmol) in CH_2Cl_2 (0.25 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **1** (256 mg, 1 mmol) in CH_2Cl_2 (0.75 mL) was added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (2.09 mL, 15 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, and was then allowed to warm to room temperature. After adding CH_2Cl_2 (15 mL), the resulting organic phase was washed with HCl (1M, 5 mL), then with water (10 mL), and was then concentrated under vacuum. The product was isolated by silica gel column chromatography (23% EtOAc/hexanes) to produce **1'** (246 mg, 0.97 mmol, 97%), which gave ^{1}H and ^{13}C spectra that are consistent with those in the literature.[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.09 (m, 1H), δ 8.02-7.98 (m, 1H), δ 7.63-7.57 (m, 1H), δ

7.51-7.45 (m, 2H), δ 7.20-7.14 (m, 1H), δ 6.82-6.62 (m, 3H), δ 5.25 (s, 2H), δ 2.54 (t, J=7.53 Hz, 2H), δ 1.66-1.56 (m, 2H), δ 0.92 (t, J=7.3 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 194.94, 157.99, 144.59, 134.62, 133.89, 130.20, 129.26, 128.83, 128.19, 121.98, 115.29, 112.6, 111.68, 70.80, 38.02, 24.37, 13.82. GC-MS m/z (relative intensity): 254(M^+,40), 236(2.5), 207(7), 178(2), 165(1), 149(1), 119(3), 105(100), 91(14), 77(23), 65(4), 51(4).

2.3.2 Oxidation of 2.

A solution of DMSO (108 μL, 1.5 mmol) in CH_2Cl_2 (0.25 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (66 μL , 0.75 mmol) in CH_2Cl_2 (0.25 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **2** (54 mg, 0.15 mmol) in CH_2Cl_2 (0.75 mL) was added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (312 μL, 2.25 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, and was then allowed to warm to room temperature. After adding CH_2Cl_2 (15 mL), the resulting organic phase was washed with HCl (1M, 5 mL), then with water (10 mL), and was then concentrated under vacuum. The product was isolated by silica gel column chromatography (23% EtOAc/hexanes) to produce **2'** (46.72 mg, 0.13 mmol, 87%), which gave ^{1}H and ^{13}C spectra that are consistent with those in the literature.[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, J=8.56, 2.08 Hz, 1H), δ 7.61 (d, J=2.11 Hz, 1H), δ 6.88 (d, J=8.64 Hz, 1H), δ 6.33-6.25 Hz (m, 3H), δ 5.40 (q, J=6.67 Hz, 1H), δ 3.94 (s, 3H), δ 3.90 (s, 3H), δ 3.71 (s, 3H), δ 2.46 (t, J=7.67 Hz, 2H), δ 1.69 (d, J=7.07 Hz, 3H), δ 1.61-1.50 (m, 2H), δ 0.88 (t, J=7.39 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 197.62, 160.62, 158.48, 153.69, 149.08, 145.25, 127.18, 123.5, 111.09, 110.10, 107.52, 107.25, 98.73, 76.59, 56.05, 55.92, 55.17, 38.24, 24.16, 19.06, 13.76. GC-MS m/z (relative intensity): 358(M+, 17), 340(52), 325(3), 311(10), 295(1), 280(6), 265(4), 249(1.5), 237(1), 225(1), 207(1), 193(12), 178(1), 165(60), 151(5), 137(4), 121(4), 105(2), 91(5), 77(6), 65(1), 51(1).

2.3.3 Oxidation of 3.

A solution of DMSO (90 μL, 1.24 mmol) in CH_2Cl_2 (0.25 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (55 μL , 0.62 mmol) in CH_2Cl_2 (0.25 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **3** (43 mg, 0.124 mmol) in CH_2Cl_2 (0.75 mL) was then added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (262 μL, 1.87 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, then allowed to warm to room temperature. After adding CH_2Cl_2 (15 mL), the resulting organic phase was washed with HCl (1M, 5 mL), then with water (10 mL), and was then concentrated under vacuum. The product was isolated by silica gel column chromatography (33% EtOAc/hexanes) to produce **3'** (21.2 mg, 0.064 mmol, 52%), which gave ^{1}H and ^{13}C spectra that are consistent with those in the literature.[11] ^{1}H NMR (400

MHz, $CDCl_3$) δ 7.19 (d, J=1.94 Hz, 1H), δ 6.92 (dd, J=8.48, 2.05 Hz, 1H), δ 6.79 (d, J=8.24 Hz, 1H), δ 6.46-6.39 Hz (m, 3H), δ 5.55 (s, 1H), δ 3.76 (s, 3H), δ 3.72 (s, 3H), δ 2.51 (t, J=7.47 Hz, 2H), δ 1.65-1.55 (m, 2H), δ 0.92 (t, J=7.40 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 160.76, 156.4, 147.15, 145.41, 127.70, 125.99, 122.29, 121.72, 114.98, 114.02, 111.59, 110.43, 108.22, 98.67, 55.19, 50.69, 38.1, 24.31, 19.63, 13.76. GC-MS m/z (relative intensity): 328(M^+, 100), 313(2), 299(2), 285(26), 270(2), 253(5), 242(5), 225(4), 211(12), 193(1), 179(2), 162(59), 147(26), 131(9), 119(7), 103(17), 91(20), 77(10), 65(8), 51(3). HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{25}O_4$ 329.1747, found 329.1748.

2.3.4 Oxidation of 4.

A solution of DMSO (108 μL, 1.5 mmol) in CH_2Cl_2 (0.25 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (66 μL, 0.75 mmol) in CH_2Cl_2 (0.25 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **4** (56.4 mg, 0.15 mmol) in CH_2Cl_2 (0.75 mL) was then added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (312 μL, 2.25 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, then allowed to warm to room temperature. After adding CH_2Cl_2 (15 mL), the resulting organic phase was washed with HCl (1M, 5 mL), then with water (10 mL), and was then concentrated under vacuum. The product was isolated by silica gel column chromatography (23% EtOAc/hexanes) to produce **4'** (49.1 mg, 0.132 mmol, 88%), which gave ^1H and ^{13}C spectra that are consistent with those in the literature.[11] ^1H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.82 (dd, J=8.50, 2.1 Hz, 1H), δ 7.56 (d, J=2.3 Hz, 1H), δ 6.79 (d, J=8.7 Hz, 1H), δ 6.56-6.52 Hz (m, 2H), δ 6.32-6.30 Hz (m, 1H), δ 3.90 (s, 3H), δ 3.88 (s, 3H), δ 3.70 (s, 3H), δ 2.43 (t, J=7.6 Hz, 2H), δ 1.56-1.46 (m, 2H), δ 0.82 (t, J=7.4 Hz, 3H). ^{13}C NMR (400 MHz, CDCl3) δ 190.7, 180.7, 160.2, 154.7, 154.6, 148.97, 144.97, 127.15, 125.0, 111.2, 110.3, 109.5, 108.98, 100.6, 97.5, 56.1, 55.9, 55.2, 38.0, 24.0, 13.5. GC-MS m/z (relative intensity): 372(M^+, 100), 342(3), 329(42), 311(9), 297(9), 281(5), 269(10), 253(3), 240(2), 224(2), 207(14), 197(3), 186(5), 165(10), 148(3), 133(2), 121(4), 77(2).

2.3.5 Oxidation of 5.

A solution of DMSO (108 μL, 1.5 mmol) in CH_2Cl_2 (0.25 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (66 μL, 0.75 mmol) in CH_2Cl_2 (0.25 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **5** (54.3 mg, 0.15 mmol) in CH_2Cl_2 (0.75 mL) was then added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (312 μL, 2.25 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, then allowed to warm to room temperature. After adding CH_2Cl_2 (15 mL), the resulting organic phase was washed with HCl (1M, 5 mL), then with water (10 mL), and was then concentrated under vacuum. The

product was isolated by silica gel column chromatography (25% EtOAc/hexanes) to produce **5'** (41.6 mg, 0.12 mmol, 81%), which gave ^{1}H and ^{13}C spectra that are consistent with those in the literature.[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.37 (dd, J=6.1, 2.06 Hz, 1H), δ 7.22-7.19 Hz (m, 1H), δ 6.99 Hz (s, 1H), δ 6.42-6.35 Hz (m, 4H), δ 6.22 (s, 1H), δ 3.76 (s, 3H), δ 3.74 (s, 3H), δ 2.485 (t, J=7.69 Hz, 2H), δ 1.64-1.52 (m, 2H), δ 0.90 (t, J=7.36 Hz, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.59, 160.78, 156.74, 146.98, 146.39, 145.58, 127.01, 126.18, 124.33, 123.89, 114.69, 111.04, 108.41, 107.62, 98.84, 55.94, 55.27, 38.17, 24.22, 13.76. GC-MS m/z (relative intensity): 342(78), 314(6), 299(11), 281(10), 267(6), 253(7), 239(8), 207(44), 191(6), 177(46), 167(100), 148(12), 138(24), 125(13), 105(14), 91(18), 77(15), 65(8), 51(8). HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{20}H_{23}O_5$ 343.1540, found 343.1541.

2.3.6 Oxidation of 6.

A solution of DMSO (224 µL, 3.12 mmol) in CH_2Cl_2 (0.8 mL) was added dropwise, under N_2, to a cold (-78°C) solution of $(COCl)_2$ (135 µL, 1.56 mmol) in CH_2Cl_2 (0.8 mL) and the resulting solution was stirred at -78°C for 15 min. A solution of **6** (100 mg, 0.31 mmol) in CH_2Cl_2 (1 mL) was then added dropwise and the resulting mixture was stirred at -40°C for 30 min. Et_3N (649 µL, 4.69 mmol) was then added dropwise, the resulting mixture was stirred at -78°C for 30 min, then allowed to warm to room temperature. After adding CH_2Cl_2 (30 mL), the resulting organic phase was washed with HCl (1M, 10 mL), then with water (20 mL), and was then concentrated under vacuum. The product was isolated by silica gel column chromatography (25% EtOAc/hexanes) to produce **6'** (15.1 mg, 0.05 mmol, 16 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.42 (dd, J=3.2, 2.0 Hz, 1H), δ 7.22 Hz (d, J=2.2, 1H), δ 6.98-6.78 Hz (m, 5H), δ 3.77 (s, 3H), δ 3.75 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.7, 155.1, 149.7, 147.7, 146.6, 146.3, 126.9, 124, 116.24, 116.19, 114.8, 112.2, 110.9, 55.9, 55.6. GC-MS *m/z* (relative intensity): 300(95), 281(33), 243(39), 207(100), 191(18), 177(20), 149(13), 133(24), 124(28), 109(22), 92(11), 77(21), 65(15), 51(10).

2.4 Oxidation of 6 with SO_3-pyridine complex.

A solution of **6** (109 mg, 0.34 mmol) in DMSO (0.38 mL) and DCM (0.19 mL) was cooled in ice. N,N-Diisopropylethylamine (0.18 mL, 1 mmol) and a suspension of SO_3-pyridine complex (166 mg, 1 mmol) in DMSO (0.19mL) were added and the resulting mixture was stirred for 30 minutes at 0°C. The mixture was diluted with EtOAc (20 mL), was washed successively with 1M HCl (20 mL), saturated $NaHCO_3$ (20 mL), and saturated NaCl (20 mL), was dried over $MgSO_4$ and then concentrated in vacuum. The product was isolated by silica gel column chromatography (25% EtOAc/hexanes) to produce **6'** (11.6 mg, 0.04 mmol, 11 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H), 7.48 (d, J=1.94 Hz, 1H), δ 7.24 Hz (d, J=1.84 Hz, 1H), δ 6.98-

6.787 Hz (m, 6H), δ 3.78 (s, 3H), δ 3.75 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.8, 155.1, 149.7, 148.24, 147.5, 146.5, 126.1, 124.8, 116.2, 114.8, 114.6, 112.2, 55.8, 55.64. GC-MS *m/z* (relative intensity): 300(100), 281(5), 272(10), 255(7), 243(72), 211(18), 197(4), 185(6), 177(24), 164(14), 149(9), 133(20), 124(18), 109(18), 89(14), 77(18), 65(10), 51(9). HRMS (ESI) *m/z* $[M+H]^+$ calcd for $C_{17}H_{17}O_5$ 301.1071, found 301.1070.

2.5 Swern Oxidation of Kraft Lignin

Kraft lignin was dried in a vacuum oven at 50°C over for 72 h before use. All glassware was purged with nitrogen for 15 minutes before use. Flask 1 was charged with lignin (2.005 g, 5.557 mmol with an assumed dimer molecular weight of 360 g/mol) and dry DMSO (20 mL). Flask 2 was charged with oxalyl chloride (2.4 mL, 10 eq.) and dry DCM (88 mL). Flask 3 was charged with DMSO (4 mL, 10 eq.) and dry (DCM 88 mL). The contents of flask 2 were then cooled to -72°C. The contents of flask 3 were then added to flask 2 slowly and the contents of flask 2 were maintained at -72°C for 15 minutes. The contents of flask 1 (containing lignin) were then slowly added to flask 2. The solution was then allowed to slowly warm to -40°C and stirred for 30 minutes. The reaction mixture was then cooled to -72°C and 12 mL (15 eq) of Et_3N was added. The mixture was then allowed to warm to room temperature and hexanes were added to bring the solvent level up to 1 L, resulting in precipitation of the lignin. The solution was then filtered with a Whatman Sharkskin filter and transferred to a Buchner funnel equipped with a PTFE membrane (Gelman Scientific, 0.2 μm 47 mm). The filter cake was washed with water (500 mL) and diethyl ether (100 mL) and was then dried in a vacuum oven overnight at 50°C. 1.788 g of lignin was collected.

2.6 Parikh Doering Oxidation of Kraft Lignin

Kraft lignin was dried in a vacuum oven at 39°C overnight before use. All glassware was flushed with N_2 for 15 minutes before use. To a round bottom flask was added 1.002 g (2.783 mmol) of lignin and 15 mL of a 2:1 mixture of dry DMSO:DCM. The resulting solution was chilled in an ice bath. Separately, SO_3-pyridine complex (1.327 g, 3 eq.) was dissolved in dry DMSO (1.6 mL) for 15 minutes in order to form the active intermediate. The SO_3-pyridine complex solution and DIPEA (Hunig's base, 1.45 mL, 3 eq.) was added to the Kraft lignin solution and the mixture was allowed to stir for 30 minutes at 0°C. HCl (100 mL, 1 M) was then added to the reaction mixture, precipitating the lignin. The round bottom flask was decanted into a Nalgene™ centrifuge bottle and the rinsed with DI water to remove residual lignin. The bottle was centrifuged and the supernatant was vacuum filtered with Whatman Sharkskin filter paper. Solids were washed with DCM and hexanes and dried in a vacuum oven overnight at 50°C. 0.658 g of lignin was collected.

2.7 HSQC NMR measurements

All samples contained 100 mg of lignin and 1 mg chromium (III) acetylacetonate (relaxation agent) in 1 mL of d_6-DMSO. In some cases the sample required sonication or mild heat (*ca.* 50°C) to improve dissolution.

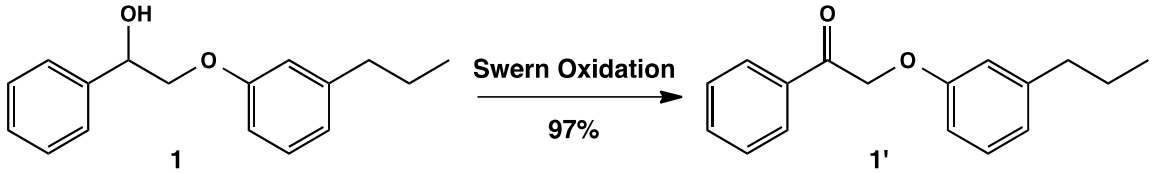
$^{1}H^{13}C$-gradient heteronuclear single quantum coherence spectra (gHSQC) were collected at 600 MHz (and 150 MHz ^{13}C) on a Unity-Inova NMR spectrometer (Varian-Agilent, Palo Alto CA) equipped with a triple-resonance H(CN) 5 mm probe, at 59 °C. The ^{13}C-^{1}H correlation experiment was collected using an Agilent pulse program 'gHSQC' which implements a gradient-selected phase-sensitive heteronuclear single quantum coherence spectrum. Proton and carbon pulses were delivered with B_1 field strengths of 39 KHz and 20 KHz, respectively. Spectra were collected with spectral widths of 8400 Hz (^{1}H) and 32 kHz (^{13}C) using an acquisition time of 80 ms (F2, 672 complex points for ^{1}H) and 12.4 ms (F1, 400 increments for the ^{13}C dimension). 160 scans were taken per increment using a delay of 1.3 times the longest measured proton T_1. Data were weighted with a 90°-shifted sine bell (^{1}H), or a matched Gaussian function (^{13}C) prior to Fourier transformation to generate a 4k x 1k spectrum. In all cases, the DMSO solvent peak was used an internal reference (δ_c 39.5 ppm , δ_H 2.5 ppm) and spectra are displayed in absolute value mode. HSQC assignments were determined using the Biological Magnetic Resonance Data Bank.[23]

2.8 ATR-FTIR Measurements

ATR-FTIR spectra were obtained using a Nicolet 6700 FT-IR instrument using a scan range of 4000-600 cm^{-1} and a resolution of 4 cm^{-1}. In all cases 16 scans were taken.

Results and Discussion

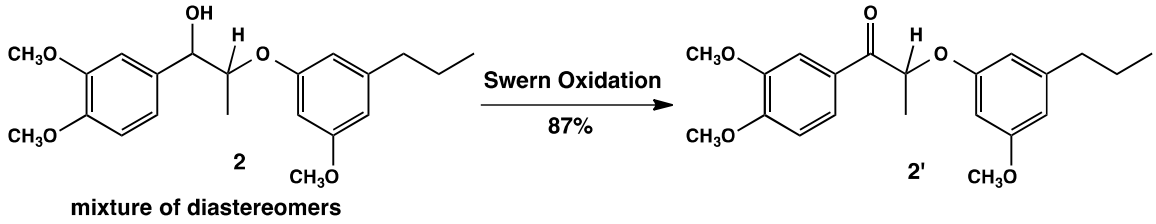
3.1 Swern Oxidation of Lignin Model Dimers



Scheme 3: Swern oxidation of model compound 1.

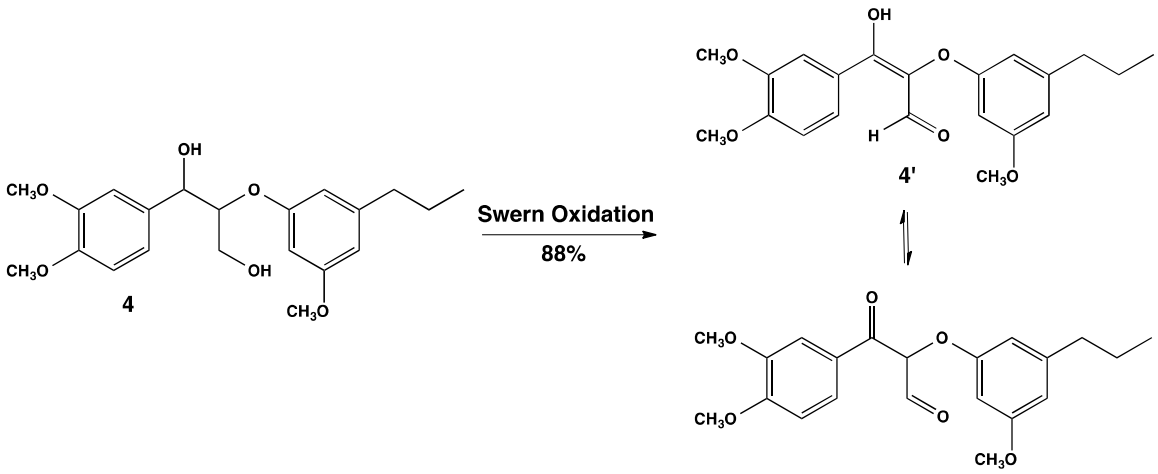
Given recent successes in the selective oxidation of lignin model compounds, in this work we employed lignin model dimers of increasing

complexity. Among the common laboratory techniques for alcohol oxidations, Swern oxidation is an obvious choice due to the mild conditions employed and high selectivity towards the carbonyl product, without over oxidation to the corresponding carboxylic acid. Oxidations utilizing activated DMSO come in many varieties, however; perhaps the most common is that which employs oxalyl chloride at -78°C to activate DMSO, producing dimethyl(chloro)sulfonium chloride.[24] The simplest lignin model compound, model **1,** was chosen as a starting point due its lack of aromatic ring functionality other than a propyl chain, the latter being used to test the selectivity of benzylic oxidation (i.e., benzylic alcohol versus benzylic methylene group). Swern oxidation of model **1** proceeded smoothly, affording a 97% isolated yield of the product **1'** (Scheme 3), evidenced by a ^{13}C NMR chemical shift for the carbonyl group at 195 ppm (see Supplementary Information Figure S5), as well as a characteristic ^{1}H NMR singlet at 5.25 ppm deriving from the two hydrogens located on the β carbon adjacent to the newly formed ketone (see Supplementary Information Figure S6). This was further confirmed by means of GC-MS (parent ion of 254 *m/z*).



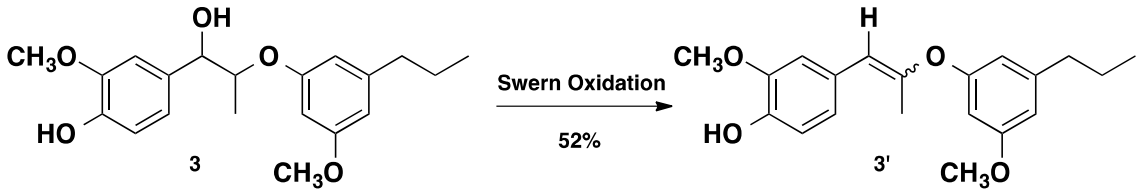
Scheme 4: Swern oxidation of model compound 2.

Compared to **1**, compound **2** contains methoxy groups in the 3- and 4-positions of the aromatic ring adjacent to the benzylic alcohol moiety as well as in the 3-position of the phenoxyl ring. Also significant is the addition of a gamma carbon, which is characteristic of phenyl propane monolignols. With this compound, Swern oxidation afforded an 87% isolated yield of the product **2'** (Scheme 4). This was confirmed *via* observation of the disappearance of signals at 4.61 and 4.96 ppm (two diastereomers) for the $\beta_{C\text{-}H}$ proton in the starting material and the appearance of a quartet at 5.4 ppm (see Supplementary Information Figure S8). The identity of the product was also confirmed by its ^{13}C NMR spectrum, which displayed a ketone peak at *ca.* 198 ppm (see Supplementary Information Figure S7).



Scheme 5: Swern oxidation of model compound 4.

In the case of compound **4,** a similar result to compounds **1** and **2** was obtained. There are two alcohol groups present in **4**, which provide multiple sites for Swern oxidation. The doubly oxidized product (**4',** Scheme 5), obtained in 88% isolated yield, was the predominant compound formed, as shown by the disappearance of the multiplet peaks at 4.97 ppm, 4.37-4.15 ppm, and 3.94-3.92 ppm corresponding to the α, β, and γ protons, respectively, in the starting material (see Supplementary Information Figure S12). Moreover, there was clear evidence of a mixture of tautomers of the α-ketone group as shown by the ^{13}C NMR shifts at 180.7 ppm, 97.5 ppm, and 190.7 ppm representing the α, β, and γ carbons (see Supplementary Information Figure S11), and by the aldehyde H peak at 9.12 ppm in the product (see Supplementary Information Figure S12).

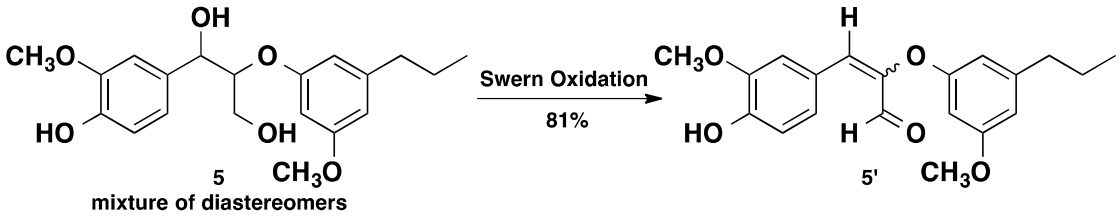


Scheme 6: Swern oxidation of compound 3.

Lignin is known to contain phenolic functionalities[25]; thus, in order to better describe lignin reactivity under Swern conditions, phenolic dimer models **3** and **5** were synthesized. Compound **3** differs from compound **2** only by replacement of compound **2**'s methoxy group in the 4-position of the alcohol adjacent ring with an alcohol moiety. This compound is of particular interest as a lignin model due to the propensity of phenolic compounds to undergo radical coupling during 1-electron processes.[26] Notably, compound **3** did not yield the expected ketone product; rather, compound **3** underwent elimination forming the enol ether product (**3'**) in 52% yield (Scheme 6). This

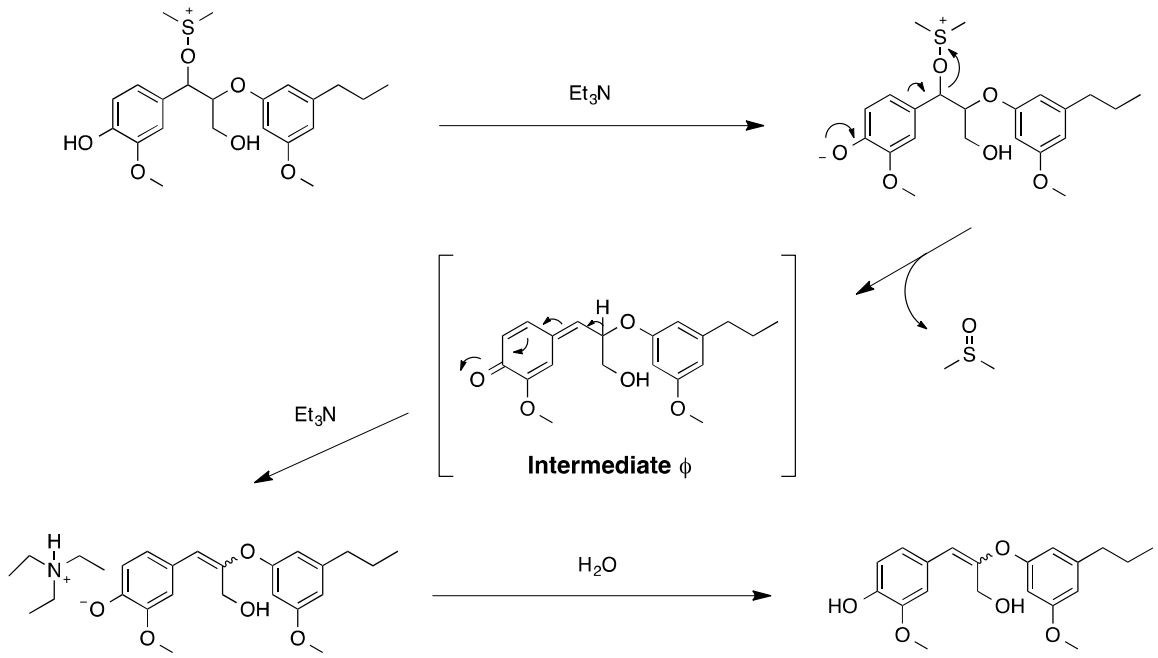
was evidenced by the absence of a $\beta_{C\text{-}H}$ in the ^1H NMR spectrum (see Supplementary Information Figure S10). Also of note is the absence of a ketone resonance in the carbon spectrum of **3'** (see Supplementary Information Figure S9). High-resolution mass spectrometry (ESI) confirmed a molecular formula ($C_{20}H_{25}O_4$) that is consistent with the $(M+H)^+$ ion of **3'**.

While the conversion of **3** to **3'** was not the expected result of Swern oxidation, it is not an undesirable one. Enol ethers are notorious for acid catalysed hydrolysis[20], thereby providing a means of cleaving appropriately functionalized β-O-4 linkages in lignin. In fact, Beckham *et al*. have reported the formation and cleavage of enol ether intermediates from lignin model compounds under acidic conditions.[27]



Scheme 7: Swern oxidation of compound 5.

In order to determine whether the formation of the elimination product was a consequence of the phenolic alcohol moiety or some other factor, Swern oxidation was carried out on compound **5**. Compound **5** is identical to compound **3** with the exception of the alcohol functionality on the γ carbon. Hence, like compound **4** there are two sites at which oxidation can occur. Interestingly, the product of the reaction (**5'**), obtained in 81% isolated yield, derives from both elimination of the benzylic alcohol group and oxidation of the primary alcohol (Scheme 7). Again, signals corresponding to $\beta_{C\text{-}H}$ protons are not present in the ^1H NMR spectrum of the Swern product, while an aldehyde proton is prominent at 9.5 ppm (see Supplementary Information Figure S14).



Scheme 8: Plausible mechanism for enol ether formation.

Given the results from Swern oxidation of models **3** and **5**, we propose that enol ethers are formed from a quinone methide intermediate (φ, Scheme 8). Evidently, deprotonation of the phenolic –OH in the initially formed sulfur ylide species is faster than deprotonation of the sulfur ylide group itself, making the quinone methide intermediate kinetically preferred. Elimination of DMSO, followed by proton abstraction at the $\beta_{C\text{-}H}$ position by additional base, restores aromaticity and produces the phenoxide, which is then re-protonated. This pathway is consistent with the one suggested by Dimmel and Gellerstedt[19] in which a quinone methide intermediate, produced by base addition in alkaline pulping, undergoes a proton abstraction from the $\beta_{C\text{-}H}$, resulting in formation of a vinyl ether. The involvement of a quinone methide intermediate φ is further supported by the formation of the elimination product between the α and β carbons in model **5,** which could easily eliminate between the β and γ position otherwise.

3.2 Swern Oxidation of Kraft Lignin

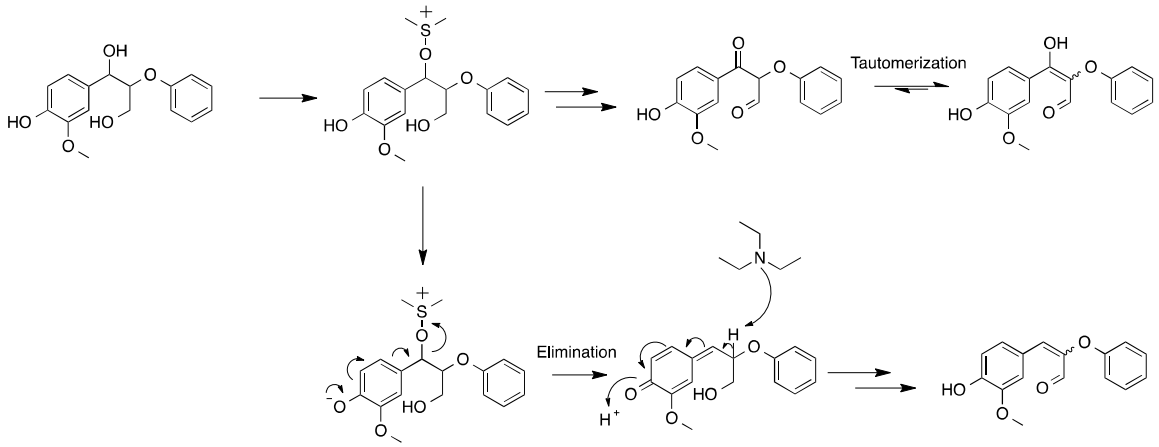
Given the encouraging results obtained with the model compounds, Swern oxidation was next applied to an industrial lignin. Indulin AT lignin is a type of softwood Kraft lignin that is produced on an industrial scale and should be representative of technical lignins produced from a biorefinery. Using Heteronuclear Single Quantum Coherence NMR (HSQC) spectroscopy, the β-O-4 linkage in Indulin AT lignin was monitored for changes arising from the application of Swern oxidation conditions, in addition to the β-5 and β-β linkages. As shown in Figure 2, $\alpha_{C\text{-}H}$ groups corresponding to benzylic alcohols

present on the β-O-4 linkage are absent after Swern oxidation. Likewise, signals for the γ_{C-H} group associated with alcohol groups in the β-O-4 and β-5 linkages were also absent in the product's HSQC spectrum. Moreover, phosphitylation followed by ^{31}P NMR analysis of the Swern oxidized lignin revealed a near absence of aliphatic hydroxyl groups (see Supporting Information), consistent with oxidation at the α and γ positions. As expected, α, β, and γ C-H groups corresponding to β-β linkages were still present in the Kraft lignin after Swern oxidation (Figure 2). Interestingly, the solubility of the lignin in DMSO decreased post-Swern oxidation (i.e., while Kraft lignin was highly soluble in DMSO, Swern oxidized lignin demonstrated decreased solubility). This is presumably due to the loss of alcohol groups upon oxidation, thereby decreasing the hydrogen bond donor ability of the lignin macromolecule. Upon further investigation of the HSQC spectrum, the cross-peak corresponding to the β_{C-H} bond (δ_C/δ_H = 84.2/5.55) in the oxidized β-O-4 linkage was not located, which may indicate enol ether formation (*vide infra*). Similarly, γ_{C-H} bonds corresponding to aldehydes were also absent. Also of note were new peaks that appeared post-Swern oxidation in the upfield region of the spectrum. Most notable were those at δ_C/δ_H 38/3.6 ppm and 13/1.8 which are assigned to methyl and methylene groups in methylthiomethyl moeities (*vide infra*).

In order to probe the chemical shifts of the β_{C-H} bonds in the β-O-4 linkage in Swern oxidized lignin, Swern oxidation was performed on phenolic β-O-4 model compound **6**. Model **6** was chosen due to the phenolic alcohol moiety and the single methoxy group on the A ring, as well as its γ alcohol substitution; all of these features are found in softwood G lignins. Additionally, unlike our other models, which contain an aliphatic propyl chain, **6** does not, which allows determination of the source of the new upfield HSQC signals. Significantly, we found that this model also failed to exhibit a β_{C-H} cross-peak (δ_C/δ_H = 84.2/5.55, as identified by model 1028 in ref. 23) corresponding to the Swern oxidized product (Figure 3). However, we were able to find faint peaks corresponding to an aldehyde γ_{C-H} group (Figure 3 inset). The faint nature of this signal is not unexpected given that aldehydes are located near the edge of the spectral window where intensity is diminished due to off-resonance effects[28]. Given that aldehyde groups are very faint in the pure sample, we propose that in the authentic lignin sample they may be equally difficult to resolve and thus not observable in the HSQC spectra.

Since the β_{C-H} group is absent in the oxidized products of model compounds **3**, **4**, **5**, and **6** we decided to look elsewhere for evidence of oxidation or elimination. Two reaction pathways exist (Scheme 9): either the alcohol in the α position of the β-O-4 linkage eliminates, forming an enol ether, or a 1,3-diketone is formed which exists in equilibrium with its enol ether tautomer. In either case, monitoring the α_{C-H} signal should allow us to determine whether the enol ether of the tautomeric 1,3-diketone or the enol ether of the elimination product is produced. In the case of the elimination

product an $\alpha_{C\text{-}H}$ cross-peak should be observed at δ_C/δ_H 137/7.26 ppm (as for related compound 3034 in ref. 23) while the 1,3-diketone tautomer will be absent of an $\alpha_{C\text{-}H}$ cross-peak. Indeed, analysis of the aromatic region of Swern oxidized model compound **6** showed a cross peak at δ_C/δ_H 137/7.26 ppm corresponding to the $\alpha_{C\text{-}H}$ of the elimination product (Figure 4).



Scheme 9: Possible reaction pathways leading to C-H bond cleavage on the β carbon.

.Notably, HSQC analysis of the Swern oxidized product of model **6** revealed similar upfield cross-peaks to those seen in Kraft lignin (Figures 3 and 2, respectively). These cross-peaks are consistent with the presence of methylthiomethyl groups resulting from [2,3]-sigmatropic rearrangements of the sulfur ylide attached to a phenol.[29] Indeed, there are numerous reports in the literature in which phenols form methylthiomethyl groups under Swern-like conditions.[30-32] This highlights the importance of choosing models which are appropriate with respect to the chemistry of lignin, given that models that are free of phenolic moieties are unable to form methylthiomethyl groups and thus would yield a different product distribution to phenolic models. Indeed, other common byproducts of Swern-like conditions involving oxalyl chloride and phenols include oxalates[33, 34], mixed O-S thioacetals[35], and α-chlorination[24], although we were unable to identify these products in the above reactions.

Given the appearance of methylthiomethyl groups, together with the presence of other unidentified cross peaks in the HSQC spectrum of Swern oxidized lignin, the use of activated DMSO under milder conditions was next examined. Parikh-Doering (PD) oxidations are a natural choice to probe the issues associated with the use of oxalyl chloride in Swern oxidations since they form the same sulfur ylide intermediate generated during Swern oxidation; however, PD oxidations are performed at room temperature, the sulfur ylide being formed *via* the less labile pyridine-SO_3 complex (zwitterionic dimethylsulfonium sulfate intermediate). NMR spectroscopic

analysis (Figure 3) of PD oxidized model **6** revealed the absence of methylthiomethyl groups in the upfield cross peak region of the HSQC spectrum, as well as the absence of the unidentified peaks resulting from Swern oxidation. Similar to the Swern oxidation of model **6**, PD oxidation led to the loss of all signals corresponding to α, β and γ C-H bonds. Moreover, the enol ether α_{CH} cross peak resulting from the elimination product was observed at δ_C/δ_H 137/7.25 ppm. In view of this encouraging result, PD oxidation was also performed on lignin. The resulting PD oxidized lignin displayed increased solubility in DMSO relative to Swern oxidized lignin and, as for model **6**, was absent of additional signals of uncertain origin in the upfield region of the HSQC spectrum (Figure 2). Indeed, the only additional peaks found in the upfield region corresponded to residual Hünig's base (ammonium salt). However, in both the Swern and PD oxidized lignin, enol ether α_{CH} peaks were not observed (Figure 5). We believe that this may be due to the relatively low abundance of β-O-4 linkages in Kraft lignin. However, it is possible that the 1,3-diketone tautomeric product is the predominant product under these conditions, resulting in loss of both the α and β C-H cross-peaks.

Finally, it should be noted that efforts to confirm the formation of carbonyl species proved inconclusive. ^{13}C NMR spectra of Swern and Parikh-Doering oxidized lignin displayed a complete lack of carbonyl signals at 185-210 ppm. Given the low sensitivity of the ^{13}C nucleus and the low relative abundance of singular carbonyl functionalities in oxidized lignin, it is unlikely that C=O chemical shifts would be easily observed. FT-IR spectra of Swern oxidized lignin displayed a small decrease in signal intensity around 3330 cm^{-1}, consistent with the loss of OH groups (Figure 6). Changes were also observed in the carbonyl stretching region, the appearance of signals at *ca.* 1690 cm^{-1} for both oxidized lignin samples being suggestive of carbonyl formation. However, conjugated enol ethers also give rise to a band in this region, as evidenced by the observation of a band at 1685 cm^{-1} in the FT-IR spectrum of the Swern oxidation product obtained from lignin model compound **5** (see Fig. S23 in Supplementary Data) which was confirmed to be an enol ether *via* multiple analytical techniques. Other enol ethers also share a C-H alkene stretch in this region.[36-38] Consequently, while it is clear that alcohol oxidation occurs at the α and γ positions in lignin under Swern and Parikh-Doering conditions, the relative importance of enol ether formation versus 1,3-diketone formation (or its tautomer) cannot be readily established. However, results obtained for model compounds **4** and **5** suggest that both products are accessible, the reaction pathway depending on whether a phenolic group is present at the 4-position of the A ring or not. This further demonstrates that lignin is more complex than our current models and that proper demonstration of lignin reactivity will rely on more complex and heterogeneously linked model polymers.

Conclusions

The stoichiometric Swern oxidation reaction was applied to a series of compounds modelling the β-O-4 linkage in lignin. Phenolic β-O-4 lignin models produced enol ethers rather than ketone products, as evidenced by multiple analytical techniques. We propose that enol ethers are formed from a quinone methide intermediate formed *via* deprotonation of the phenolic –OH in the initially formed sulfur ylide species. When applied to Kraft lignin, alcohol oxidation was observed at both the α and γ positions in lignin under both Swern and Parikh-Doering conditions, although analytical data were unable to shed light on the relative importance of enol ether versus 1,3-diketone formation (or its tautomer). Given the abundance of phenolic moieties in technical lignins and the susceptibility of enol ethers to cleavage *via* acid-catalyzed hydrolysis, enol ether formation in lignin may provide a means of cleaving at least a portion of the β-O-4 linkages present. These results also emphasize the importance of working with realistic lignin model compounds in order to understand and develop lignin chemistry.

Acknowledgments

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References

1. P. D. Sainsbury, E. M. Hardiman, M. Ahmad, H. Otani, N. Seghezzi, L. D. Eltis and T. D. H. Bugg, *ACS Chemical Biology*, 2013, **8**, 2151-2156.
2. R. Busch, T. Hirth, A. Liese, S. Nordhoff, J. Puls, O. Pulz, D. Sell, C. Syldatk and R. Ulber, *Biotechnology Journal*, 2006, **1**, 770-776.
3. J. Zakzeski, P. C. A. Bruijnincx, A. L. Jongerius and B. M. Weckhuysen, *Chemical Reviews*, 2010, **110**, 3552-3599.
4. W. Boerjan, J. Ralph, M. Baucher, A. JC, B. A, P. G, L. M and L. C, *Annual Review of Plant Biology*, 2003, **54**, 519-546.
5. R. J. A. Gosselink, E. de Jong, B. Guran and A. Abächerli, *Industrial Crops and Products*, 2004, **20**, 121-129.
6. G. Henriksson, J. Li, L. Zhang and M. E. Lindstrom, in *Thermochemical Conversion of Biomass to Liquid Fuels and Chemicals*, The Royal Society of Chemistry, Editon edn., 2010, pp. 222-262.
7. M. P. Pandey and C. S. Kim, *Chemical Engineering & Technology*, 2011, **34**, 29-41.
8. A. Rahimi, A. Azarpira, H. Kim, J. Ralph and S. S. Stahl, *Journal of the American Chemical Society*, 2013, **135**, 6415-6418.
9. M. Dawange, M. V. Galkin and J. S. M. Samec, *ChemCatChem*, 2014, n/a-n/a.
10. C. S. Lancefield, O. S. Ojo, F. Tran and N. J. Westwood, *Angewandte Chemie*, 2014, n/a-n/a.
11. N. D. Patil, S. G. Yao, M. S. Meier, J. K. Mobley and M. Crocker, *Organic & Biomolecular Chemistry*, 2015.

12. S. K. Hanson, R. T. Baker, J. C. Gordon, B. L. Scott and D. L. Thorn, *Inorganic Chemistry*, 2010, **49**, 5611-5618.
13. S. Son and D. Toste, *Angew. Chem., Int. Ed.*, 2010, **49**, 3791.
14. S. K. Hanson, R. Wu and L. A. P. Silks, *Angew. Chem., Int. Ed.*, 2012, **51**, 3410.
15. B. Biannic and J. J. Bozell, *Organic Letters*, 2013, **15**, 2730-2733.
16. J. Mottweiler, M. Puche, C. Räuber, T. Schmidt, P. Concepción, A. Corma and C. Bolm, *ChemSusChem*, 2015, **8**, 2106-2113.
17. Y. Ma, Z. Du, J. Liu, F. Xia and J. Xu, *Green Chemistry*, 2015.
18. Y. Z. Lai and X. P. Guo, *Wood Science and Technology*, 1991, **25**, 467-472.
19. D. Dimmel and G. Gellerstedt, in *Lignin and Lignans*, CRC Press, Editon edn., 2010, pp. 349-391.
20. M. B. Smith and J. March, in *March's Advanced Organic Chemistry*, John Wiley & Sons, Inc., Editon edn., 2006, pp. 425-656.
21. A. Rahimi, A. Ulbrich, J. J. Coon and S. S. Stahl, *Nature*, 2014, **515**, 249-252.
22. D. B. G. Williams and M. Lawton, *The Journal of Organic Chemistry*, 2010, **75**, 8351-8354.
23. S. A. Ralph, L. L. Landucci and J. Ralph, *NMR Database of Lignin and Cell Wall Model Compounds*, http://www.bmrb.wisc.edu/metabolomics/metabolomics_standards_jr.shtml - jr_cat_3, Accessed 9/14/15.
24. T. T. Tidwell, *Synthesis*, 1990, 857-870.
25. H. Sadeghifar, C. Cui and D. S. Argyropoulos, *Industrial & Engineering Chemistry Research*, 2012, **51**, 16713-16720.
26. A. I. Scott, *Quarterly Reviews, Chemical Society*, 1965, **19**, 1-35.
27. M. R. Sturgeon, S. Kim, K. Lawrence, R. S. Paton, S. C. Chmely, M. Nimlos, T. D. Foust and G. T. Beckham, *ACS Sustainable Chemistry & Engineering*, 2013, **2**, 472-485.
28. J. Cavanagh, W. J. Fairbrother, A. G. Palmer Iii, M. Rance and N. J. Skelton, in *Protein NMR Spectroscopy (Second Edition)*, eds. J. Cavanagh, W. J. Fairbrother, A. G. Palmer, M. Rance and N. J. Skelton, Academic Press, Burlington, Editon edn., 2007, pp. 114-270.
29. P. G. Gassman and D. R. Amick, *Journal of the American Chemical Society*, 1978, **100**, 7611-7619.
30. Y. Hiraki, M. Kamiya, R. Tanikaga, N. Ono and A. Kaji, *Bulletin of the Chemical Society of Japan*, 1977, **50**, 447-452.
31. K. Sato, S. Inoue, K. Ozawa and M. Tazaki, *Journal of the Chemical Society, Perkin Transactions 1*, 1984, 2715-2719.
32. P. Claus, *Monatshefte für Chemie*, 1968, **99**, 1034-1044.
33. R. Koike, Y. Kato, J. Motoyoshiya, Y. Nishii and H. Aoyama, *Luminescence*, 2006, **21**, 164-173.
34. Z. S. Şahin, G. K. Kantar, S. Şaşmaz and O. Büyükgüngör, *Journal of Molecular Structure*, 2015, **1087**, 104-112.
35. K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651-1660.
36. T. Baumann, H. Vogt and S. Bräse, *European Journal of Organic Chemistry*, 2007, **2007**, 266-282.
37. E. Pretsch, P. Bühlmann and M. Badertscher, *Structure Determination of Organic Compounds*, 4 edn., Springer-Verlag Berlin Heidelberg, 2009.
38. J. Dabrowski and M. Tencer, *Bulletin of the Chemical Society of Japan*, 1976, **49**, 981-986.

39. Cross-peaks assigned to methylthiomethyl groups may also represent dithioacetals which are known bi-products of activated DMSO oxidations as noted by Gassman ref. 29.

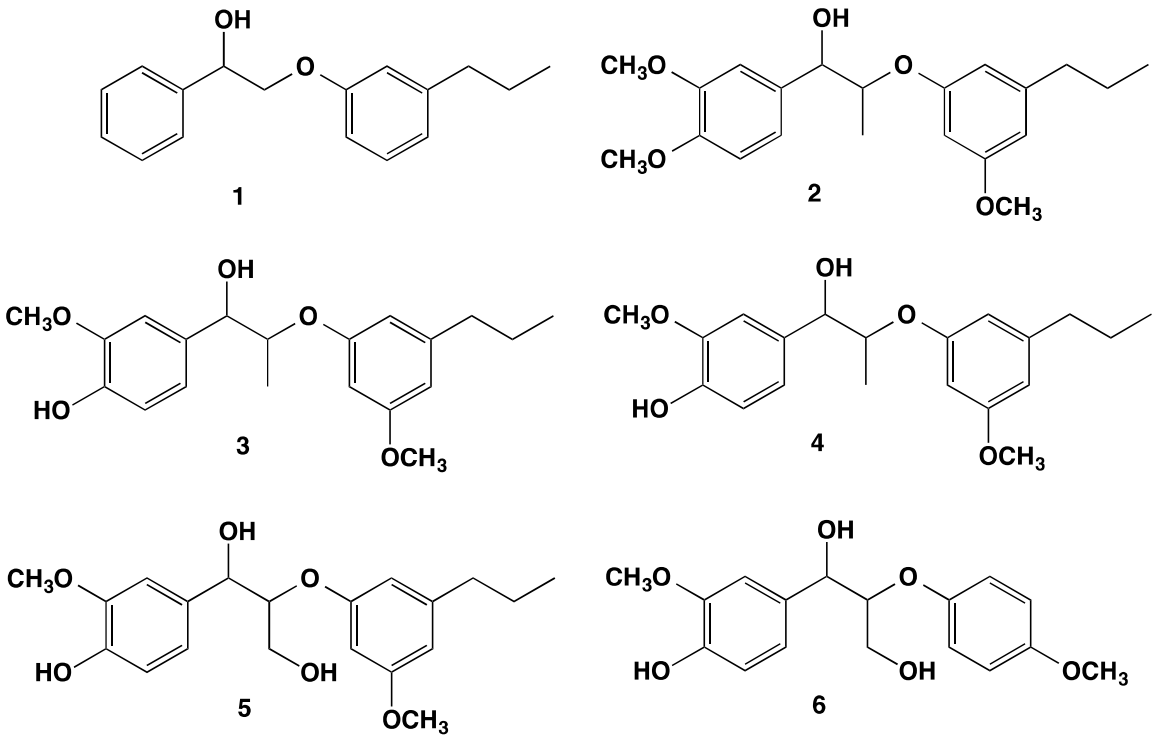

Figure 1: Lignin model dimer compounds 1-6

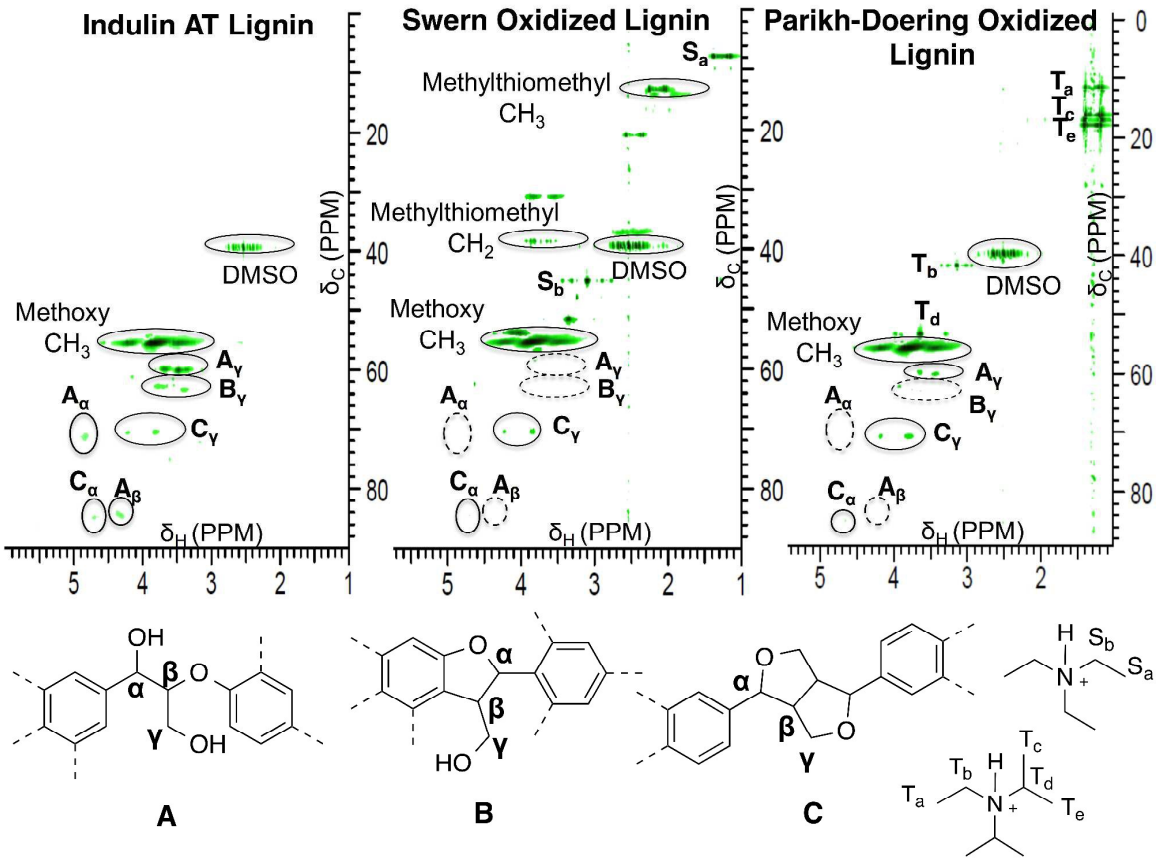

Figure 2: HSQC spectra of Kraft lignin, Swern oxidized Kraft lignin, and Parikh-Doering oxidized Kraft Lignin[39]

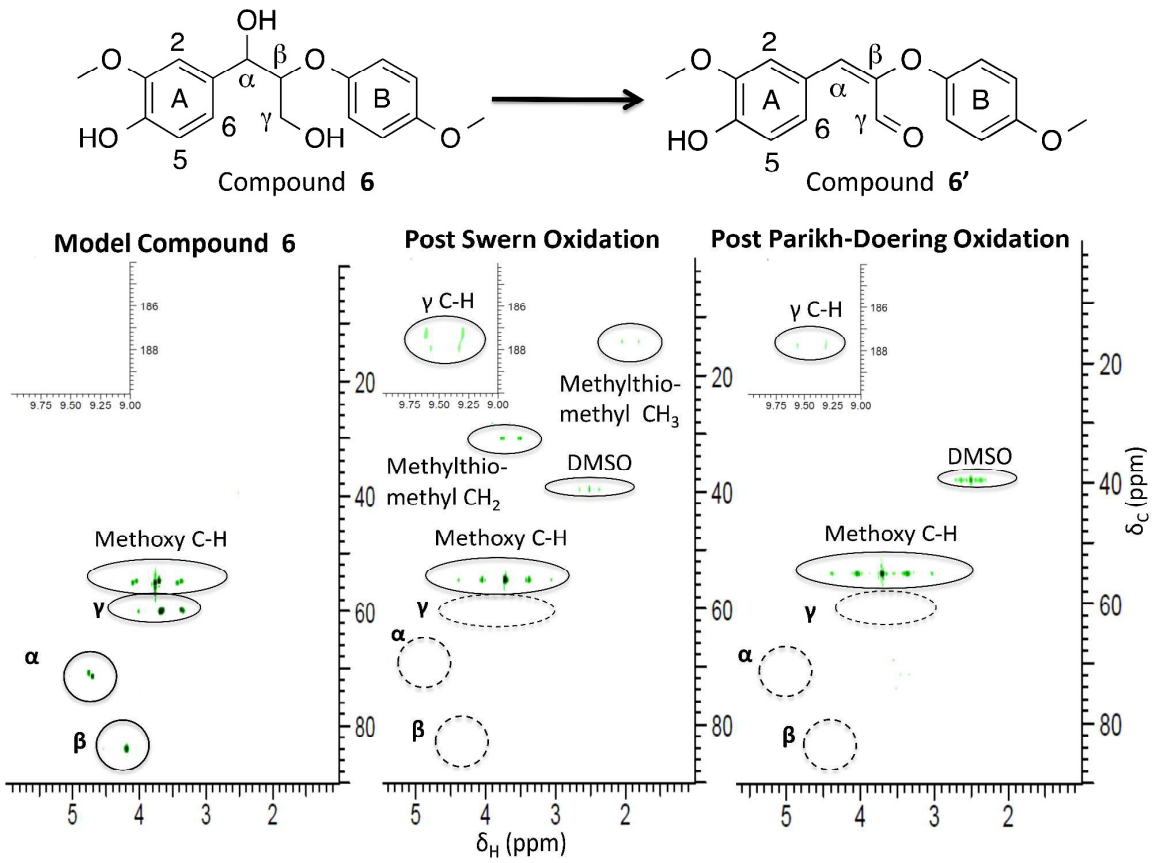

Figure 3: HSQC spectra of compound 6, Swern oxidation of compound 6, and Parikh-Doering oxidation of compound 6.

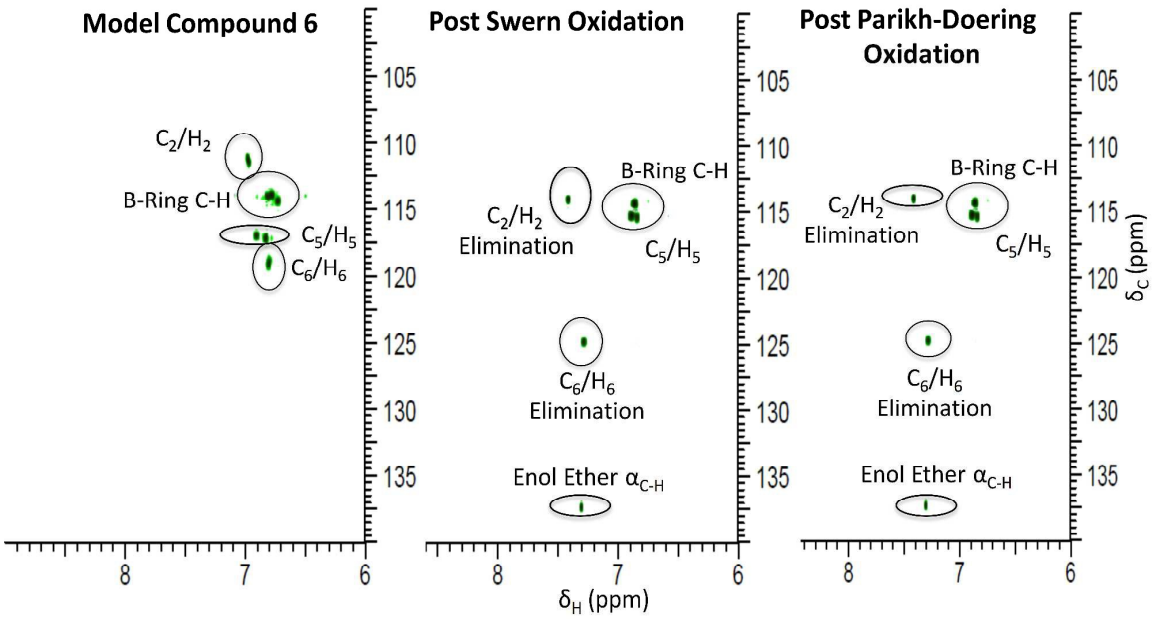

Figure 4: HSQC NMR spectra showing the aromatic region of the products obtained from Swern and Parikh-Doering oxidation of model 6.

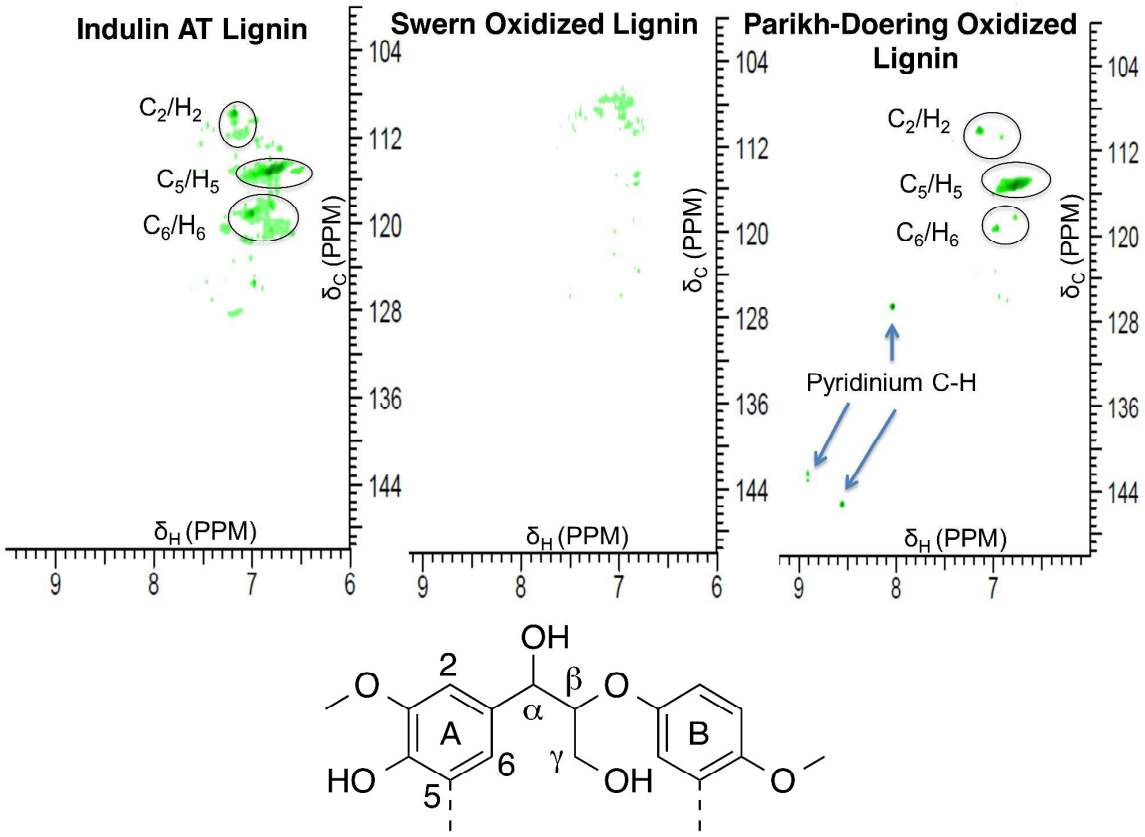

Figure 5: HSQC NMR spectra showing the aromatic region of Swern and Parikh-Doering oxidized Kraft Lignin

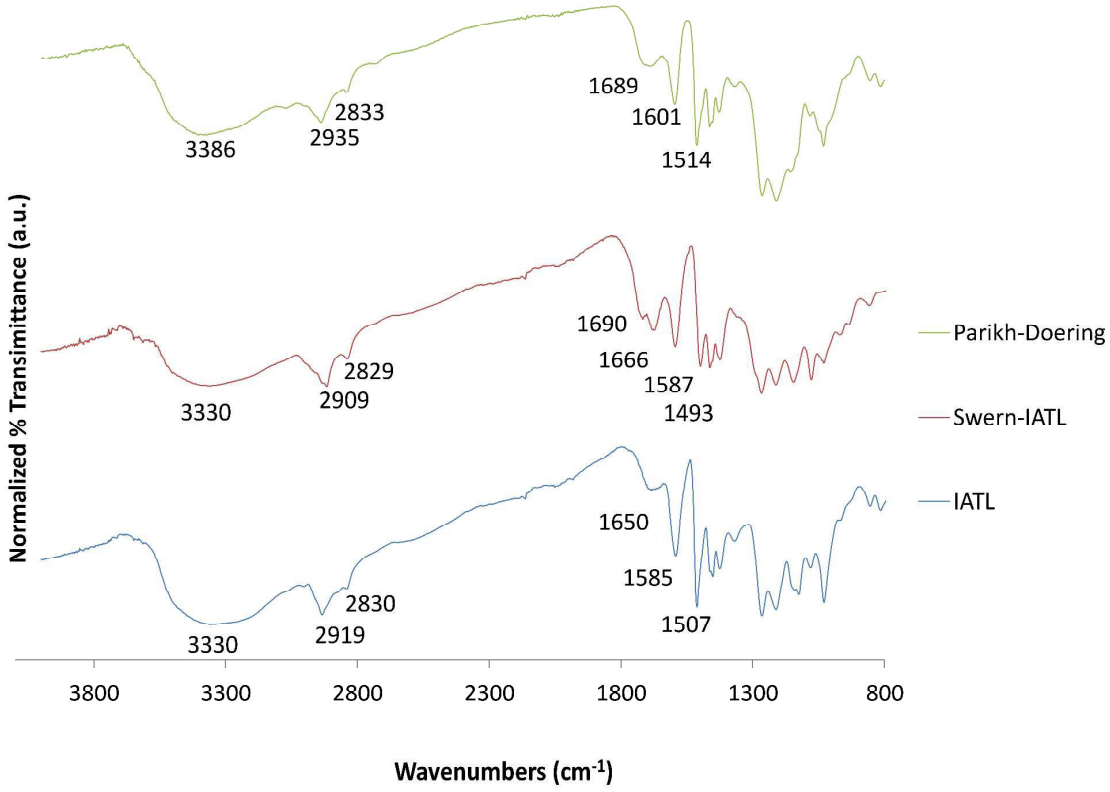

Figure 6: ATR-FTIR analysis of (Kraft) lignin and lignin subjected to oxidation under Swern and Parikh-Doering conditions

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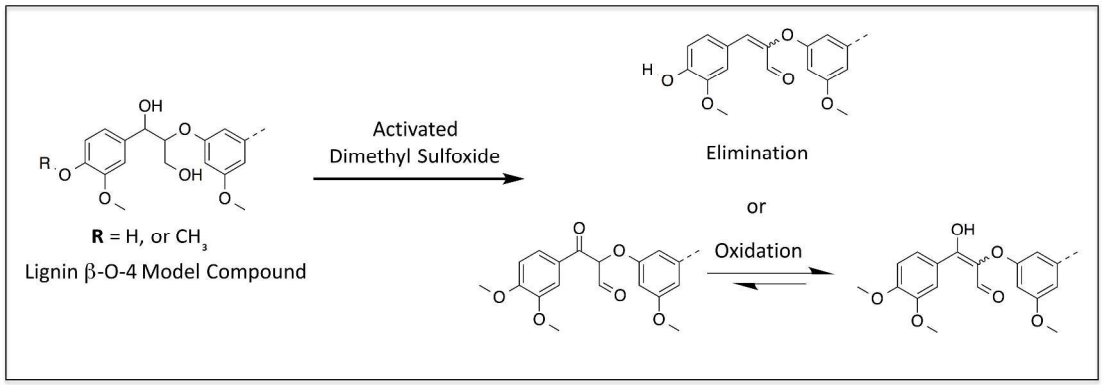

One sentence of text:

Oxidation of lignin and β-O-4 models using activated DMSO compounds can give ketones or enol ethers