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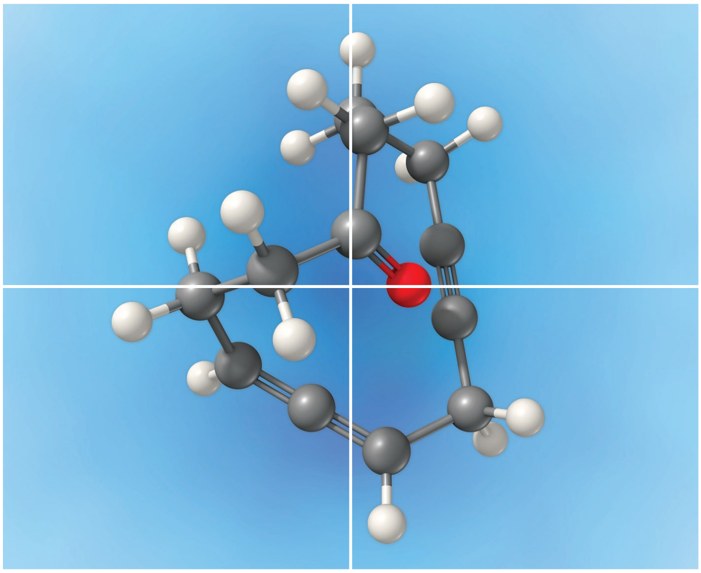

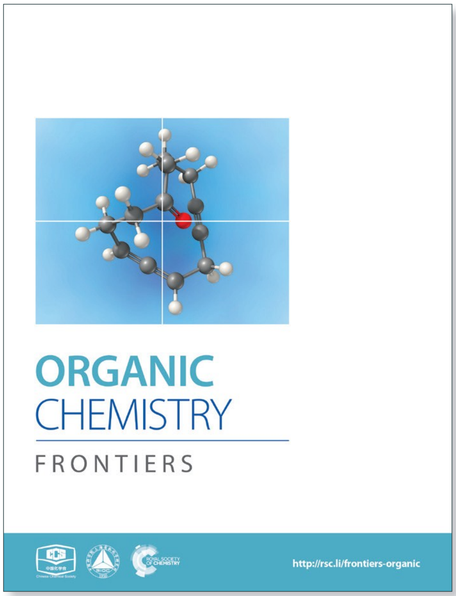

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ARTICLE TYPE

Fragmentation of Structural Units of Lignin Promoted by Persulfate through Selective C-C Cleavage under Mild Conditions

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A concise and environmentally benign protocol for lignin model fragmentation was developed by using cheap and commercially available sodium persulfate as an oxidant. The predominant lignin *β*-O-4 or *β*-1 model was fragmented into high-valued aromatic aldehydes. The other lignin models, such as *α*-O-4, 4-O-5, and 5-5', showed good reactivity in this system.

Energy and environment problems became serious to human beings and urgent solutions toward these serious challenges are highly required by finding renewable energy sources and sustainable synthetic transformations[1]. Conversion of non-food biomass lignocelluloses is a highly potential alternative for the production of valuable chemicals and fuels. Lignin, as the second most abundant biopolymer, constitutes up to 15-30% of the weight and 40% of the energy content of lignocellulosic biomass. However, the achievement on conversion of lignin is far behind its family of cellulose and hemicellulose due to its structural complexity and stability[2].

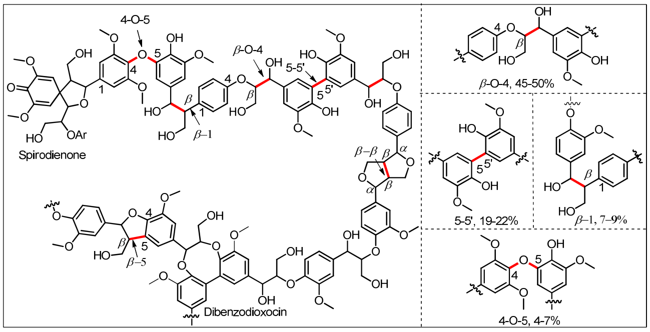
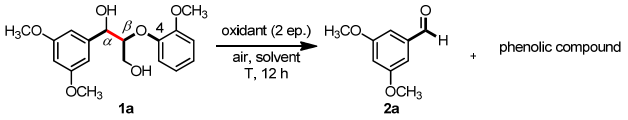


Figure 1. Representative Structures of a Fragment of Lignin and Some Prevalent Chemical Linkages Characterized in Lignin from Spruce trees

This predicament of lignin is attributed to its complexity of irregular structure with methoxyl substituted phenyl and phenolic subunits[3] (**Figure 1**). Indeed in recent years, much attention has been paid to lignin fragmentation due to its potential feedstock for high-valued chemicals, pharmaceuticals and fuels[4]. Different oxidative[5], reductive[6], and redox-neutral[7] lignin protocols have been demonstrated to fragmentate lignin, native lignin, and lignin model systems. More encouragingly, beautiful examples on the promising catalytic lignin degradation have been recently developed by using transition-metal catalysts. Vanadium complexes showed a promising ability on aerobic oxidative degradation lignin to afford C−C/C−O cleavage products [5g-h, 5k]. Aerobic oxidation of lignin models with amide bond formation was developed by using Cu catalyst[8]. Cobalt exhibited a credible ability to catalyze the oxidative conversion of lignin models to benzoquinones in an O_2 atmosphere[5i]. During our preparation this manuscript, a chemical selective oxidation through C-O bond cleavage of *β*-O-4 lignin to isolate phenolic monomers was reported[9]. Under reductive conditions, nickel carbene complex was an effective catalyst for hydrogenolysis of aryl ether bonds in several lignin model compounds under alkaline condition in H_2 atmosphere[6f]. Fe catalyst also showed good reductive activity for hydrogenolysis of aryl ether bonds in lignin models[10]. With hydrogenation transfer strategy, Ru-catalzyed C-O cleavage of lignin model compounds under neutral conditions has been developed by Bergman's group[7a] and other groups[7b-7f]. These methods represented diverse strategies toward lignin degradation utilizing transition-metal catalysis.

Other than transition metal catalysis, Stahl and co-workers developed a chemoselective metal-free aerobic secondary alcohol oxidation in lignin models and further converted the generated ketones to corresponding products in two steps[11]. Continuous efforts from Stahl's group have been made to explore formic-acid-induced depolymerization of oxidized lignin to aromatics[12]. Interestingly, Stephenson and coworkers developed a photochemical strategy for lignin degradation at room temperature *via* chemoselective secondary alcohol oxidation and photocatalytic cleavage C-O bond by using an iridium complex photosensitizer[13]. More recently, a frustrated Lewis pair $B(C_6F_5)_3$ as catalyst has been applied into reductive cleavage of C-O bonds of *β*-O-4 model[14]. Obviously, the protocols are still facing significant challenges that have yet to be addressed to some extent, such as the step economy, and the frequent use of expensive and high loading of transition-metal catalysts. Therefore, new methods to convert the lignin models to valuable chemicals are still appealing. Herein, we reported a convenient and transition-metal free protocol for fragmenting lignin models to aromatic aldehydes through selective C-C cleavage in the presence of persulfate.

Table 1. Optimization Study.



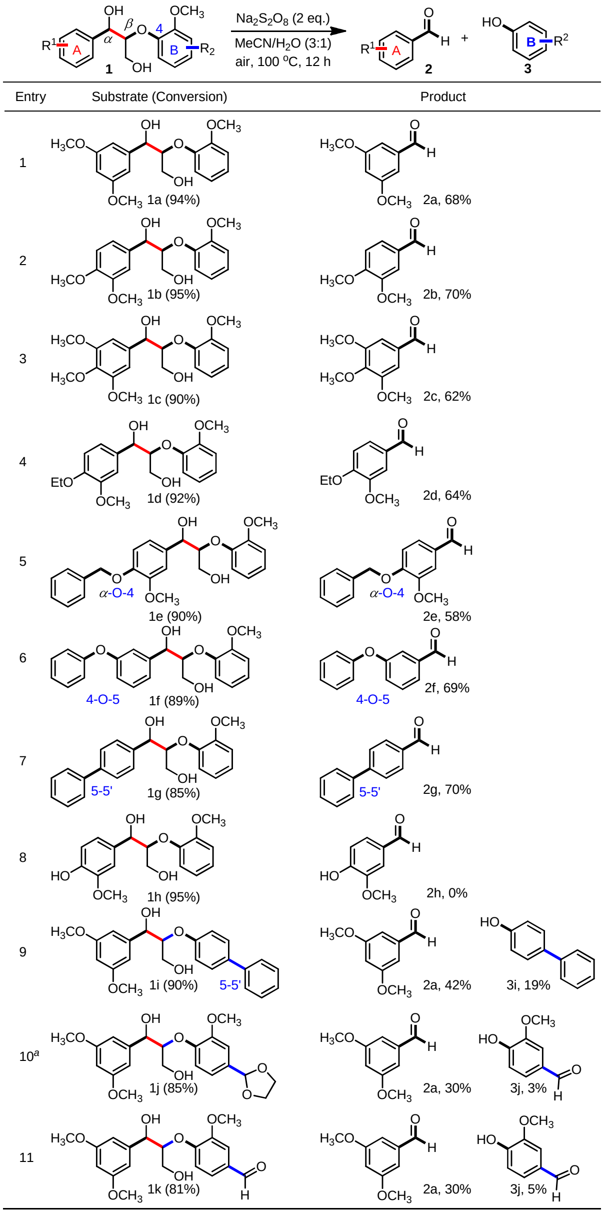
Entry[a]	[Oxidant]	T(°C)	Solvent(v/v)	Result
1	$Na_2S_2O_8$	80	MeCN / H_2O (3:1)	51%
2	$K_2S_2O_8$	80	MeCN / H_2O (3:1)	41%
3	$(NH_4)_2S_2O_8$	80	MeCN / H_2O (3:1)	42%

4	Oxone	80	MeCN / H_2O (3:1)	DP[b]
5	$Na_2S_2O_8$	60	MeCN / H_2O (3:1)	34%
6	$Na_2S_2O_8$	100	MeCN / H_2O (3:1)	61%
7	$Na_2S_2O_8$	120	MeCN / H_2O (3:1)	50%
8	$Na_2S_2O_8$ / O_2	100	MeCN / H_2O (3:1)	53%
9	$Na_2S_2O_8$ / N_2	100	MeCN / H_2O (3:1)	44%
10	$Na_2S_2O_8$	100	MeCN / H_2O (1:1)	36%
11	$Na_2S_2O_8$	100	MeCN (4eq. H_2O)	DP[b]
12	$Na_2S_2O_8$(1.0 eq.)	100	MeCN / H_2O (3:1)	29%
13	$Na_2S_2O_8$(2.5 eq.)	100	MeCN / H_2O (3:1)	55%
14	$Na_2S_2O_8$ (9 h)	100	MeCN / H_2O (3:1)	47%
15	$Na_2S_2O_8$ (15 h)	100	MeCN / H_2O (3:1)	55%
16[c]	$Na_2S_2O_8$	100	MeCN / H_2O (3:1)	65%(68%[d])
17[e]	$Na_2S_2O_8$	100	MeCN / H_2O (3:1)	55%[f]+7%[g]

[a] 0.05 mmol of lignin model **1a** and 0.1mmol of $Na_2S_2O_8$, 0.75 mL of organic solvent and 0.25 mL of H_2O, 100 °C, 12 h. NMR yield with using CH_2Br_2 as internal standard reagent. [b] DP = decomposed product, No product was identified from the decomposed starting material. [c] 0.1 mmol of lignin model **1a** and 0.2 mmol of $Na_2S_2O_8$, 1.5 mL of organic solvent and 0.5 mL of H_2O, 100 °C, 12 h. [d] isolated yield. [e] 0.2 mmol of **2a** and 0.4 mmol of $Na_2S_2O_8$ in 4.0 mL mixture of MeCN/H_2O (v/v = 3:1) were reacted at 100 °C for 12 h. [f] isolated yield of the recovery of aldehyde **2a**; [g] isolated yield of the corresponding acid of **2a**.

Persulfates are cheap and commercially available inorganic chemicals, which have been widely applied in chemical industry and researches in laboratory as radical initiator and/or oxidant[15].We envisaged that the electron-rich lignin models probably transferred an electron to persulfate and formed a radical cation, which could further fragment to small molecules through C-C or/and C-O bond cleavage. To examine our hypothesis, we chose and synthesized the predominant lignin β-O-4 model (**1a**) as the model compound to screen the reaction conditions (**Table 1**). To our delight, lignin β-O-4 model reacted with two equivalent of sodium persulfate in a mixture of MeCN/H_2O (3:1, v/v) under air at 80 ºC and aromatic aldehyde **2a** was isolated in 51% yield (entry 1). Unfortunately, the desired phenolic compound guaiacol was failed to isolate, which may be over-oxidized to a water-soluble and/or polymeric species. This observation was consistent with previous reported oxidation systems *via* radical mechanism using peroxidase[16,17] or Fe/PhI(OAc)$_2$[5e] as oxidant. Different persulfates (entries 2-4) were screened and sodium persulfate outperformed the others. Further screening of the reaction temperature found that the best result was obtained at 100 ºC (entry 6) (entries 5-7). Interestingly, the air was shown the best performance for this fragmentation than O_2 or N_2 (entry 6 and entries 8 and 9). To our interest, the ratio of the mixed solvent was critical for high efficiency. Decreasing or increasing the amount of water diminished the efficacy (cf: entries 10 and 11, and entries 11-14 in **Table S1**). No desired product **2a** was obtained at all when only 4.0 equivalent of water was added (entry 11). After carefully screening of other parameters in this transformation (**Table 1** and **S1**), the best condition was fixed in the presence of 2.0 equivalent of sodium persulfate and **1a** was fragmented into aromatic aldehyde in the mixture of MeCN/H_2O (3:1, v/v) at 100 °C. Encouragingly, when the reaction was conducted in 2.0 mL of mixture of MeCN/H_2O (3:1, v/v) with 0.1 mmol of **1a** and 0.2 mmol of persulfate at 100 °C for 12 h, the best result was obtained in a 68% isolated yield (entry 16). More importantly, when the product **2a** as substrate was subjected into reaction system, it was successfully recovered in an acceptable isolated yield, accompanying with its oxidized acid product in 7% yield (entry 17). This observation exhibited that the aldehyde exhibited good compatibility in the oxidation system. Recently, it was reported that the lignin, lignin models and hydroxy-aromatics were breakdown to C1 and C2 chemicals (mainly methanol, formate, carbonate, and oxalate) *via* metal-free oxidation using persulfate or peroxide as oxidant in alkaline condition[18]. In contrast to this result, we developed an alternative method to fragment the lignin models to high-valued aldehydes using metal-free persulfate as oxidant in neutral condition. The difference results may be attributed to the solvent and the reaction pH value condition.

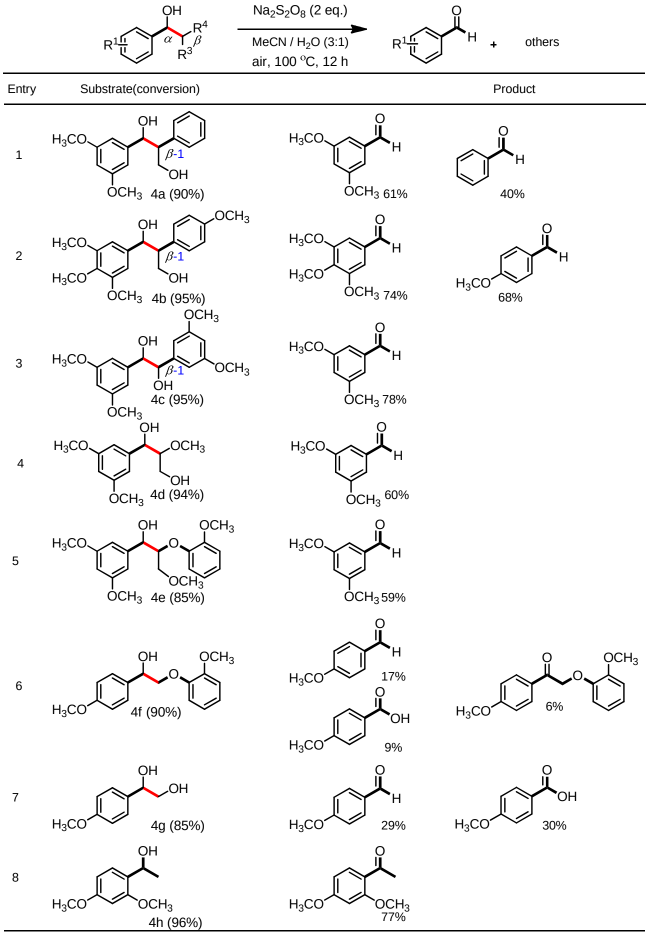
Table 2. Investigation on Fragmentation of β-O-4 Lignin Models



[a] 15% of its deprotected product **1k** was recovered.

With the optimized conditions in hand, we continued to examine other lignin β-O-4 model with different substituents. As shown in **Table 2**, different substituents on the left phenyl ring A proceeded smoothly to give the corresponding valuable aromatic aldehyde **2** in good yields. Methoxyl group on different position of ring A exhibited good activities and gave the corresponding aldehydes in good yields (**1a**-**1c**). More importantly, the models with other general substituents in lignin, including ethoxyl (**1d**), benzoxyl (**1e**), phenoxyl (**1f**), phenyl (**1g**), were fragmented to high-valued aromatic aldehydes in good yields, respectively. It is worthy to note that the models with benzoxyl (**1e**), phenoxyl (**1f**), and phenyl (**1g**) substituents, are belonging to the α-O-4, 4-O-5, and 5-5' lignin models, respectively[2a]. This observation was well documented that our methodology exhibited a high selectivity for β-O-4 lignin models from other structural units in lignin. Unfortunately, the phenolic model (**1h**) and desired phenol guaiacol were decomposed in our system, which was consistent with the previous reported results[5e, 16, 17]. Encouragingly, when phenyl group was equipped at the para-position of right phenyl ring B (**1i**), 19% of 4-phenylphenol and 42% of **2a** were successfully isolated, thus providing indirect proof for the formation of the corresponding phenol under this condition. The electron withdrawing groups, such as the acetyl (**1j**) or formyl (**1k**), at the para-position, affected the efficacy of this fragmentation and **2a** was isolated in much lower yields with the recovery of starting materials. The isolation of vanillin, despite in a low yield, further solidated the formation of phenol to some extent.

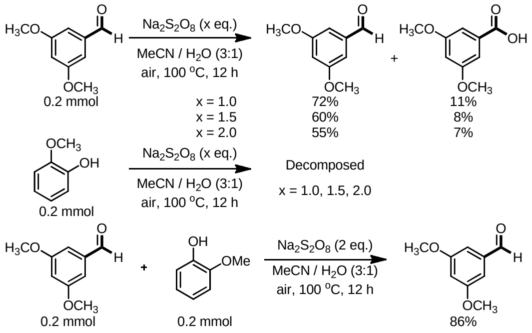
Table 3 Substrate Scope of Other Lignin Models



Further investigation was focused on the lignin model analogues with different substituents on β position of the bridge between two aromatic rings (**Table 3**). Encouragingly, the β-phenyl substituted models (**4a-4c**), attributed to β-1 lignin model[2a, 5k], were fragmented into two different benzaldehydes in good yields. It was obvious that the β-1 lignin model could be fragmented into different valuable aromatic aldehydes *via* selective C-C bond cleavage. The β-alkyloxyl substituted models could be also fragmented to aldehyde. The lignin model, in which hydroxymethyl substituent on β position was replaced with methoxymethyl group (**4e**) was converted into aldehyde in 59% yield. Finally, the lignin models with only one substituent on the β position (**4f** and **4g**) were also degraded into 4-methoxy benzaldehyde and 4-methoxy benzoic acid, while the secondary benzyl alcohol (**4h**) was oxidized to ketone product in 77% yield.

To highlight our protocol in real lignin fragmentation, We have attempted to add the alkaline lignin and dealkaline lignin to our standard reaction system. Unfortunately, the real lignin cannot be soluble well in this system. We failed to observe and isolate aldehydes or phenols.

To understand the stability of the products, 3, 5-dimethoxy benzaldehyde **2a** was submitted to the standard condition. With the increasing amount of persulfate (from 1 equivalent to 2 equivalent), the recovering yield of **2a** was reduced, while to our interest, the oxidized benzoic acid was kept at a very low level. Thus, the relative lower yields in some cases might arise from the over-oxidation of the products. Moreover, when the 2-methoxy phenol was delivered into the flask with a different amount of persulfate, the phenol was completely decomposed, which was consistent with the observed results and previous reports[5e, 16, 17]. Finally, when **2a** and 2-methoxy phenol were added into the same pot, only 86% of the **2a** was recovered, which further enhanced our conclusion. Thus, it is understandable that β-O-4 lignin models were fragmented into arylaldehydes in good yields and the phenols were given the poor yield due to its over-oxidation.



Conclusions

In conclusion, we had successfully developed a concise and environmentally benign protocol to fragment lignin models to valuable aldehydes by using sodium persulfate as oxidant. The predominant lignin β-O-4 model was fragmented into high-valued aromatic aldehydes in moderate to good yields. The β-1 lignin model was also converted into two different aromatic aldehydes in excellent yields. The other lignin models, such as α-O-4, 4-O-5, and 5-5', show good reactivity in this transformation. Further efforts to optimize the reaction condition for improving the efficacy and using this protocol to real lignin are underway.

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Notes and references

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† Electronic Supplementary Information (ESI) available: lignin meodels preparation procedure and their ^{1}H NMR, ^{13}C NMR and FTMS-ESI data See DOI:10.1039/b000000x/

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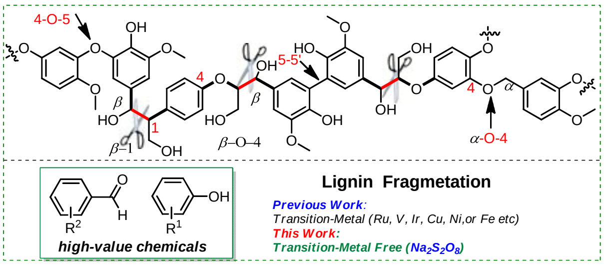
TOC



High selectivity and activity for fragmentation of β-O-4 and β-1 lignin models to high–valued chemicals were developed by using persulfate.