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# Photocatalytic Oxidation of Lignin Model Systems by Merging Visible-Light Photoredox and Palladium Catalysis

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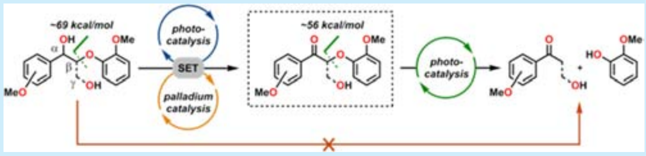
Supporting Information

**ABSTRACT:** Lignin valorization has long been recognized as a sustainable solution for the renewable production of aromatic compounds. Two-step oxidation/reduction strategies, whereby the first oxidation step is required to "activate" lignin systems for controlled fragmentation reactions, have recently emerged as viable routes toward this goal. Herein we describe a catalytic protocol for oxidation of lignin model systems by combining photoredox and Pd catalysis. The developed dual catalytic protocol allowed the efficient oxidation of lignin model substrates at room temperature to afford the oxidized products in good to excellent yields.



Lignocellulose is an integral structural component of plant cell walls and is considered as a potential feedstock for the production of nonfossil-based fuels and platform chemicals.[1,2] Because lignin is the largest renewable feedstock containing an aromatic backbone, the development of efficient processes for its exploitation as a renewable resource—so-called "valorization"—is a well-recognized objective. Approximately 20−35% of lignocellulose consists of lignin, which itself is comprised primarily of three cinnamyl alcohols: *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol (Figure 1). While considerable effort has been devoted to chemical depolymerization of lignin,[3−6] its rigid, irregular, and highly cross-linked structure renders effective degradation a challenging goal. If accomplished, this would provide access to discrete low-molecular weight aromatic building blocks and other commodity aromatic fine chemicals and would complement the products obtained from cellulose and bio-oil.

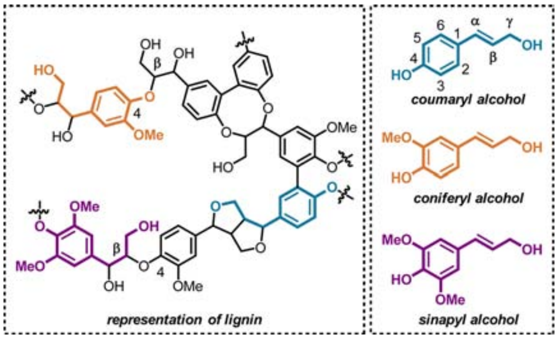


**Figure 1.** (Left) Representative depiction of lignin and (right) its main building blocks.

Building upon our previous understanding of photoredox catalysis,[7−9] our laboratory recently reported a method for the controlled cleavage of *β*-O-4 linkages in oxidized lignin model systems at room temperature using visible-light photoredox catalysis (Figure 2a).[10] This protocol relied on a two-step oxidation/reduction sequence whereby initial oxidation of the benzylic alcohol significantly weakens the C−O bond of the *β*-O-4 linkage[11] and has proven to be essential for fragmentation.[4d,10] Subunits containing a *β*-O-4 linkage constitute 45−60% of the polymer connectivity;[12] thus, the controlled cleavage of this linkage represents an attractive route for converting lignin into value-added aromatic products.

Dual catalytic systems which merge photoredox and transition metal catalysis have been used to mediate functionalizations under mild conditions that would otherwise be difficult to achieve using either system independently.[13] This is particularly important within the context of lignin depolymerization, where traditional methods employing elevated temperatures and/or the use of acids or bases can significantly and irreversibly modify the native lignin structure. Herein, we disclose the successful combination of visible-light photoredox and Pd catalysis for the efficient oxidation of relevant lignin model substrates at room temperature (Figure 2b). The designed oxidative transformation represents a vital step toward the chemoselective valorization of lignin using a two-step oxidation/reduction strategy.

For oxidation of the *α*- or *γ*-carbons, we targeted the use of Pd in the presence of sodium persulfate ($Na_2S_2O_8$) as an inexpensive terminal oxidant. We reasoned that $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]PF_6$ {**1**($PF_6$); where dF($CF_3$)ppy) = 2-(2,4-difluorophenyl)-5-trifluoro-methylpyridine and dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridyl} would constitute the preferred photoredox catalyst since the photoexcited state of this complex (**1**$^{*+}$) has previously been reported to undergo quenching in the presence of the persulfate anion ($S_2O_8^{2-}$).[14] The envisioned dual catalytic system was initially evaluated with photocatalyst **1**($PF_6$) (1 mol %), $Pd(OAc)_2$ (10 mol %), and $Na_2S_2O_8$ (1 equiv) in MeCN using 4.4 W blue LEDs at room temperature; however, this

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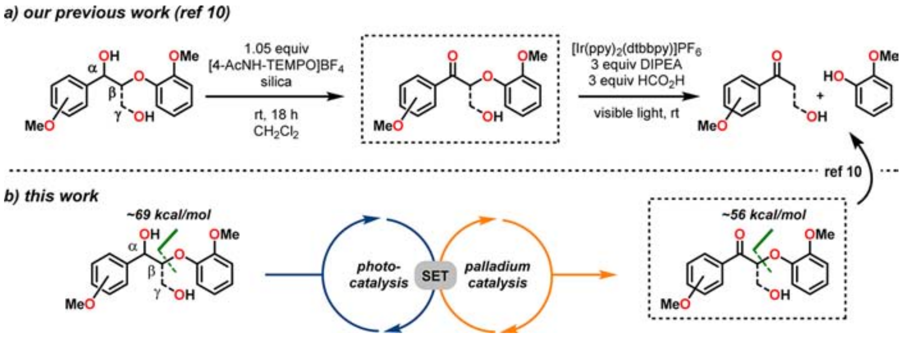
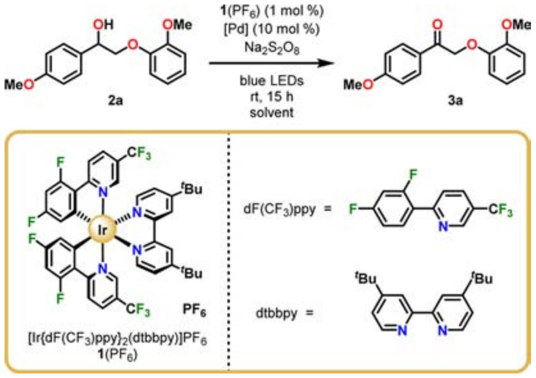


**Figure 2.** (a) Two-step visible-light mediated depolymerization strategy for lignin and lignin model systems, and (b) oxidation of lignin model systems by merging photoredox and Pd catalysis.

resulted in merely 11% of the oxidized product (Table 1, entry 1). By changing the reaction media to DMF, the desired oxidized product could be produced in 53% yield (Table 1, entry 2). Increasing the amount of persulfate to 2 equiv further improved the yield, furnishing the product in 85% yield (Table 1, entry 3). Pd(TFA)$_2$ was also evaluated as the Pd source but did not improve the outcome (Table 1, entry 4). Subsequent control experiments highlighted the essential roles of the photocatalyst, Pd catalyst, oxidant, and light in this transformation (Table 1, entries 5−8). With the optimized reaction conditions in hand, a variety of lignin model systems were subjected to the dual oxidative catalytic system to probe the scope (Scheme 1). Several simplified $\beta$-O-4 model systems (**2b**−**e**) were screened and could all be oxidized to their corresponding ketone in high yields. Electron-rich arenes were essential to reaction efficiency as substrate **2f** showed only moderate yield as compared to more electron-rich substrates.

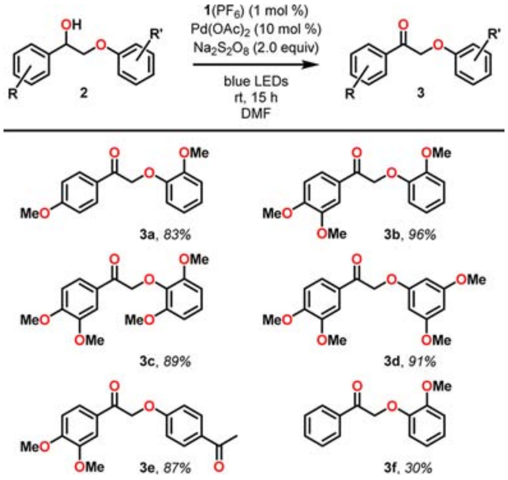
### Table 1. Optimization of Model Reaction[a]



| entry | photocatalyst | [Pd] | yield (%)[b] |
|---|---|---|---|
| 1[c,d] | 1(PF$_6$) | Pd(OAc)$_2$ | 11 |
| 2[d] | 1(PF$_6$) | Pd(OAc)$_2$ | 53 |
| **3** | **1(PF$_6$)** | **Pd(OAc)$_2$** | **85** |
| 4 | 1(PF$_6$) | Pd(TFA)$_2$ | 83 |
| 5 | none | Pd(OAc)$_2$ | 21 |
| 6 | 1(PF$_6$) | none | 10 |
| 7[e] | 1(PF$_6$) | Pd(OAc)$_2$ | 4 |
| 8[f] | 1(PF$_6$) | Pd(OAc)$_2$ | 19 |

[a] Reactions were conducted with photocatalyst **1**(PF$_6$) (1 mol %), Pd(OAc)$_2$ (10 mol %), and Na$_2$S$_2$O$_8$ (2.0 equiv) in DMF at room temperature if not otherwise stated. [b] Yields determined by $^1$H NMR using 1,3,5-trimethoxybenzene as internal standard. [c] Reaction performed in MeCN. [d] 1.0 equiv Na$_2$S$_2$O$_8$ was used. [e] Reaction performed in the absence of Na$_2$S$_2$O$_8$. [f] Reaction performed in the absence of light. dF(CF$_3$)ppy = 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine. dtbbpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine. TFA = trifluoroacetate.

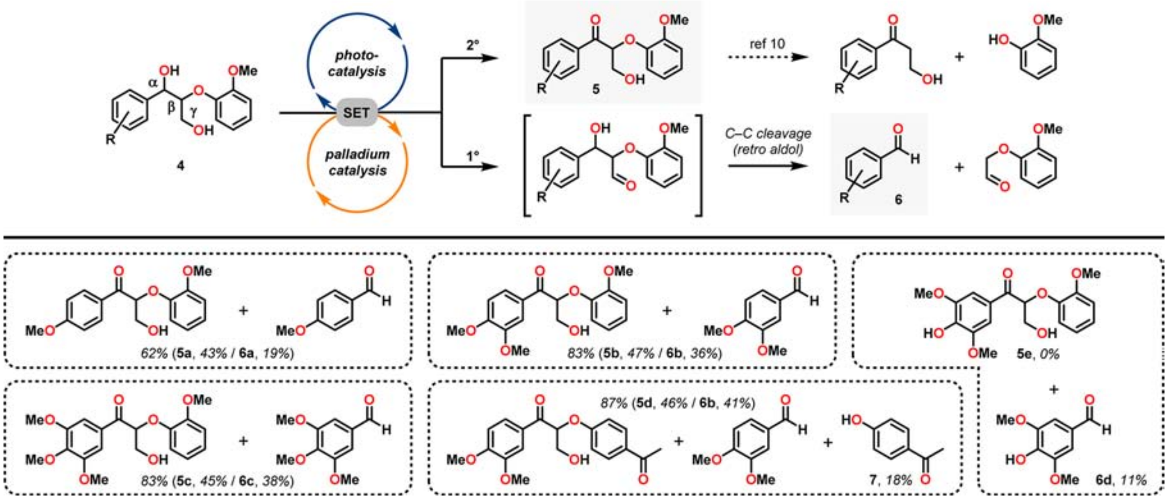
### Scheme 1. Oxidation of Lignin Model Systems[a]



[a] Reactions were conducted with photocatalyst **1**(PF$_6$) (1 mol %), substrate **2** (1.0 equiv), Pd(OAc)$_2$ (10 mol %), Na$_2$S$_2$O$_8$ (2.0 equiv) in DMF at room temperature. All reaction yields are of isolated products.

These results further prompted the examination of diol compounds **4**, which are good representations of the different units present in native lignin (coumaryl, coniferyl, and sinapyl alcohols). For these compounds, oxidation could potentially occur either at the 2° benzylic position or the 1° alcohol (i.e., oxidation at the $\alpha$- or $\gamma$-carbon), each of which have previously been observed.[4d] This would yield two different products, which could undergo separate C−O and/or C−C cleavage pathways to ultimately furnish distinct products (see Scheme 2). By subjecting diol **4a** to the optimized oxidation conditions, both ketone **5a** (43%) and aldehyde **6a** (19%) were isolated in a combined yield of 62%. Formation of benzaldehyde **6a** is likely the result of a retro-aldol reaction after initial oxidation of the 1° ($\gamma$) alcohol. Similar reactivity was observed for model systems **4b** and **4c**, which afforded the oxidized products in a combined yield of 83% and 83% yield, respectively. Here, the benzylic ketones **5b** and **5c** were isolated in 47% and 45% yield, together with veratraldehyde (**6b**) and 3,4,5-trimethoxybenzaldehyde (**6c**) in 35% and 38% yield, respectively.[15] Keto-lignin substrate **4d** was also successfully oxidized and afforded benzylic ketone **5d** and aldehyde **6b** in 46% and 41% yield, respectively. In addition to ketone **5d** and aldehyde **6b**, this reaction also provided 4-

**Scheme 2. Chemoselective Oxidation of Lignin Model Systems 4 by Merging Photoredox and Pd Catalysis**[a]

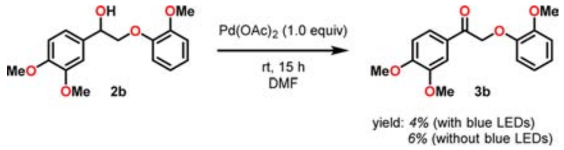


[a]Reactions were conducted with photocatalyst **1**($PF_6$) (1 mol %), substrate **4** (1.0 equiv), $Pd(OAc)_2$ (10 mol %), $Na_2S_2O_8$ (2.0 equiv) in DMF at room temperature. All reaction yields are of isolated products.

hydroxyacetophenone (**7**) in 18% yield.[16] Model systems containing free phenolic moieties[17] present exceptional challenges for chemoselectivity, as such systems have previously been shown to afford complex product mixtures with other catalytic systems.[4a,6a,b] In line with previous reports, reaction of the free phenol substrate **4e** produced only ∼11% of 4-hydroxy-3,5-dimethoxybenzaldehyde (**6d**), with no observable formation of ketone **5e** (see Supporting Information for further details).

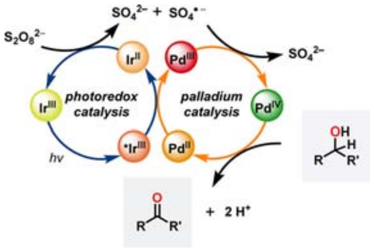
To gain insight into the mechanistic cycle, experiments were conducted with a stoichiometric amount of $Pd(OAc)_2$. Combining model substrate **2b** with 1 equiv of $Pd(OAc)_2$, in the presence or absence of light, resulted in low conversion and yielded just ∼5% of the oxidized product (Scheme 3). This suggests that $Pd^{II}$ is not the catalytically competent species at ambient temperature and that higher redox states are involved in the catalytic cycle. This highlights the concept of combining metal and photoredox catalysis for accessing reactivity that is not attainable using either catalytic system independently. To assess the possibility of heterogeneous Pd species being involved in the catalytic system, filtration and mercury poisoning tests[18] were carried out. Both studies suggest that the observed catalytic activity does not originate from in situ generated heterogeneous Pd species. Luminescence quenching experiments were subsequently performed to study the quenching process. It was found that neither substrate **2b** nor $Na_2S_2O_8$ was able to quench the photocatalyst efficiently (Figures S3 and S7, respectively). However, $Pd(OAc)_2$ exhibited significant fluorescence quenching, with a Stern−Volmer quenching rate constant ($k_q$) of $3.44 \times 10^8$ $M^{-1}$ $s^{-1}$ (Figure S5, Table S1), suggesting that $Pd^{II}$ is the most efficient quencher in the catalytic system.

**Scheme 3. Stoichiometric Oxidation of Lignin Model System 2b with $Pd(OAc)_2$ in the Presence or Absence of Light**



Based on the aforementioned observations, a tentative mechanistic proposal for oxidation of lignin model systems with the developed dual catalytic system is outlined in Scheme 4.

**Scheme 4. Proposed Mechanism for Oxidation of Lignin Model Systems**



The mechanism is initiated with irradiation of the photocatalyst $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]^+$ ($\mathbf{1}^+$) and results in metal-to-ligand charge transfer to produce a long-lived excited state, $[Ir\{dF(CF_3)ppy\}_2(dtbbpy)]^{*+}$ ($\mathbf{1}^{*+}$). As suggested by the luminescence quenching studies, the produced photoexcited state, which is a strong oxidant ($E_{1/2}$ $Ir^{III*}/Ir^{II}$ = +1.21 V vs SCE[19]), can undergo reductive quenching with $Pd(OAc)_2$ to generate a $Pd^{III}$ species. The reduced $Ir^{II}$ photocatalyst (**1**) is a strong reductant ($E_{1/2}$ $Ir^{III}/Ir^{II}$ = −1.37 V vs SCE[19]) and subsequently reacts with $S_2O_8^{2-}$ to regenerate the ground-state $Ir^{III}$ photocatalyst $\mathbf{1}^+$ and produce $SO_4^{2-}$ and $SO_4^{•-}$. The sulfate radical, $SO_4^{•-}$, is a potent oxidant ($E_{1/2}$ = +2.2 V vs SCE[20]) and has sufficient potential to facilitate the oxidation of $Pd^{III}$ to $Pd^{IV}$. The high-valent $Pd^{IV}$ species is expected to oxidize the substrate to afford the desired oxidized product, regenerating $Pd^{II}$ to complete the proposed dual catalytic cycle.

In conclusion, a novel approach toward the valorization of lignin and related systems has been developed by combining photoredox and Pd catalysis. The unique cooperative interplay of photoredox and Pd catalysis has allowed for the efficient oxidation of lignin related systems at room temperature and constitutes a vital step toward converting lignin to value-added, low-molecular weight aromatics. Current efforts to improve this process and to develop further the use of dual catalytic systems incorporating visible-light active complexes are underway.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02651.

Detailed experimental details and characterization data (PDF)

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### Notes

The authors declare no competing financial interest.

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(16) ~40% degradation of 4-hydroxyacetophenone was observed when subjecting it to the optimized reaction conditions.

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