

# Solar-powered Biorefinery

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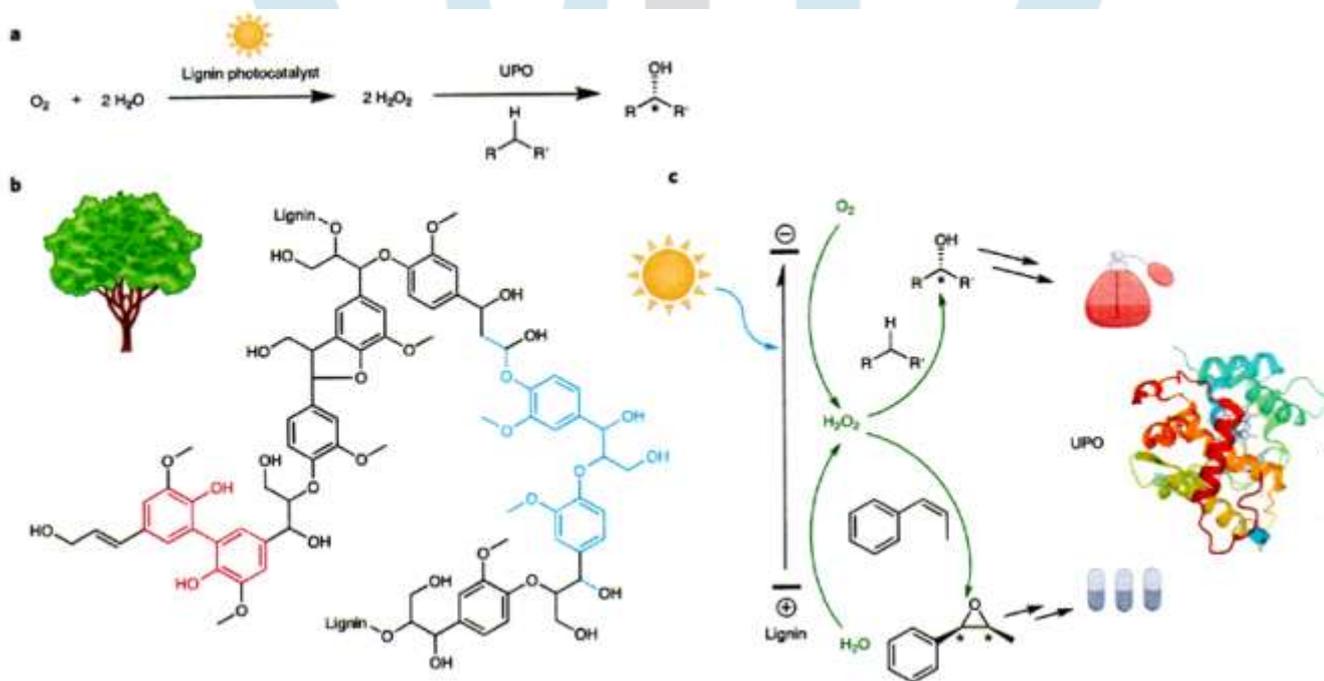
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**Abstract:** ‘Solar chemical’ production can be limited by the need for sacrificial reagents, metal-containing catalysts and low product values. Now,  $\text{H}_2\text{O}_2$  is generated from  $\text{H}_2\text{O}$  and air using lignin as a photocatalyst. Combining lignin with enzymatic catalysis enables selective oxyfunctionalization.

**Keywords:** Photocatalyst, Oxyfunctionalization, Artificial Photosynthesis, Asymmetric Synthesis, Enantioselective

## Macromolecules.

Using solar energy to produce chemicals and fuels, namely artificial photosynthesis, has steadily gained momentum owing to the increasing recognition of global climate change and a need for more sustainable production of chemicals. The upscaling of artificial photosynthesis has, thus far, been hampered by the low economic value of products such as  $\text{O}_2$ , even when sacrificial reagents are not required<sup>1</sup>. Consequently, there is growing interest to move beyond simple reactions like water splitting to the production of more value-added solar chemicals<sup>2</sup>. Accordingly, semi-artificial photosynthetic systems have been developed to combine light harvesting with enzymatic catalysis<sup>3</sup>, with the additional advantage of enantioselectively oxyfunctionalizing aliphatic hydrocarbons<sup>4</sup>. The union of light and enzymatic catalysis has also been applied to the asymmetric synthesis of complex natural products and active pharmaceutical ingredients. Nonetheless, these seminal reports required excess sacrificial redox agents, such as alcohols, or expensive platinum group photocatalysts<sup>5</sup>, which will limit their large-scale deployment for artificial photosynthesis. Non-food biomass lignin has previously been shown to be concurrently oxidized by a photoelectrochemical platform in combination with the enzymatic reduction of  $\text{CO}_2$  or  $\alpha$ -ketoglutarate, although the substrate scope was severely limited, and toxic lead-containing perovskites were needed for light harvesting<sup>6</sup>. Now, writing in *Nature Synthesis*, Park, Hollmann and co-workers report the use of lignin as a photocatalyst to produce hydrogen peroxide from air and water without sacrificial reagents. Coupling of this reaction with unspecific peroxygenases (UPOs) achieves the oxyfunctionalization of aliphatic hydrocarbons (Fig. 1a) with quantitative enantioselectivity<sup>7</sup>



**Fig. 1 | Cooperation of lignin photocatalysts with unspecific peroxygenases (UPOs) for the enantioselective oxyfunctionalization of hydrocarbons. a, Overall semi-artificial photosynthetic reaction. b, Adding value to non-food biomass-derived lignin by using it as a multifunctional photocatalyst. The photoactive motif includes the  $\beta$ -O-4 linkage dimer (blue), while phenolic groups (red) can serve as antioxidative hydroxyl radical quenchers. c, After visible light illumination, lignin photocatalyses the simultaneous reduction of  $\text{O}_2$  from air and the oxidation of water to produce hydrogen peroxide as a solar fuel, without the need for sacrificial reagents. By coupling the in situ generated hydrogen peroxide with UPOs (PDB ID: 7O2G), this biohybrid system achieves the enantioselective, regioselective oxyfunctionalization of aliphatic hydrocarbons and the enantioselective epoxidation of alkenes, with excellent enantiocontrol and record-high UPO turnover numbers owing to the protective capabilities of the phenolic sub-**

**units in lignin. The chiral alcohol and epoxide products can be precursors to fragrances and active pharmaceutical ingredients, respectively.**

In a twist on biomass valorization, lignin is used as a multifunctional photocatalyst to harvest light and quench hydroxyl radicals, rather than as a substrate. Unlike Hollmann's previous report<sup>4</sup> where the photosynthetic oxidative half-reaction generated the low-value O<sub>2</sub>, in the present study, both half-reactions productively yielded hydrogen peroxide under ambient, atmospheric conditions. The hydrogen peroxide produced in situ then facilitated a UPO-biocatalysed epoxidation of a styrene or the hydroxylation of aliphatic C–H bonds, achieving unprecedented UPO turnover numbers for the hydroxylation of ethylbenzene. Given that UPOs are extracellular enzymes secreted by fungi, these experiments could model natural biodegradation and nutrient recycling in the environment. More generally, this bioinspired approach can sustainably generate value-added fine chemicals from abundant feedstocks by semi-artificial photosynthesis<sup>2</sup>.

Park and co-workers identify the functional groups and compare the structural changes in lignosulfonate and kraft lignin relative to native lignin, and then use optical and photoelectron spectroscopy to estimate the photoexcited state redox potentials. Having established the thermodynamic feasibility of the reactions, kraft lignin and lignosulfonate are used as photocatalysts for hydrogen peroxide production from ambient air and water. Both forms of processed lignin generate hydrogen peroxide in neutral solutions upon irradiation with visible light. The researchers conducted radical scavenging and <sup>18</sup>O isotope labelling experiments to suggest that O<sub>2</sub> was likely reduced to hydrogen peroxide in two sequential steps via superoxide radicals, whereas water was directly oxidized to hydrogen peroxide without the intermediacy of O<sub>2</sub>.

Park and co-workers also screen different models and types of lignin to pinpoint the photoactive motifs within lignin. More specifically, they investigate the production of hydrogen peroxide under dark and light conditions by cellulolytic enzyme lignin (a realistic model of native lignin), a synthetic lignin dehydrogenation polymer, guaiacylglycerol-β-guaiacyl ether as a phenolic β-O-4 linkage dimer, coniferyl alcohol, and sinapyl alcohol. Notably, all these lignin models except for coniferyl and sinapyl alcohol, which do not contain β-O-4 linkages, are effective photocatalysts for hydrogen peroxide production, indicating the indispensable role of the β-O-4 linkage (Fig. 1b). Their proposed mechanism involves the reduction of O<sub>2</sub> to hydrogen peroxide by the visible-light photoexcited electron, with concomitant β-O-4 benzylic alcohol oxidation, while the transient hole oxidizes water to hydrogen peroxide (Fig. 1c). Spectroscopic analyses verified the benzylic alcohol oxidation to a carbonyl group in lignin.

To add value to their artificial photosynthetic system, Park and co-workers harness the in situ generated hydrogen peroxide for the enantioselective oxyfunctionalization of aliphatic hydrocarbons, which is a synthetic challenge in the presence of oxidizable arenes<sup>8</sup>. UPOs have been previously reported<sup>4</sup> by Hollmann for the oxyfunctionalization of aliphatic hydrocarbons; however, expensive gold-loaded TiO<sub>2</sub> photocatalysts were needed for water oxidation, the reactions showed poor chemoselectivity for alcohols, and the turnover numbers did not exceed 38,000. In this collaboration, Park, Hollmann and co-workers report the use of lignosulfonate as a photocatalyst with UPO to yield exclusively alcohols, with higher enantioselectivities and 30–83% higher turnover numbers, leading to a remarkable UPO catalysis benchmark of 81,000 turnovers for the production of (*R*)-1-phenylethanol (Fig. 1c). Furthermore, the versatile UPO epoxidized *cis*-β-methylstyrene to (1*R*,2*S*)-*cis*-β-methylstyrene oxide (Fig. 1c) with quantitative enantiocontrol and respectable turnovers. This improved enantioselectivity and catalytic longevity (over 130 hours) is attributed to the hydroxyl radical-quenching capabilities of the phenolic groups within lignin (Fig. 1b), which helped to alleviate the oxidative damage to the UPO.

Despite the limited substrate scope, this method has immense promise to be adopted by researchers in academia and industry for the synthesis of bioactive chiral molecules. The outstanding enantiopurity of the products, high turnover numbers, and simple, benign, aqueous reaction media make the method attractive for sustainable industrial applications. However, one of the remaining challenges is the insolubility of aliphatic hydrocarbons in water, which severely limits the reaction rates. The nonuniform, complex nature of both lignin and UPOs makes it difficult to systematically improve the macromolecules in a fashion similar to small molecules.

Nevertheless, these limitations offer opportunities for exploration. A deeper understanding of the role of β-O-4 linkages in the lignin photocatalyst and insights into the interfacial processes between O<sub>2</sub>, hydrogen peroxide, lignin, and UPO through in operando spectroscopy and computational calculations could be fruitful for improving catalytic performances and expanding the substrate scope. UPOs enhanced by directed evolution or artificial intelligence, or more generally by other enzymes, can be integrated to create semi-artificial photosynthetic systems capable of the late-stage functionalization of complex molecules or the activation of more inert feedstocks, such as methane. Accordingly, I expect synthetic chemists to take inspiration from these findings to develop biohybrid systems for the sustainable manufacturing of chiral fine chemicals.

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