

# LIGHT-MEDIATED ENZYMATIC CATALYSIS IN ORGANIC SYNTHESIS

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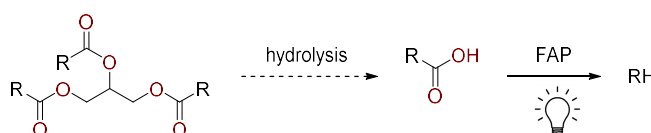
## NATURAL PHOTOENZYMES IN ORGANIC SYNTHESIS

### Photoenzymes in Nature

To date, there are four kinds of photoenzymes discovered: *photosystem* (PSI and PSII), *photolyase*, *light-dependent protochlorophyllide-reductases* and *photodecarboxylases*.<sup>1</sup> PSI and PSII enable the process of biosynthesis; photolyases repair the DNA by splitting the DNA dimer formed under UV; light-dependent protochlorophyllide-reductases reduce the protochlorophyllide to chlorophyllide in the biosynthesis of chlorophyll; photodecarboxylases catalyze the decarboxylation of free fatty acids to n-alkanes or alkenes.

### Application of in Photodecarboxylases Organic Synthesis

However, most of the photoenzymes catalyze sophisticated reactions and/or have complex structure, which limits their substrate scope and potential to be applied in biocatalysis, the only enzymes that can be applied are light-driven fatty acid photodecarboxylases (FAPs). Started from 2018, Hollmann group studies on the enzymatic catalysis with FAPs, focus on the transformation of cheap, available triglycerides to valuable biofuels (**Scheme 1**).<sup>2</sup>



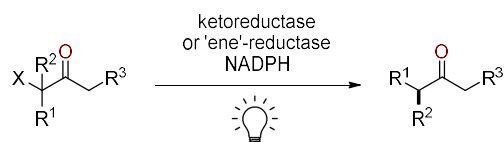
**Scheme 1.** Biofuels from Triglycerides Catalyzed by FAPs

## PHOTOINDUCED ENZYMATIC PROMISCUITIES IN ORGANIC SYNTHESIS

### Radical Reductions Catalyzed by Enzymes under Irradiation

In addition to photoenzymes, chemists have been exploring enzymatic promiscuities under irradiation as well. In 2018, the Hyster group reported an enantioselective photo-enzymatic debromination of  $\alpha$ -brominated lactones (**Scheme 2**).<sup>3</sup>

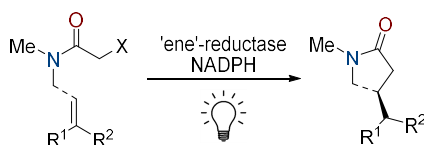
This reaction is catalyzed by ketoreductase (KR) under irradiation with visible light. The substrate binds to the active site of KR, then forms the electron donor–acceptor (EDA) complex with NADPH, followed by the single-electron reductive debromination. With careful choice of mediator for this transformation, they later achieved the  $\alpha$ -debromination on broader substrate scope, as well as other  $\alpha$ -reduction of ketones.



**Scheme 2.** Photo-enzymatic  $\alpha$ -reductions

### Intra- and Intermolecular Coupling Reactions Catalyzed by Enzymes under Irradiation

On the basis of previous studies of radicals, the Hyster group reported a photo-enzymatic enantioselective intramolecular hydroalkylation with an ERED.<sup>4</sup> Flavin is photoexcited to become a strong reductant to transfer electrons to the substrate. In 2020, the Zhao group reported the intermolecular version of this transformation (**Scheme 3**).<sup>5</sup>



**Scheme 3.** Photo-enzymatic Hydroalkylation

In 2022, an intermolecular C(sp<sup>3</sup>)-C(sp<sup>3</sup>) cross-electrophile coupling reaction between alkyl halides and nitroalkanes catalyzed by an ERED was reported by the Hyster group (**Scheme 4**).<sup>6</sup> The enzyme acts as a template to stabilize the charge-transfer complex formed between substrates, mediate the reactivities, and control the stereochemistry.



**Scheme 4.** Photo-enzymatic Cross-Coupling

### Reference

- [1] Kroutil, W., *ACS Catal.* **2019**, *9*, 4115 [2] Hollmann, F., *Angew. Chem. Int. Ed.* **2018**, *57*, 13648. [3] Hyster, T. K., *Nature* **2016**, *540*, 414. [4] Hyster, T. K., *Science* **2019**, *364*, 1166–1169. [5] Zhao, H., *Nature* **2020**, *584*, 69–74. [6] Hyster, T. K., *Nature* **2022**, ASAP.