

Photoenzymatic Enantioselective Intermolecular Radical Hydroalkylation

Background/objective

Photochemistry may be used to elicit new reactions from existing enzymes, expanding the suite of compounds that can be synthesized via enzymatic catalysis. Photoenzyme use to achieve intermolecular cross-coupling was previously hampered by poor enzymatic photoreactivity and difficulty in achieving stereochemical control. Here, researchers expand the reactivity of ene-reductase (ER) for the synthesis of γ -chiral carbonyl compounds using visible-light-enabled intermolecular radical hydroalkylation of terminal alkenes with α -halo carbonyls.

Approach

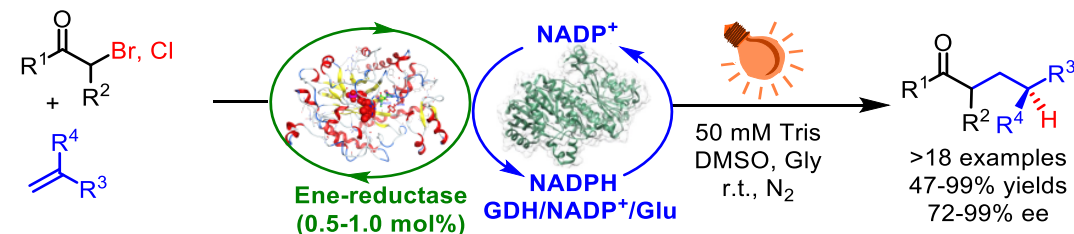
- ❖ Achieved the novel reaction by combining reactants with a catalytic amount of ene-reductase and the cofactor regeneration system under visible-light-illumination.
- ❖ Established a detailed reaction mechanism.

Results

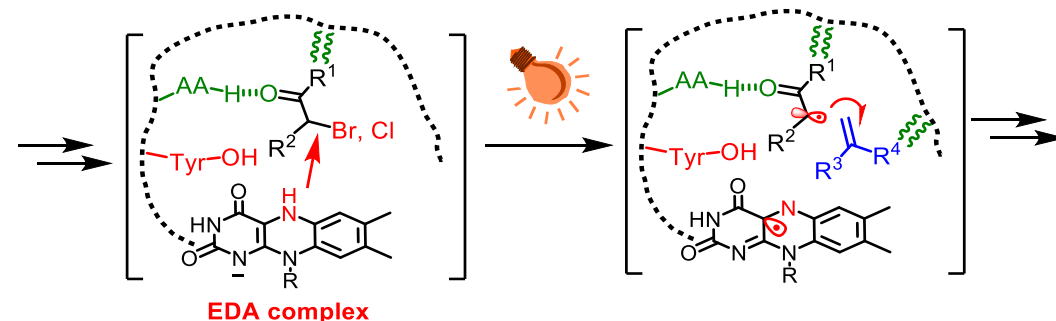
- ❖ Developed a photoenzyme with new-to-nature intermolecular cross coupling reactivity, broad substrate scope, and high yield (up to 99%) and enantioselectivity (up to 99% enantiomeric excess).
- ❖ Established a detailed reaction mechanism in which visible light induces generation of radical intermediates within the enzyme active site, leading to asymmetric cross-coupling of terminal alkenes with α -halo carbonyls to form γ -chiral carbonyl compounds.

Significance

This work demonstrates that combined photoenzymatic catalysis can expand enzyme reactivity to catalyze new-to-nature reactions. The photoenzyme developed here can be used to upgrade alkenes, which can be produced from biomass-derived alcohols or fatty acids. It serves as a proof-of-concept for development of other photoenzymes for bioproduct upgrading.



mechanism



Visible light-driven ene-reductase catalysis for radical hydroalkylation full reaction schematic (top) and key mechanistic steps (bottom).