

Cooperative Asymmetric Reactions Combining Photocatalysis and Enzymatic Catalysis

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<https://cabbi.bio/research/conversion-theme/>

Project Goals: The goal of this work was to develop a novel cooperative chemoenzymatic reaction capable of stereoconvergent reduction of a mixture of alkenes.

Living organisms rely on simultaneous reactions that are catalyzed by mutually compatible and selective enzymes to synthesize complex natural products and other metabolites. To combine the advantages of these biological systems with the reactivity of artificial chemical catalysts, chemists have devised sequential, concurrent, and cooperative chemoenzymatic reactions that combine enzymatic and artificial catalysts. Cooperative chemoenzymatic reactions consist of interconnected processes that generate products in yields and selectivities that cannot be obtained from the two reactions run sequentially with their respective substrates. This feature of cooperative reactions makes them particularly valuable among chemoenzymatic systems. However, such reactions are difficult to develop because chemical and enzymatic catalysts generally operate in different media at different temperatures and can deactivate each other. As a result of these constraints, the vast majority of cooperative chemoenzymatic processes that have been reported over the last 30 years can be divided into just two categories: 1) chemoenzymatic dynamic kinetic resolutions of alcohols and amines, and 2) enzymatic reactions requiring the simultaneous regeneration of a cofactor. New approaches to the development of chemoenzymatic reactions are needed to enable valuable chemical transformations beyond dynamic kinetic resolutions of alcohols and amines and cofactor regenerations. University of Illinois researchers can report a new class of cooperative chemoenzymatic reactions that combine photocatalysts that isomerize alkenes with ene-reductases that reduce carbon-carbon double bonds to generate valuable enantioenriched products. This method enables the stereoconvergent reduction of E/Z mixtures of alkenes or reduction of the unreactive stereoisomers of alkenes in yields and enantiomeric excess (ee's) that match those obtained from the reduction of the pure, more reactive isomers. The system affords a range of enantioenriched precursors to biologically active compounds. More generally, these results show that the compatibility between photocatalysts and enzymes enables chemoenzymatic processes beyond cofactor regeneration and provides a general strategy for converting stereoselective enzymatic reactions into stereoconvergent ones. We are developing a cooperative system by coupling photocatalyst-catalyzed co-factor regeneration and isomerization with enzymatic reduction in one pot. By doing so, we can realize stereoconvergent reduction of a mixture of alkenes without using an expensive and unstable co-factor such as NADPH.

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