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Unlocking Promiscuous Activity of the Photoenzyme Fatty Acid Photodecarboxylase from C. variabilis

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PURPOSE OF THE ABSTRACT

Strategic C-C bond formations are among the most important synthetic reactions in organic chemistry to construct the carbon backbone of complex molecules from small building blocks. Traditional organic approaches often display low atom economy, thus producing higher amounts of waste compared to applying enzymes because of the need of sophisticated reagents. The photoenzyme Fatty Acid Photodecarboxylase (CvFAP) from the microalgae C. variabilis, was recently identified and characterized to decarboxylate fatty acids into their corresponding Cn-1 alkanes or alkenes under a continuous flux of blue light via a radical mechanism [1-3]. Inspired by precedence in chemical photocatalysis utilizing carboxylic acids for radical decarboxylative couplings, [4] we investigated the capability of CvFAP to catalyze the decarboxylation of unsaturated fatty acids, bearing an internal electron acceptor within the chain. The intermediate radical generated upon decarboxylation then undergoes an intramolecular cyclization leading to alkylated ring systems.

Herein we demonstrate the proof-of-concept for the desired promiscuity by illuminating suitable fatty acids bearing internal electron acceptors, with variants of CvFAP, in an in-house built photoreactor (Figure 1, A and B). Suitable variants resulted in different ratios of cyclized and decarboxylated product.

FIGURES

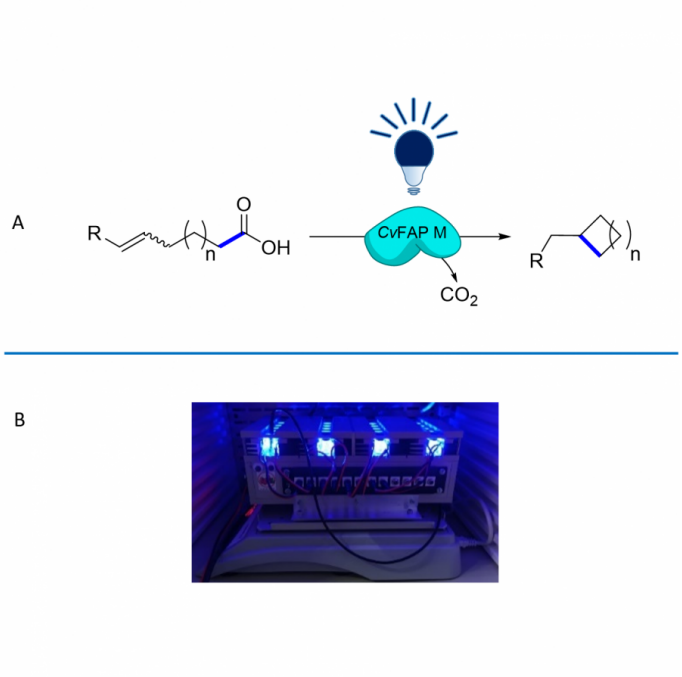

FIGURE 1

Promiscuous activity of CvFAP towards radical intramolecular cyclizations.
(A) Generalized scheme for promiscuous intramolecular C-C bond formations using a suitable CvFAP mutant. (B) Photodecarboxylation in an in-house built photoreactor.

FIGURE 2

KEYWORDS

enzyme promiscuity | photobiocatalysis | C-C-bond formations | protein engineering

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