**PRENYLATED FLAVIN-DEPENDENT DECARBOXYLASES: STRUCTURE-GUIDED ENGINEERING AND SYNTHETIC APPLICABILITY**

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The recently discovered prenylated flavin (prFMN) cofactor is utilised by UbiD enzyme family to catalyse non-oxidative decarboxylation of precursors of respiratory quinones. Mechanistic aspect of prFMN-mediated decarboxylation has attracted interests and studies of fungal ferulic acid decarboxylases (FDCs), members of the UbiD enzyme family reveal a rare enzymatic 1,3-dipolar cycloaddition mechanism for the decarboxylation of cinnamic aid.

We have demonstrated the applicability of prFMN-dependent FDCs for both isolated enzyme and whole-cell biocatalysis. Using in-vitro (de)carboxylase activity of prFMN bound-FDCs, we performed a substrate profiling study of four FDCs, providing insights into structural determinants of activity (Figure 1). The FDC-UbiX system enables access to a variety of industrially relevant terminal alkenes from acrylic acid derivatives bearing (hetero)cyclic or olefinic substituents at C3; affording conversions of up to >99 %.

Importantly, the application of the FDC in carboxylation direction has been achieved allowing the functionalisation of unactivated terminal alkenes under mild reaction conditions. By applying structure-guided protein engineering, we have developed FDC variants acting on a wide range of unactivated (hetero)aromatic carboxylic acids, hence expanding the product profile of enzymatic (de)carboxylation. Development of efficient prFMN-dependent enzymes will immensely expand the scope of biocatalytic (de)carboxylation reactions.

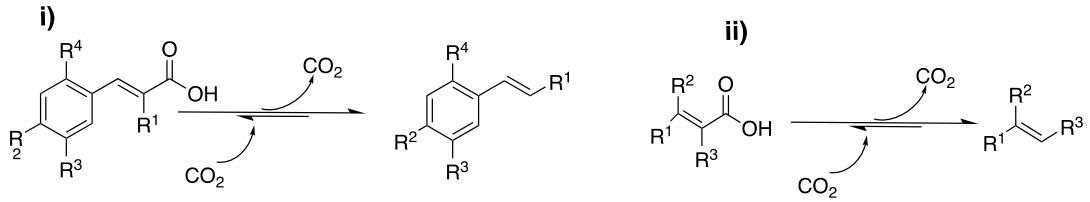


*Figure 1. Overview of substrate specificity of prFMN-dependent ferulic acid decarboxylases (FDCs).*

References

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