J. M. ELLIS, M. E. CAMPBELL, P. KUMAR, E. P. GEUNES, C. A. BINGMAN, A. R. BULLER*
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Biocatalytic Synthesis of Non-Standard Amino Acids by a Decarboxylative Aldol Reaction
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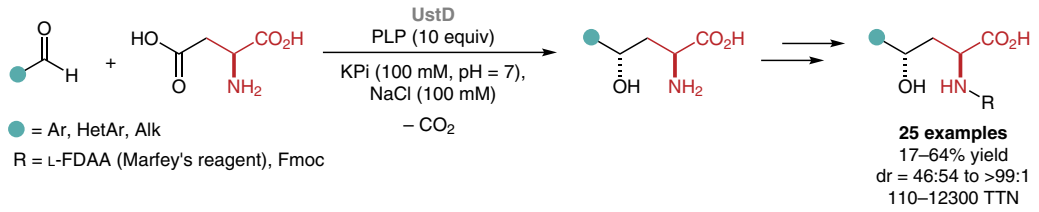
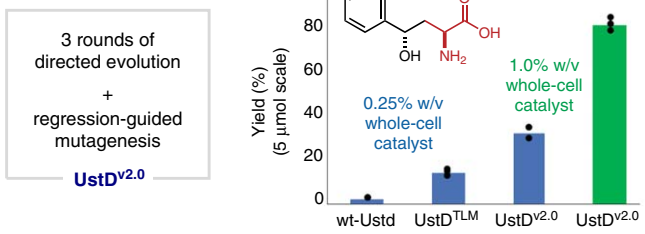
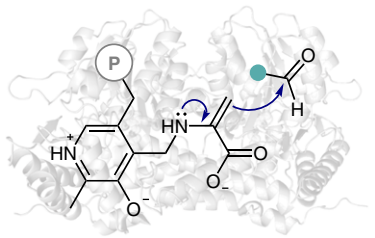
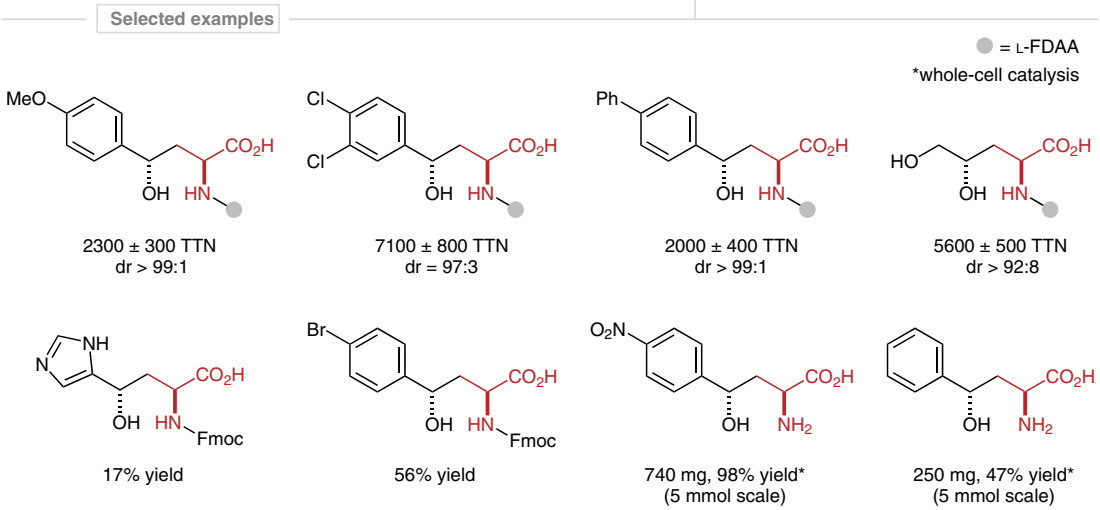
Directed Evolution Toward Nonstandard Amino Acids by a Decarboxylative Aldol Reaction









Significance: Buller and co-workers disclose an enantioselective synthesis of γ-hydroxy amino acids catalyzed by engineered variants of a pyridoxal 5′-phosphate (PLP)-dependent enzyme. Various products of C–C bond-forming reactions were obtained in moderate to excellent yields and enantioselectivities. The optimized enzyme UstD$^{v2.0}$ is efficient in a whole-cell biocatalysis format, thereby eliminating the need for enzyme purification in gram-scale syntheses.

Comment: Unlike other classic aldolases, UstD is capable of decarboxylating the side chain of pyridoxal-bound L-aspartate to form a putative nucleophilic enamine intermediate, which renders the enantioselective C–C bond-forming reaction effectively irreversible. An X-ray crystal-structure analysis of UstD$^{v2.0}$ revealed the active site and provides a foundation for probing the UstD mechanism. A broader scope of gram-scale whole-cell applications is anticipated.

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Category
Organo- and Biocatalysis

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decarboxylation
aldol reaction
amino acids
directed evolution

Synfact of the Month