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TOPIC(s) : Biocatalytic cascade reactions / (Chemo)enzymatic strategies

?1-Piperidine-2-carboxylate/?1-pyrroline-2-carboxylate reductase from Pseudomonas syringae (DpkAPsyrin) as catalyst for the synthesis 2-hydroxy-4-arylbut-3-enoic acid derivatives

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PURPOSE OF THE ABSTRACT

NAD(P)H-dependent Δ1-piperideine-2-carboxylate/Δ1-pyrroline-2-carboxylate reductase from Pseudomonas syringae pv. tomato (DpkAPsyrin, EC 1.5.1.21) catalyzes the stereoselective reduction of Δ1-piperideine-2-carboxylate and Δ1-pyrroline-2-carboxylate to L-pipecolic acid and L-proline respectively. Furthermore, DpkAPsyrin is also able to catalyze the enantioselective synthesis of N-methyl-L-amino acids from methylamine and various 2-oxo acids [1]. In our research group, we observed that in addition to the imine reductase activity, DpkAPsyrin have a promiscuous ketoreductase activity and, consequently, we consider interesting to exploit its underdeveloped synthetic capabilities for the synthesis of 2-hydroxy-4-arylbut-3-enoic acid (4). These 2-hydroxyacids are intermediates in the synthesis of 2-hydroxy-4-arylbutanoic acid, important building blocks for the production of a variety of angiotensin converting enzyme (ACE) inhibitors (e.g. enalapril, lisinopril, cilapril, and benazepril) [2].

In this communication we reported the preparation of structurally diverse (S)-2-hydroxy-4-arylbut-3-enoic acid (4) (isolated yield: 57%-78% and ee: 87%->99%) from aromatic aldehydes (1) and pyruvate (2) by enzymatic cascade reaction using trans-o-hydroxybenzylidene pyruvate hydratase-aldolase from Pseudomonas putida HBPAPputida) [3] and DpkAPsyrin (Scheme 1). The cascade process was possible because it was found that the ketoreductase preferentially reduced the aldol condensation adducts (3) rather than the pyruvate (2). This allows for high levels of 2-hydroxy-4-arylbut-3-enoic acids (4) conversions (>95% after 24 h).

FIGURES

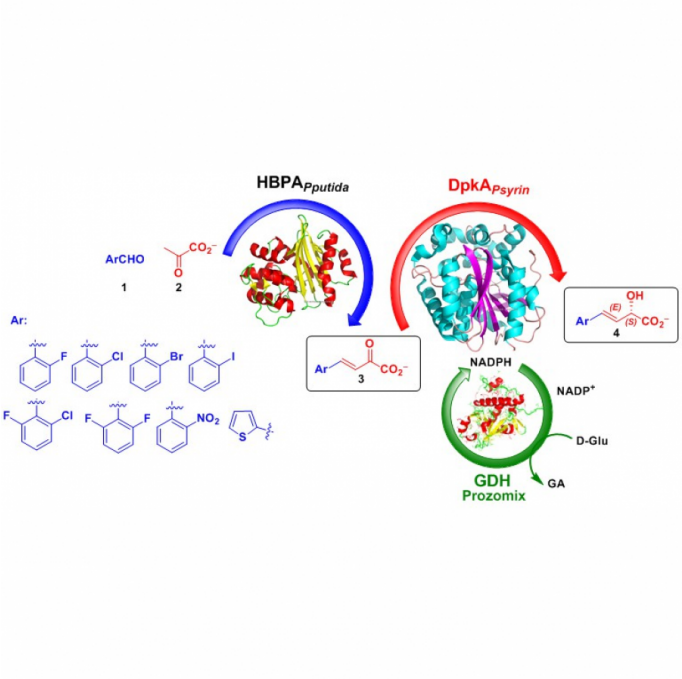

FIGURE 1

Scheme 1

Synthesis of (S)-2-hydroxy-4-arylbut-3-enoic acid (4) through enzymatic cascade reaction.

FIGURE 2

KEYWORDS

Ketorreductase | trans-o-hydroxybenzylidene pyruvate hydratase-ald | 2-Hydroxy-4-arylbut-3-enoic acids | biocatalytic cascade

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