BIOTRANS
LA ROCHELLE 2023

N°1065 / PC
TOPIC(s) : (Chemo)enzymatic strategies / Enzyme discovery and engineering

P450 peroxygenases – regio- and stereoselective hydroxylation of fatty acids

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PURPOSE OF THE ABSTRACT
P450 peroxygenases, a subgroup of the cytochrome P450s, allow a similar oxy-functionalization as P450 monooxygenases but are independent of reduced nicotinamide cofactors and rely on hydrogen peroxide only. [1] The mechanism relies on the hydrogen peroxide-shunt. [2] These peroxygenases can for instance be used for the biocatalytic α-functionalization of medium-chain fatty acids. Six potential enzyme candidates of the CYP152 family, P450Spα [3], P450CLA [4], P450Bsβ F79L/G290F [5], P450Exα [6], CYP152K6 [7] and P450Jα [8] were expressed, purified and the conversions of caproic acid (C6:0), caprylic acid (C8:0) and capric acid (C10:0) were investigated (Figure 1).

Biotransformations with P450CLA, P450Spα, P450Exα, and CYP152K6 led to successful conversion giving the corresponding α-hydroxylated fatty acids. The most promising results were obtained with P450Spα whereby C8:0 and C10:0 were very well converted (>99% conv.) and a high percentage of α-hydroxylated products was achieved (for C8:0 and C10:0 89% and 85% α-hydroxylation, respectively). P450Exα, is an excellent candidate for the conversion of C6:0 (95% conv.) and showed high regioselectivity (70% α-hydroxylation). The main side-product was the β-hydroxylated product in the conversion of C8:0 and C10:0. All tested CYP152 are (S)-stereoselective. P450Spα, P450Exα, and CYP152K6 displayed high stereoselectivity for the conversion of C6:0, C8:0 and C10:0. In addition, P450Exα successfully converted the dicarboxylic acids nonane-1,9-dioic acid and decane-1,10-dioic acid exclusively to the corresponding monohydroxylated 2-hydroxynonane-1,9-dioic acid and 2-hydroxydecane-1,10-dioic acid, the latter with >99% conversion.

This project has received funding from the European Union's Horizon 2020 research and innovation program under Marie Skolodowska-Curie grant agreement ID: 956621.

FIGURES

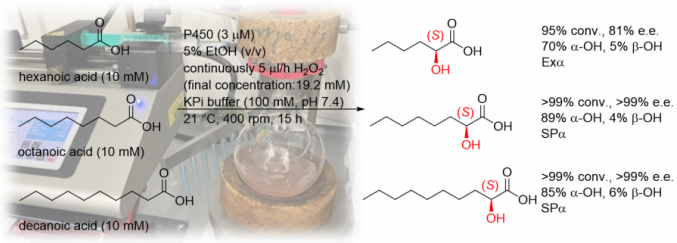

FIGURE 1

FIGURE 2

KEYWORDS

P450 Peroxygenases | Fatty Acids | Regioselectivity | Stereoselectivity

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