MULTIENZYME-CASCADES FOR THE FUNCTIONALIZATION OF FATTY ACIDS

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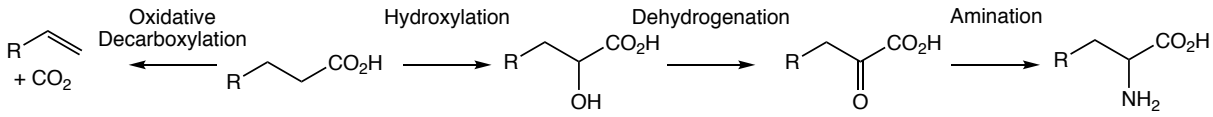
The vast majority of carbon-based starting materials (>90%) for organic synthesis are petroleum-derived alkanes and alkenes, which are oxidatively functionalized by introduction of functional groups. With few exceptions, C-H oxo-functionalization of alkanes using chemical methodologies is impeded by insufficient catalytic activities and imperfect (regio)selectivities. Bio-hydroxylation mediated by cytochrome P450 enzymes, which may be operated in the mono- or per-oxygenase-mode using O_2/NAD(P)H or H_2O_2 as oxidant, respectively, are able to hydroxylate fatty acids as renewable substitutes for petroleum-based carbon feedstocks. Whereas bio-hydroxylation of the ω- or (ω-1) position is well understood,[1a] α- and β-hydroxylation is scarcely exploited.[1b]

Recently, we developed several multistep cascade-processes for the functionalization of fatty acids:
— Oxidative decarboxylation of fatty acids by P450 OleT yields the corresponding terminal alkenes.[2]
— α-Hydroxylation of fatty acids by P450 enzymes yields the corresponding α-hydroxy acids, which are further oxidized by stereo-complementary α-hydroxyacid-oxidases or -dehydrogenases to furnish α-keto acids. In-situ amination of the latter gives α-amino acids as final products. The efficiency of these cascades was optimized by re-cycling of redox equivalents [H_2O_2 or NAD(P)H] in a redox-neutral mode.[3]



Acknowledgements: Financial support by Evonik Industries (Germany) and the Austrian FFG-COMET-Funding is gratefully acknowledged.

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