Enzymatic cascade for the production of halogenated API precursors

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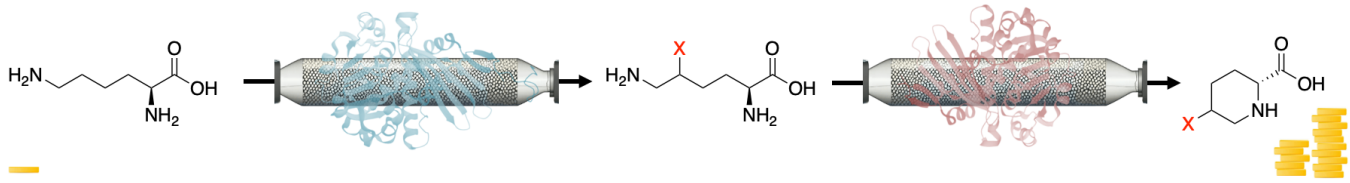
The synthesis of pipecolic acid derivatives is critical for the development of bioactive molecules and pharmaceutical compounds, particularly local anaesthetics and antibiotics. Halogens are known to enhance the pharmacokinetic and pharmacodynamic profiles of APIs and facilitate cross-coupling reactions essential for complex drug synthesis.[1] However, traditional synthetic methods struggle with the regioselective halogenation of unactivated sp^3 C-H bonds, a challenge overcome by our biocatalytic approach. We report the usage of engineered variants of Lysine Cyclodeaminase and a Hydroxylase in a two-enzyme cascade to produce chiral halogenated pipecolic acid from cost-effective starting materials.[2] The process is designed for scalability and high efficiency by utilising immobilised enzymes, with the potential of future integration in continuous flow reactors for enhanced performance.



[1] G. Gerebtzoff, X. Li-Blatter, H. Fischer, A. Frentzel, *ChemBioChem*, **2004**, 5, 676–684.
[2] Neugebauer, M.E., Sumida, K.H., Pelton, J.G. *et al. Nat Chem Biol*, **2019,** 15, 1009–1016