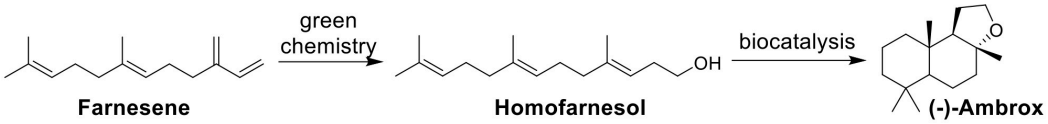
Sustainable (-)-ambrox production: chemistry meets biocatalysis

A. Bombrun[1], E. Eichhorn[1], S. Schilling[1], F. Schröder[1]

[1]Givaudan Schweiz AG, Ingredients CoE, Fragrance S&T, Kemptpark 50, CH-8310 Kemptthal

(-)-Ambrox, the most prominent olfactive component of ambergris is one of the most widely used biodegradable fragrance ingredients. It is traditionally produced from the diterpene sclareol, transformed into (-)-ambrox by classical synthetic chemistry. The availability of the new feedstock farnesene opened new pathways to homofarnesol for (-)-ambrox production. *Alicyclobacillus acidocaldarius* Squalene Hopene Cyclase (SHC) was evolved by means of random mutagenesis to biocatalysts suitable for (-)-ambrox production at industrial scale. Amino acid mutations responsible for improving homofarnesol cyclization were identified. Enzyme evolution together with process optimization produced improved SHC variants allowing for the diastereo- and enantioselective conversion of up to triple digit gram per liter homofarnesol to (-)-ambrox [1]. In parallel, access to the required homofarnesol precursor was investigated. Routes starting from farnesene were developed [2], delivering efficient processes for homofarnesol and its precursors at multi-ton scale for (-)-ambrox production. This double invention led to a sustainable production of the fragrance ingredient (-)-ambrox as a drop-in quality for Ambrofix™ [3].



[1] E. Eichhorn, E. Locher, S. Guillemer, D. Wahler, L. Fourage, B. Schilling.*Adv. Synth. Catal.*, **2018**, *360*, 2339-2351.
[2] F. Schröder, F. Rüthi, WO2015059290, Givaudan SA, Amyris Inc.; F. Schröder, WO2015059293, Givaudan SA, Amyris Inc.; S. Ellwood, C.-L. Tse, WO 2022136232, Givaudan SA.
[3] E. Eichhorn, F. Schröder. *J. Agric. Food Chem.*, **2023**, *71*, 5142-5052.