BIOTRANS
LA ROCHELLE 2023

N°917 / PC
TOPIC(s) : Biocatalytic cascade reactions / (Chemo)enzymatic strategies

From smelly sulphur substrates to fragrant flavours – enzymatic synthesis of L methionine analogues and their usage for alkylation

AUTHORS

Michael MOHR / ALBERT-LUDWIGS-UNIVERSITÄT, FREIBURG, ALBERTSTR. 25, FREIBURG
Raspudin SALEEM-BATCHA / ALBERT-LUDWIGS-UNIVERSITÄT, FREIBURG, ALBERTSTR. 25, FREIBURG
Corresponding author : Jennifer N. ANDEXER / jennifer.andexer@pharmazie.uni-freiburg.de

PURPOSE OF THE ABSTRACT

Regio- and stereoselective alkylation of small molecules can impact their physicochemical and pharmaceutical properties.[1,2] Highly selective methyltransferases (MTs) are promising tools for the transfer of alkyl chains onto various substrates.[1,3,4] S-adenosyl-L-methionine (SAM) analogues are utilised for the alkylation and can either be generated from L-methionine analogues and ATP by an L methionine adenosyltransferase (MAT) or by using the analogues in combination with 5´-chloro adenosine and the SAM chlorinase SalL.[5,6] So far most of the commercially unavailable L-methionine analogues have to be chemically synthesised.[7]

We explored an alternative approach, following the enzymatic synthesis of L-ethionine. The simplest modified L-methionine analogue can be synthesised from L-homocysteine and ethanthiol using the O-acetyl-L-homoserine sulfhydrolase from S. cerevisiae (ScOAHS). Investigation on the substrate scope of ScOAHS revealed a promiscuous enzyme. Starting from L homocysteine and organic thiols, different L methionine analogues with newly introduced functionalities at the transferable thioether residue could be synthesised.

Based on these results we expanded our selective alkylation cascade,[3] using the O MT from Rattus norvegicus with the substrate protocatechuic aldehyde. We successfully transferred alkyl chains onto the substrate and thereby synthesised new derivatives of the flavour vanillin (s. Figure 1).[8]

FIGURES

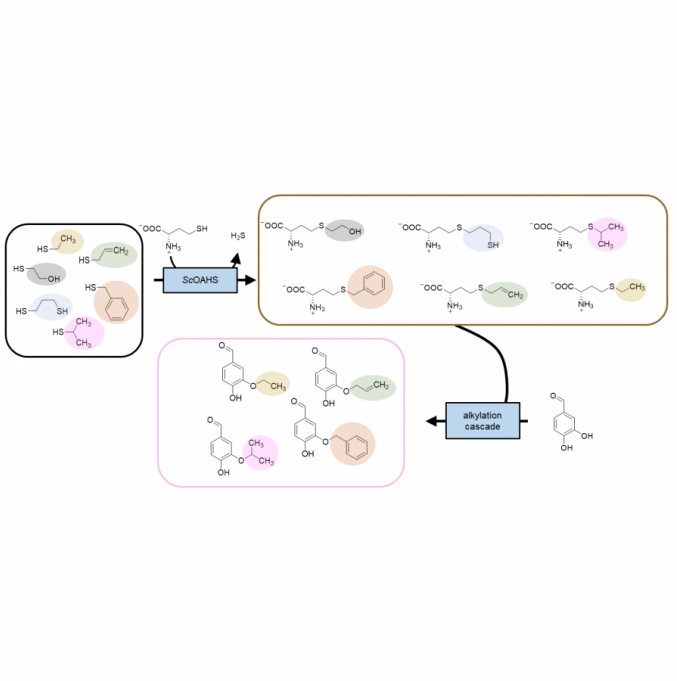

FIGURE 1

Figure 1

Utilisation of sulphur substrates for alkylation. Organic thiols (black box) are used by ScOAHS with L-homocysteine to synthesise the L-methionine analogues (blue box). When this set up is combined with the alkylation cascade enzymes the utilised RnCOMT t

FIGURE 2

KEYWORDS

unnatural amino acids | SAM analogues | enzymatic alkylation | enzyme cascade

BIBLIOGRAPHY