BIOTRANS
LA ROCHELLE 2023

N°232 / PC
TOPIC(s) : Biocatalytic cascade reactions

A single biocatalyst for an alcohol oxidation ? conjugated addition cascade reaction

AUTHORS
Mathias PICKL / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28/II, GRAZ
Andrea RAAB / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28/II, GRAZ
Jasper S. MÖHLER / ETH ZÜRICH, VLADIMIR-PRELOG-WEG 3, ZURICH
Helma B. WENNEMERS / ETH ZÜRICH, VLADIMIR-PRELOG-WEG 3, ZURICH
Corresponding author : Wolfgang KROUTIL / wolfgang.kroutil@uni-graz.at

PURPOSE OF THE ABSTRACT

Aldehydes offer the reactivity as starting material to access many compound classes. Biocatalysis has a strong record in carbonyl modifying redox chemistry and a plethora of potent catalysts is available to produce e.g. aldehydes from primary alcohols via oxidation. However, utilizing aldehydes in carbon-carbon bond formations, biocatalysis is outperformed by the reaction portfolio of organocatalysis. The enzymatic equivalents for reactions such as Michael additions, Mannich reactions or Knoevenagel condensations are inconceivably underexplored.[1] Remarkably, many organocatalytic reactions such as the Michael addition are mediated by proteinogenic amino acids or peptides.[2] Hence, we envisioned that a biocatalyst can be designed that has the ability to oxidize a primary alcohol to the corresponding aldehyde and in parallel enables enamine catalysis allowing the ?-carbon of the aldehyde to act as a nucleophile in a Michael addition.

Several alcohol dehydrogenases and alcohol oxidases were screened for their ability to mediate the redox reaction.[3] To enable the carboligation, a peptide sequence known to mediate Michael additions was N-terminally attached, or alternatively, it was tested whether amino acid side chains such as the ?-amino groups of lysine can catalyze a Michael addition (Figure 1). It turned out that several designed candidates mediate the desired conjugated addition. In case an appropriate co-factor recycling system is chosen, a one-pot, one-step cascade system is feasible starting from aliphatic alcohol and yielding g-nitro aldehydes.

FIGURES

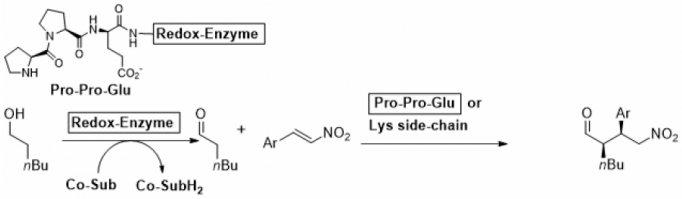

FIGURE 1

Scheme 1

FIGURE 2

KEYWORDS

Cascade | Alcohol Oxidation | Conjugated Addition

BIBLIOGRAPHY

[1] G. Xu, G. J. Poelarends, Angew. Chem. Int. Ed.2022, 61, e202203613.

[2] M. Wiesner, J. D. Revell, H. Wennemers, Angew. Chem. Int. Ed. 2008, 47, 1871-1874.

[3] J. Dong, E. Fernández-Fueyo, F. Hollmann, C. Paul, M. Pasic, S. Schmidt, Y. Wang, S. Younes, W. Zhang, Angew. Chem. Int. Ed. 2018, 57, 9238-9261.