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Biocatalytic hydronitration of α,β-unsaturated carboxylic acids

AUTHORS
Matteo ALEOTTI / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28 / II, GRAZ
Hannah DREISBACH / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28 / II, GRAZ
Rémi CORLAY / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28 / II, GRAZ
Mélanie HALL / UNIVERSITY OF GRAZ, HEINRICHSTRASSE 28 / II, GRAZ

PURPOSE OF THE ABSTRACT
The nitro functionality (-NO2) is one of the most versatile groups in chemistry. Indeed, due to its strong electron-withdrawing properties, it confers exceptional reactivity in a myriad of synthetic reactions. Moreover, nitro compounds are notorious precursors to amines, and they are widely exploited as chemotherapeutic agents, prodrugs, explosives and as building blocks for dyes and polymers.[1] Despite the synthetic difficulties related to the introduction of the nitro group, such as the requirement for high temperatures and mixtures of strong acids, and the poor selectivity of the synthesis, this reaction is still exploited on industrial scale due to a lack of milder approaches. A few enzymes however can handle the nitro moiety in the context of natural metabolic pathways under mild conditions.[2] Thus, biocatalysis may provide a suitable alternative to perform selective nitration reactions under environmentally friendly conditions.
In this work, the enzymatic nitration of α,β-unsaturated carboxylic acids by the nitrosuccinate lyase (CreD)[3] was investigated. We could demonstrate that the enzyme can catalyze the hydronitration of fumaric acid on 50 mM substrate loading with high catalytic efficiency (TTN up to 20,000). In order to expand the substrate scope to a variety of conjugated carboxylic acids, and due to the substrate selectivity of the enzyme for fumaric acid, the re-design of the active site is currently being explored and will be discussed, along with recent findings on the promiscuity within this enzyme family.

FIGURES

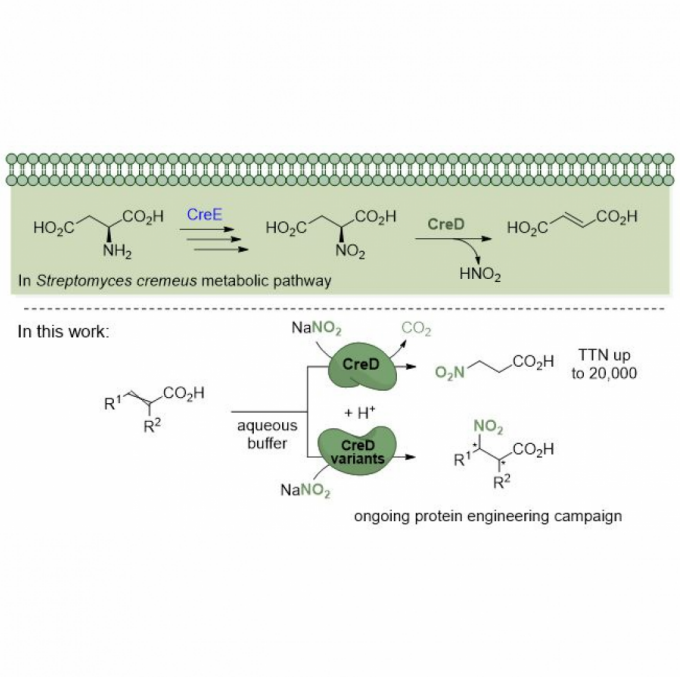

FIGURE 1

Figure 1:

Occurrence of the nitrosuccinate lyase activity of CreD in Streptomyces cremeus (above) and enzymatic strategies for the hydronitration of unsaturated carboxylic acid using CreD (below).

FIGURE 2

KEYWORDS

Enzymatic hydronitration | α,β-unsaturated carboxylic acids | Protein engineering | Nitrosuccinate lyase

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[3] Y. Katsuyama, Y. Sato, Y. Sugai, Y. Higashiyama, M. Senda, T. Senda, Y. Ohnishi, FEBS J 2018, 285, 1540-1555.