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Pyrrolnitrin congeners: Selective access via biocatalytic halogenation

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PURPOSE OF THE ABSTRACT
Pyrrolnitrin is an antifungal agent that requires two halogenating enzymes in its biosynthesis.[1,2] Halogenating enzymes have evolved several times in nature,[3] yet their biocatalytic use remains limited. Obvious arguments are that biocatalytic use may be more sustainable, which needs to be proven, but undisputed is the argument that toxic elemental halogens are avoided here. In this study, however, we were able to show above all that halogenating enzymes may well have advantages, particularly in regioselectivity.
The flavin-dependent halogenase PrnC from Pseudomonas protegens Pf-5 was successfully heterologously expressed in Escherichia coli and isolated. The enzyme requires an electron transport protein namely a flavin reductase for function. The use of the E. coli homolog SsuE[4] failed because of solubility issues during hmologoues expression, thus, the natural flavoprotein PrnF from the same biosynthetic cluster proved to be advantageous for biocatalytic conversions. Overall, an in vitro system consisting of the halogenase, the flavoreductase, and a glucose dehydrogenase for cofactor recycling was optimized by a design-of-experiment in such a way that it could be used for the synthesis of non-natural congeners.
It is worth noting that these halogenations could not be introduced by chemical methods, so that this approach provides access to such pyrrolnitrin analogs for the first time.

FIGURES

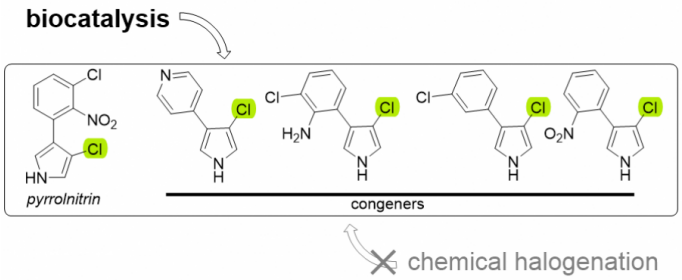

FIGURE 1

Pyrrolnitrin and synthesized congeners

Marked in green is the halogen that has been introduced by PrnC.

FIGURE 2

KEYWORDS

Halogenation | Antifungal Agent | flavin-dependent halogenase

BIBLIOGRAPHY