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Homospermidine synthase facilitated N-cross coupling and applications in N-heterocycle synthesis.

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PURPOSE OF THE ABSTRACT

Polyamines (PAs) are a diverse and ubiquitous class of molecules with essential cellular functions including cell proliferation, apoptosis, and DNA stabilization. Additionally they are a utilitarian intermediates for the biosynthesis of pyrrolizidine and indolizidine alkaloids, a potent class of therapeutics with antiviral and anticancer properties. Despite the abundance and diversity of polyamines in nature, bulk chemical syntheses of such molecules remains a challenge due to selectivity issues associated with traditional chemical synthesis.

Homospermidine synthase (HSS) is a key enzyme in the biosynthesis of PAs, with HSS from Blastochloris viridis (BvHSS) able to catalyse the synthesis of homospermidine from two molecules of putrescine in a hydrogen borrowing type mechanism that can be described as an N-cross coupling reaction. In this work, we present the use of BvHSS as a biocatalyst to produce homospermidine, and structurally related PAs, as well as several non-natural PA analogues via BvHSS catalysed N-cross coupling between diamine donors and non-biogenic amine acceptors including amino alcohols, amino acids, and alkylamines.

Subsequently, we combined BvHSS with diamine oxidases, transaminases, and choline oxidase in order to obtain a number of N-heterocycles.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

biocatalysis | heterocycle | poly-amine | enzyme cascades

BIBLIOGRAPHY

Krossa, S., Faust, A., Ober, D. et al. . Sci Rep 6, 19501 (2016).

Ramsden, J., Turner, N J,. et al.. J. Am. Chem. Soc. 141, 3, 1201-1206 (2019)