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The Biocatalytic Synthesis of Indoles from Indolines

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PURPOSE OF THE ABSTRACT

The indole scaffold is a prominent structure in organic chemistry due to its prevalent presence in both natural products and in the pharmaceutical industry [1]. Examples of its use as a building block for pharmaceutical compounds include frovatriptan, indomethacin, sumatriptan and rizatriptan [2]. Indole- containing natural products include examples such as vincamine, psilocin, melatonin and tryptophan [3]. The evolution of methods to synthesise this important heterocycle has been a key concern for organic chemists for years. However, many methods that have been developed, such as the well-known Fischer synthesis of indoles [4] utilise harsh reaction conditions and often require the use of rare metals and stoichiometric amounts of oxidising agents. This is unappealing in a world striving towards green chemistry. An alternative approach which has scarcely been explored in literature is the use of chemo-enzymatic and biocatalytic methods inspired by nature to synthesise indoles and their derivatives [5]. Enzymes are now widely exploited to construct stereospecific chemical bonds, however their use as biocatalysts has seldom been explored. This work has been inspired by natural metabolic transformations and demonstrates the aromatization of indoline derivates into indoles biocatalytically, exploiting monoamine oxidase (MAO-N) enzymes. MAO-N D11 whole cell biocatalyst was used to chemoselectively aromatize indoline substrates. The substrates for biocatalysis were prepared either by arylative dearomatization of unsubstituted indoles or by photocatalytic cyclisation of arylaniline precursors. The biocatalytic mechanism and experimental results were explained by computational docking studies of the indoline substrates in the MAO-N active site. The findings of this study show an efficient way to biocatalytically synthesise nonchiral aromatic molecules under mild reaction conditions and the huge potential of MAO-N enzymes to be used as aromatizing biocatalysts.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

indole | monoamine oxidase | chemoenzymatic cascade | biocatalysis

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