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Enantioselective Synthesis of Pyrroloindolines Bearing Heteroaromatic Side-Chains

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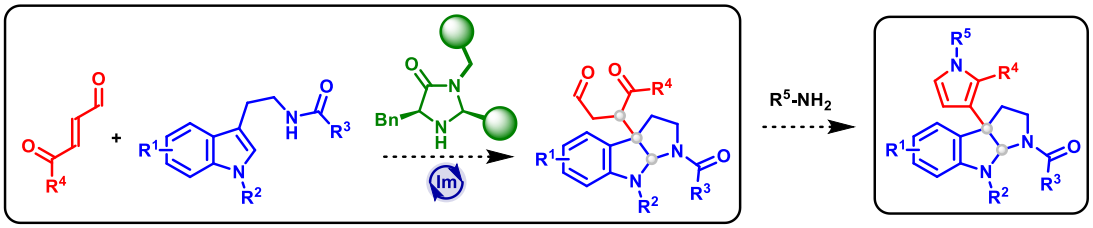
ABSTRACT

Pyrroloindoline is a tricyclic benzofused heterocyclic system found in several bioactive compounds with pharmaceutical potential.[1] Natural and synthetic compounds bearing pyrroloindolines in their structure were found to have antitumor and antibacterial activity.[2] Given the growing impact of neurodegenerative diseases, pyrroloindolines acting as cholinesterase inhibitors were investigated for the treatment of Alzheimer's disease.[3]

In 2004, MacMillan and co-workers described the enantioselective synthesis of pyrroloindolines from unsaturated aldehydes and tryptamines. In his work, MacMillan reacted *α,β*-unsaturated aldehydes and *N*-carbamoyl-tryptamines using enantioselective iminium-ion catalysis.[4]

In this work, pyrroloindolines bearing heteroaromatic side-chains are prepared using chiral iminium ions formed *in situ* from *γ*-keto-*α,β*-unsaturated aldehydes. The initially formed 1,4-dicarbonyl compounds are then subjected to different Paal-Knorr reactions. The loss of the stereocenter initially formed *β* to the aldehyde moiety means that the enantioselectivity of the final product is dependent on the diastereoselectivity of the first step.



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