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Exploring the Bifunctional Organocatalysts for Asymmetric Synthesis of 3-Substituted-3-Aminooxindoles

Authors : Jasneet Kaur, Swapandeep Singh Chimni

Abstract : The unfavorable use of metal-based catalysts that are often extortionate and toxic can be overcome by using small organic molecules known as organocatalysts. A variety of small organic molecules, including Brønsted/Lewis bases and acids, based on sulfonic acids, phosphoric acids, amines, phosphines or carbenes, Cinchona alkaloids, have been used as organocatalysts. One of the key reasons for using organocatalysis is their ability to be effectively removed from the final product in comparison to the metallic counterparts, which are exceedingly difficult to remove. The present investigation seeks to explore the catalytic nature of Cinchona alkaloids as an organocatalyst for enantioselective synthesis of 3-substituted-3-aminooxindole, which is known to exhibit a variety of biological activities and pharmacological activities. In this context, an organocatalytic asymmetric route for the synthesis of 3-aminooxindoles via reaction of isatin imine with α-acetoxy-β-ketoesters has been developed. The bifunctional Cinchona derived thiourea catalyzed the reaction of α-acetoxy-β-ketoesters derivatives with isatin imine to afford 3-substituted-aminooxindole derivatives in up to 93% yield, 95% enantiomeric excess and >20:1 diastereomeric ratio. The reaction was performed at room temperature for two hours using 10 mol% of catalyst, in the presence of 4Å molecular sieves in tetrahydrofuran as a solvent at ambient temperature. After the completion of the reaction, the pure product could be easily separated by using column chromatography using hexane and ethyl acetate as solvents. In conclusion, the catalytic potential of Cinchona derived chiral thiourea-tertiary amine catalyst was explored for an organocatalytic enantioselective Mannich reaction of β-ketoester derivatives with various isatin imine derivatives under mild conditions.

Keywords : asymmetric synthesis, aminooxindoles, enantioselective, isatin imine
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