MULTICOMPONENT ORGANOCATALYTIC SYNTHESIS OF ISOXAZOLIDIN-5-ONES

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Isoxazolidin-5-one derivatives are important heterocyclic building blocks in organic synthesis.[1] This heterocyclic ring has been used for the elaboration of bioactive compounds such as nucleoside analogues or steroidal compounds.[2] Moreover, isoxazolidin-5-ones are useful precursors of β-amino acids after reductive cleavage of the N-O bond[1] or by making use of the KAHA ligation process, developed by the Bode group.[3]

Our team have developed an efficient racemic and diastereoselective multicomponent reaction (MCR) involving Meldrum’s acid, various aldehydes and N-acylhydroxylamines upon a Knoevenagel-azaMichael-cyclocondensation (KaMC) domino process.[4] In the context of more recent development, we tackled an organocatalytic enantioselective synthesis of isoxazolidin-5-one derivatives through the multicomponent KaMC reaction.[5] Thanks to an original chiral Brønsted base catalyst (R₃N⁺), a series of chiral isoxazolidin-5-one derivatives were obtained in moderate to high yields and up to 81% ee. We are pleased to describe herewith the development of a stereoselective KaMC reaction together with the use of isoxazolidin-5-one derivatives as precursors of β-amino acid derivatives.

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