

An Organocatalytic Construction of Vicinal Tetrasubstituted Stereocenters via Mannich Reaction of 2-Substituted Benzofuran-3-One with Isatin-Derived Ketimine

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Abstract : 3-substituted 3-amino-2-oxindole skeleton bearing adjacent tetrasubstituted stereogenic centers is of great importance because of these heterocyclic motifs possess a wide range of pharmacological activity. The catalytic asymmetric construction of multi functionalised heterocyclic compound with adjacent tetrasubstituted stereocenters is one of the most difficult tasks in organic synthesis. To date, the most straightforward methodologies have been developed for synthesis of chiral 3-substituted 3-amino-2-oxindoles through the addition of carbon nucleophiles to isatin-derived ketimines. However, only a few successful examples have been described for the assembly of vicinal tetrasubstituted stereocenters using isatin derived ketimines as electrophiles. On the other hand, 2,2-Disubstituted benzofuran-3(2H)-ones and related frameworks are characteristic of a quaternary stereogenic center at C2 position present in quite a number of natural products and bioactive Molecules. Despite the intensive efforts devoted for the construction of 2,2-Disubstituted Benzofuran-3[2H]-one, there are only a few asymmetric methods such as organocatalytic Michael addition and enantioselective halogenations were reported till now. Due to the biological importance of oxindole and benzofuran-3-one, it is proposed here with the synthesis of hybrid molecule containing tetrasubstituted stereo centers through asymmetric organocatalysis. The addition of 2-substituted Benzofuran-3-one(1a) to isatin-derived ketimines(2a) using a bifunctional organocatalyst(catalyst IV or V), leading to chiral heterocyclic compounds containing both 3-amino 2-oxindole and benzofurn-3-one bearing vicinal quaternary stereocenters with good yields and excellent enantioselectivity. The present study extends the scope of the catalytic asymmetric Mannich reaction with isatin-derived ketimines, providing a new class of amino oxindole derivatives having benzofuran-3-one.

Keywords : asymmetric synthesis, benzofuran-3-one, isatin-derived ketimines, quaternary stereocenters

Conference Title : ICOC 2018 : International Conference on Organic Chemistry

Conference Location : Copenhagen, Denmark

Conference Dates : June 11-12, 2018