Organocatalyzed Reductive Amination and its Application in the Construction of Biologically Significant Molecules

Pavel Kočovský

Department of Organic Chemistry, Charles University
12843 Prague 2, Czech Republic

pavel.kocovsky@natur.cuni.cz

A new class of amino acid-derived *N*-methyl formamides, such as the **Sigamide** (now commercially available), have been developed as Lewis-basic organocatalysts for asymmetric reduction of imines with Cl_3SiH (≤97% ee at ≥1 mol% loading). Their application will be highlighted by the enantioselective synthesis of *N*-acetyl colchinol (a potent anti-cancer agent with a mode of action similar to that of taxol) and SCH 48461 (a drug that reduces the intake of cholesterol from food). The reaction also works as a direct, one-pot reductive amination, starting with the corresponding ketone, and without the need for isolation of the imine. With aldehydes, the reaction does not require a sophisticated chiral entity and works perfectly well with both primary and secondary amines and DMF as the Lewis basic catalyst. Tolerance of a wide range of functional groups and heteroaromatic moieties can be demonstrated by the reductive amination of keto aldehydes, where the aldehyde group reacts with excellent chemoselectivity. Being not experimentally demanding, the method is particularly suitable for parallel chemistry, generating libraries of secondary and tertiary amines.