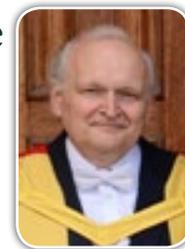


Organocatalyzed Reductive Amination with Trichlorosilane and its Synthetic Applications

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Abstract

The 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 ($\leq 97\%$ ee at ≥ 1 mol% loading). Their application will be highlighted by the enantioselective synthesis of N-acetyl colchicinol (a potent anti-cancer agent with a mode of action similar to that of taxol) and SCH 48461 and its analogue Ezetimibe (drugs reducing the intake of cholesterol from food). The key reaction also works as a direct, one-pot reductive amination, starting from the corresponding ketone, with no need for isolation of the imine. In the case of aldehydes, the reaction does not require a sophisticated chiral entity and proceeds perfectly well with both primary and secondary amines and DMF as the Lewis-basic catalyst. Tolerance to a wide range of functional groups and heteroaromatic moieties can be demonstrated, e.g., by the reductive amination of keto aldehydes, where the aldehyde group reacts with excellent chemoselectivity. Another notable feature is, e.g., retention of the azido group. Being not experimentally demanding, the method is particularly suitable for parallel chemistry, generating libraries of secondary and tertiary amines.

Biography

Pavel Kočovský was raised and educated in Prague, Czechoslovakia (now Czech Republic). He received an MSc (1st class) in 1974 from the Institute of Chemical Technology (ICT), Technical University, Prague, where he did his diploma work with Prof. O. Červinka in the area of asymmetric reactions. He obtained a PhD in 1977 from the Czechoslovak Academy of Sciences, Institute of Organic Chemistry and Biochemistry (IOCB), Prague, where he worked on steroid chemistry under the guidance of Dr. V. Černý and Prof. F. Šorm. He was then appointed to an academic position at the same Institute, which he held for fourteen years (1977-1991). He did his postdoctoral work with Prof. J. E. McMurry at Cornell University, Ithaca, NY, USA (1983-84), and later spent a sabbatical year with Prof. J.-E. Bäckvall at the University of Uppsala, Sweden (1989-1990).

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