Jürgen Brem, László-Csaba Bencze, Arto Liljeblad, Mihaela C. Turcu, Csaba Paizs, Florin-Dan Irimie, Liisa T. Kanerva

Chemoenzymatic preparation of 1-heteroarylethanamines of low solubility

Eur. J. Org. Chem. **2012**, *17*, 3288-3294

Abstract

Both enantiomers of biologically and pharmaceutically interesting benzofuran-, benzothiophen-, and phenylfuran-based 1-heteroarylethanamines were prepared at close to theoretical yields by using *Candida antarctica* lipase B (Novozym 435) catalyzed (*R*)-selective *N*-acylation with isopropyl butanoate (enantiomeric ratio $E > 200$). The use of *N*-methyl-2-pyrrolidinone (NMP) as a cosolvent (1:30) in isopropyl butanoate solved the problem of low solubility of the compounds. Instability of the heterocyclic ring systems against traditional acid- and base-catalyzed hydrolysis was solved by using *Candida antarctica* lipase A as a commercial CAL-A-CLEA preparation for deprotection of the *N*-acylated (*R*) enantiomers in water. The slow, highly enantioselective ($E > 200$) hydrolyses of racemic butanamides was also observed in the presence of Novozym 435.