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.