Annotation

KRÁTKÝ, Martin. *Synthesis of Salicylanilide Prodrugs.* Hradec Králové: Faculty of Pharmacy of Charles University, 2008. 75 pp. Diploma Thesis.

This diploma thesis is concerned with synthesis of antibacterial prodrugs based on esters of salicylanilides with amino acids. First there are characterized prodrugs and their importance and then biological activities and application of salicylanilides. The main goal of this work was the synthesis of prodrugs of salicylanilides amino acids esters. Some synthesized compounds were evaluated especially for their activity against atypical *Mycobacteria* strains. These compounds possess antimycobacterial activity, but it is lower than initial salicylanilide 5-chloro-*N*-(3-chlorophenyl)-2-hydroxybenzamide.

This diploma thesis acknowledges rearrangement after *N*-deprotection and α-amino group liberation of *N*-protected amino acids esters with salicylanilides to furnish diamides. The diamide was esterified by Z-amino acids (L-phenylalanine and glycine). These obtained esters were *N*-deprotected and the amino group was liberated. After this liberation there was described rearrangement to furnish probably triamides, analogously to furnishing of diamides. There are discussed two possible mechanisms of rearrangement – with forming of seven-membered benzoxazepinedione rings or with five-membered hydroxyimidazoline intermediates. The second version is considered to be more probable because of new knowledge. This diploma thesis contributed to these findings. It seems that this type of rearrangement could be generally a running reaction of the esters of salicylanilides with α-amino acids.

Keywords:

Salicylanilides, biological activity, antimycobacterial activity, amino acids esters, prodrugs, rearrangement.