Abstract

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Title of diploma thesis: **Synthesis of tetrazoles as antituberculotics**

Although significant progress in therapy of tuberculosis has been made since effective drugs were discovered in the second half of the 20th century, it is still widespread and refractory curable disease. The situation is complicated with growing appearance of resistant strains and for that reason it is necessary to search for new potential antituberculotics. The aim of this work was to continue with synthesis of antimycobacterial-efficient structures based on tetrazole.

Firstly, we synthesised derivates of 1-aryl-5-[(3,5-dinitrobenzyl)sulfanyl]-1*H*-tetrazole by the method of Williamson's synthesis, when the reaction of 1-aryl-1*H*-tetrazol-5-thiol with 3,5-dinitrobenzylchloride was performed. Conditions of the reactions were further optimalised. We prepared by the same way derivates of 1-fenyl-5-[(3,4,5-trimethoxybenzyl)sulfanyl]-1*H*-tetrazole afterwards, as analogues of previous tetrazoles missing the electron withdrawing 3,5-dinitrosubstitution.

Furthermore, we concentrated on synthesis of substituted 1,5-diphenyl-1*H*-tetrazoles. Substituted *N*-phenylbenzamides, prepared from appropriate benzoylchlorides and anilines, were used as the initial structures for formation of these tetrazoles. Then we tried three different pathways for preparation of the final tetrazoles:

1. formation of imidoylchloride of initial benzamide followed by its cyclization with sodium azide on tetrazole in condition of phase-transpher catalysis;
2. formation of imidoylbenzotriazole of initial benzamide followed by its cyclization with azoimide on tetrazole in condition of phase-transpher catalysis;
3. variation of Mitsunobu reaction using trimethylsilylazide.

The second mentioned method led to isolation of two substituted 1,5-difenyl-1*H*-tetrazoles, but not in sufficient amount and purity.

We obtained 12 final tetrazoles altogether and antimycobacterial activity *in vitro* was investigated in nine of them. 9 substituted *N*-phenylbenzamides and 3 substituted *N*-benzylbenzamides we prepared were tested as well. Some of these compounds shown higher antimycobacterial activity than isoniazid. The products were characterised with ^{1}H NMR and ^{13}C NMR spectroscopy and with melting points.