ABSTRACT

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Diploma Thesis

Synthesis Of Antimicrobial Active Anilides and Their Sulphur Analogues

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Implementation of *tert*-butyl group into the molecule of benzoxazoles leads to enhancement of lipophility and therefore better penetration through lipoid mycobacterial cell-wall. Several derivates had shown 100-90 % activity in concentration 6,25 μg/ml against *Mycobacterium tuberculosis* $H_{37}Rv$ in our series of 5,7-di-*tert*-butyl-benzoxazoles substituted in position No. 2 with aromatic substituent. Metabolism of benzoxazoles probably includes the opening of their structure. The goal of this thesis is to synthesize substituted *N*-(3,5-di-*tert*-butyl-2-hydroxyphenyl)benzamides and pyridinecarboxamides, their so-called ”open forms“. These structures could be also considered as ”reversed salicylanilides“ which have also a significant antitubercular activity.

The first step of the synthesis of these analogues is preparation of 2-amino-3,5-di-*tert*-butylphenol. It was prepared by reaction of 3,5-di-*tert*-butylbenzo-1,2-quinone with ammonia and following reduction by $NaBH_4$. Resulting DTB-aminophenol has been condensed with appropriate aromatic or heteroaromatic acids, while PCl_3 in chlorobenzene was added. Quite a long reaction time increased the fraction of tinted by-products at the expense of the amount of the requested product. Therefore the reaction was moved into the microwave reactor, which considerably shortened the reaction time (from hours to minutes). Benzoxazoles, unexpected by-products, were also isolated. These by-products, due to their hydroxyl group, laminate in UV light (254 nm). However the best method to synthesize these amides is condensation of DTB-aminophenol with separately prepared acid chloride. Resulting amides has been transferred into their appropriate thioamides, by-products of these reactions were benzothiazoles. The final products will be tested for antitubercular activity and their results will be compared to benzoxazolic patterns.

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