ABSTRAKT

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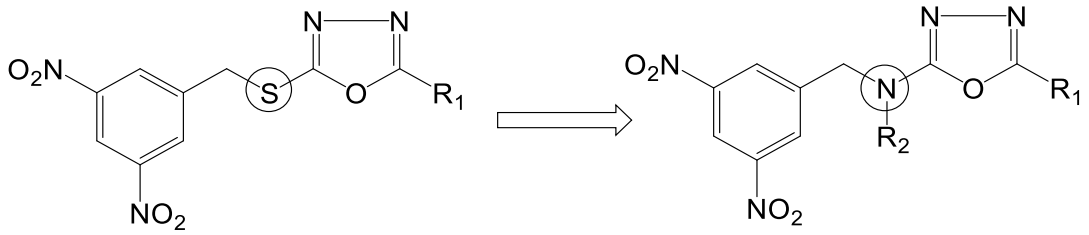
Title of Diploma Thesis: Synthesis of aza-analogs of compounds with high antimycobacterial activity

Tuberculosis (TB) is widespread disease, caused by bacteria *M. tuberculosis*. TB is the 13th leading cause of death and was the 2nd leading cause of death from infectious diseases in 2020. TB is also the most common cause of death in HIV-positive people. Due to increasing resistance to 1st line and 2nd line drugs, research into new anti-TB drugs is needed.

This diploma thesis is based on previous results obtained at KOBCH FaF UK, where 5-alkyl/aryl-2-((3,5-dinitrobenzyl)sulfanyl)-1,3,4-oxadiazoles were invented. These 1,3,4-oxadiazoles showed excellent antimycobacterial activity with minimal inhibitory concentration (MIC) values of 0.03 μM. This activity is much higher than that of isoniazid, first-line antituberculotic drug, which has MIC values of 0.5 μM.

In previous work, it has been shown that the 3,5-dinitrophenyl fragment is crucial to the high antimycobacterial activity and that derivatives with a 1,3,4-oxadiazole cycle show the highest potency compared to 1*H*/2*H*-tetrazole and 1,2,4-triazole derivatives. However, the question of the effect of sulfur in the linker chain on the activity remained. Therefore, the aim of this work was to synthesize 5-alkyl/aryl-*N*-(3,5-dinitrobenzyl)-1,3,4-oxadiazole-2-amines in which the sulfur in the linker chain is replaced by a nitrogen atom.



The synthesis of 5-alkyl/aryl-*N*-(3,5-dinitrobenzyl)-1,3,4-oxadiazole-2-amines is based on the reaction of acylhydrazides with (3,5-dinitrobenzyl)isothiocyanate followed by cyclization of formed 1-acyl-4-(3,5-dinitrobenzyl)thiosemicarbazides. In the present work, attempts were made to optimize the synthesis of (3,5-dinitrobenzyl)isothiocyanate, and the effect of solvent, temperature and ratio of starting materials was investigated. The cyclization of 1-acyl-4-(3,5-dinitrobenzyl)thiosemicarbazides was carried out under two reaction conditions and the yields of the reactions were compared. Alkylation of the prepared 5-alkyl/aryl-*N*-(3,5-dinitrobenzyl)-1,3,4-oxadiazol-2-amines was also attempted.

In the current work, 5 final compounds were prepared and their antimycobacterial activity was evaluated.