ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Organic and Bioorganic Chemistry

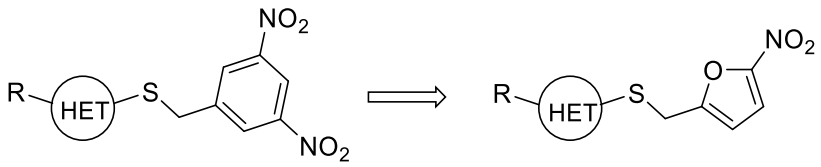
Author: Lukáš Bartoš

Supervisor: doc. PharmDr. Jaroslav Roh, Ph.D.

Title of Diploma Thesis: Synthesis of nitroheteroaromatic compounds with potential antimycobacterial activity

Tuberculosis (TB) is widespread infectious disease which is mainly caused by *Mycobacterium tuberculosis*. Referring to the World Health Organization, it is still among the top 10 causes of death in the world. Around 10 million people worldwide suffered from TB and 1.4 million died of TB only in 2019. TB is also a leading-killer in the group of HIV-positive people.

This work is based on a previous successful discovery of new compounds with significant antitubercular activity, namely 1,5- and 2,5-disubstituted tetrazoles and 2,5-disubstituted oxadiazoles bearing 3,5-dinitrobenzylsulfanyl fragment, that showed minimal inhibitory concentration (MIC) values as low as 0.03 μM (i.e. lower MIC compared to first line anti-TB drugs isoniazid or rifampicin). In this work we studied the influence of the replacement of 3,5-dinitrophenyl fragment with 5-nitrofuryl group and of the position of this fragment in the molecule on the antimycobacterial activity. We also attempted to prepare several 5-nitropyridin-3-yl analogues.



HET = 1,3,4-oxadiazole, tetrazole

Hence, three series of nitrofuryl–substituted tetrazoles and oxadiazoles were prepared and their antimycobacterial activity against *M. tuberculosis* and non-tuberculous *M. avium* and *M. kansasii* were studied. Some of the compounds showed good antimycobacterial activity with MIC in low micromolar range. However, all of them were less active than original 3,5-dinitrophenyl containing compounds.