ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

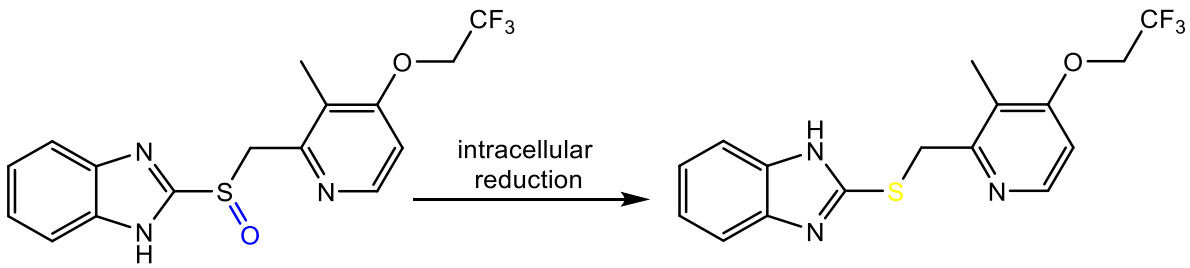
Department of Organic and Bioorganic Chemistry

Author: Mária Murínová

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

Title of diploma thesis: **Synthesis of lansoprazole analogs with potential antimycobacterial activity**

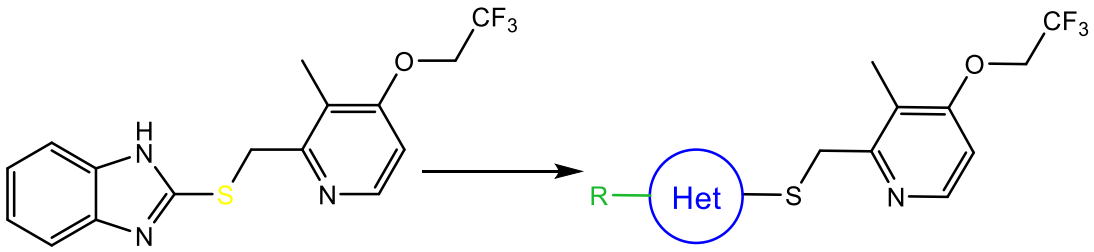
Mycobacterium tuberculosis is a bacterium that causes a serious infectious disease, tuberculosis. Recent studies show an increase in the number of patients suffering from this disease, pointing to the increasing resistance of this bacterium to most antibiotics. Given the current globalization of the world, as another factor contributing to the spread of tuberculosis in areas where the disease has been under control so far, it is essential to focus on the development of new antituberculosis drugs. Recent studies have reported that a promising candidate is lansoprazole, which is known primarily as gastric proton pump inhibitor. The mechanism of the antimycobacterial effect is that lansoprazole, after intracellular reduction to lansoprazole sulfide, kills *M. tuberculosis* by inhibiting cytochrome bc-1. This makes lansoprazole sulfide an excellent compound for further structural optimization and study of its structure-activity relationships.



lansoprazole lansoprazole sulfide

The aim of this work was to modify the structure of the lansoprazole and to prepare its anologs by altering the benzimidazole heterocycle. Thus, a series of substituted imidazole, 1,2,4-triazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole and 1*H*-tetrazole analogs of

lansoprazole sulfide were prepared and tested for their antimycobacterial activity against *M. tuberculosis* H37Rv and against *M. avium* and *M. kansasii*.



lansoprazole sulfide

Het: imidazole
1,2,4-triazole
1,3,4-oxadiazole
1,3,4-thiadiazole
1H-tetrazole