SYNTHESIS AND ANTIMYCOBACTERIAL ACTIVITY OF 1,3,4-OXADIAZOL-2-ONE DERIVATIVES

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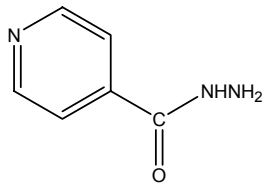
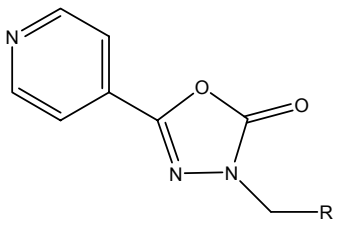
Tuberculosis is a contagious disease with high mortality worldwide. The recent emergence of cases of multidrug resistant tuberculosis (MDR-TB) becomes a serious problem to the treatment of the disease. The disease resurgence in most countries is due to the human immunodeficiency virus (HIV) epidemic, in addition to the emergence of drug-resistant strains and immigration from high-prevalence countries.
Moreover, species of mycobacteria other than *M. tuberculosis* (MOTT) are able to cause a wide range of infections. Among these bacteria, the most dangerous for humans are *M. avium*, *M. fortuitum*, *M. kansasii*, *M. chelonei* and the *M. avium-intracellulare* complex (MAC).
Therefore, new drugs for the treatment of infection sustained by MOTT and strains of MDR mycobacteria are indispensable.

Our search consists on the design, synthesis and *in vitro* evaluation of antimycobacterial activity of new isoniazid analogues. We observed [1] that the conversion of isoniazid **1** in 3-substituted 5-(pyridin-4-yl)-3*H*-1,3,4-oxadiazol-2-one derivatives **2** gave compounds whit interesting antimycobacterial activity**:**



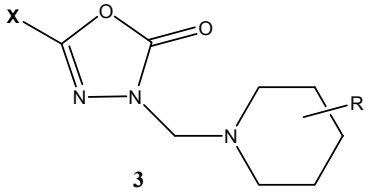
1



2

R= various cyclic amines

Trying to increase the antimycobacterial activity of the compounds **2**, we synthesized 3-(2, 3, and 4-methyl-piperidin-1-ylmethyl)-5-heteroaryl-3*H*-1,3,4-oxadiazol-



3

R= -CH_3

X=Ar, 2-,3-Pyr

2-one derivatives **3**, characterized by the presence of piperidine moiety:

We projected the substitution of the pyridin-4-yl ring with others heteroaryl rings maintaining the best pharmacophoric group in the 3- position of our precedent work [1].

[1] M.G.Mamolo, D.Zampieri, L.Vio – M.Fermeglia, M.Ferrone, S.Pricl – G.Scialino, E.Banfi; Biorg. Med. Chem (2005) in press.