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ЭКСПЕРТНОЕ ЗАКЛЮЧЕНИЕ О ВОЗМОЖНОСТИ ОПУБЛИКОВАНИЯ

Руководитель-эксперт Федерального государственного бюджетного учреждения науки Института элементоорганических соединений им. А.Н.Несмеянова Российской академии наук, рассмотрев аннотацию *коллективной монографии* под руководством V.L.M. Silva & A.M.S. Silva **«Recent Advances in the Synthesis, Functionalization and Applications of Pyrazole-Type Compounds I»**, подготовленную для печати в издательстве *"MDPI"* (Basel, Switzerland), подтверждает, что в материале *не содержатся* сведения, предусмотренные Постановлением Правительства РФ №1233 от 30.11.1994г. и на публикацию материала *не следует* получать разрешение *Минобрнауки и/или Президиума РАН*

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Recent Advances in the Synthesis, Functionalization and Applications of Pyrazole-Type Compounds I

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Boulton-Katritzky Rearrangement of 5-Substituted Phenyl-3-[2-(morpholin-1-yl)ethyl]-1,2,4-oxadiazoles as a Synthetic Path to Spiropyrazoline Benzoates and Chloride with Antitubercular Properties

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Abstract: The analysis of stability of biologically active compounds requires an accurate determination of their structure. We have found that 5-aryl-3-(2-aminoethyl)-1,2,4-oxadiazoles are generally unstable in the presence of acids and bases and are rearranged into the salts of spiropyrazolinium compounds. Hence, there is a significant probability that it is the rearranged products that should be attributed to biological activity and not the primarily screened 5-aryl-3-(2-aminoethyl)-1,2,4-oxadiazoles. A series of the 2-amino-8-oxa-1,5-diazaspiro[4.5]dec-1-en-5-ium (spiropyrazoline) benzoates and chloride was synthesized by Boulton–Katritzky rearrangement of 5-substituted phenyl-3-[2-(morpholin-1-yl)ethyl]-1,2,4-oxadiazoles and characterized using FT-IR and NMR spectroscopy and X-ray diffraction. Spiropyrazolylammonium chloride demonstrates in vitro antitubercular activity on DS (drug-sensitive) and MDR (multidrug-resistant) of MTB (*M. tuberculosis*) strains (1 and 2 μg/mL, accordingly) equal to the activity of the basic antitubercular drug rifampicin; spiropyrazoline benzoates exhibit an average antitubercular activity of 10–100 μg/mL on MTB strains. Molecular docking studies revealed a series of *M. tuberculosis* receptors with the energies of ligand–receptor complexes (−35.8–−42.8 kcal/mol) close to the value of intermolecular pairwise interactions of the same cation in the crystal of spiropyrazolylammonium chloride (−35.3 kcal/mol). However, only in complex with transcriptional repressor EthR2, both stereoisomers of the cation realize similar intermolecular interactions.

Keywords: 1,2,4-oxadiazoles; spiropyrazolinium compounds; in vitro antitubercular screening; X-ray diffraction; molecular docking

1. Introduction

There are pyrazoline-containing compounds that act as active pharmaceutical ingredients of such commercially available drugs as *aminopyrine* (*aminophenazone*; analgesic and antipyretic), *dipyrone* (*metamizole*, *noramidopyrine*; analgesic), *antipyrine* (*benzocaine*; non-narcotic analgesic, an antipyretic and antirheumatic), *zaleplon*(hypnotic and sedative), *celecoxib* (*Aclarex*, *Celebrex*; anti-inflammatory and antirheumatic drug), *allopurinol* (uricostatic agent, xanthine oxidase inhibitor) [1]. Therefore, there is always a demand for new molecules, methodologies and improved synthetic approaches to novel pyrazoline derivatives.

Pyrazolines, as noticeable, practically meaningful nitrogen-containing heterocyclic compounds, can be synthesized by a variety of methods. However, one of the most popular