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Abstract

Design, Synthesis, and Biological Evaluation of New Benzoxaborole Derivatives as Potential Antimycobacterial Agents †

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Abstract: The current study is focused on the combination of pyrazinamide with 6-aminobenzo[c][1,2]oxaborol-1(3*H*)-ol, which is a crucial pharmacophore of several antimicrobial agents. The use of benzoxaborole moiety could afford the formation of a spiro adduct between benzoxaborole moiety and 3'-terminal adenosine nucleotide Ade76 of $tRNA^{Leu}$. In the form of this spiro adduct, it may potentially inhibit the enzyme leucyl-tRNA synthetase (LeuRS). A large heterocyclic substitution in position 6 of the benzoxaborole moiety could lead to the enhanced selectivity of the intended compounds to the bacterial enzyme due to steric clashes with eukaryotic types of LeuRS. The target compounds were synthesized by condensation of 6-aminobenzo[c][1,2]oxaborol-1(3*H*)-ol with variously substituted heteroaromatic acids that underwent previous activation. The synthetic products and the isolated condensation intermediates were subjected to biological in vitro screening against fungi and bacteria, including mycobacteria and in vitro cytotoxicity screening against the HepG2 cancer cell line. Some of the compounds showed moderate antimycobacterial activity with persisted low toxicity.

Keywords: benzoxaborole; Mycobacterium tuberculosis H37Rv; Mycobacterium tuberculosis H37Ra; HepG2 cancer cell line; leucyl-tRNA synthetase

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