

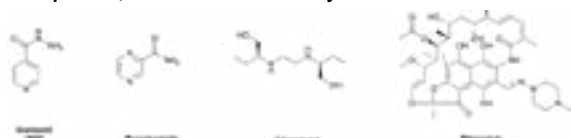
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DESIGN, SYNTHESIS AND TARGET IDENTIFICATION OF NOVEL ANTI-TUBERCULAR AGENTS

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Tuberculosis (TB) is recognized as a lethal bacterial infection that caused by the bacterium *Mycobacterium tuberculosis* (Mtb). According to the World Health Organization in 2017, Mtb is mainly found in developing countries such as India and South Africa. Consequently, an estimated 9.6 million people became ill from *M. tuberculosis* in 2014 with 1.5 million deaths, 27 % of which were complicated by co-morbid HIV.(1) However, the present day chemical synthesis could be used to produce a set of novel medicinal compounds that can selectively show bactericidal activity against *Mycobacterium tuberculosis* (Mtb). The continued development of novel benzo-[2,1,3]-diazole molecules may be used to solve antitubercular resistance because multi-drug resistant bacteria are unaffected by front-line therapies including Isoniazid 1, Rifampicin 2, Ethambutol 3 and Pyrazinamide 4 .

Figure 1: Front line treatments for *Mycobacterium tuberculosis*

Background: In the past two decades, the synthesis of bioactive heterocyclic compound had a significant role in discovery of novel and active medicinal agents. The good example of heterocyclic compounds is benzimidazole moiety 5 (Figure 2) that has been widely used for synthesis of a large number of bioactive agents. Furthermore, any substitution of one or more heteroatoms and any change in any position within heterocyclic system can clearly influence on benzimidazole's behaviors such as acidity, basicity, solubility and susceptibility to attack by electrophiles or nucleophiles. Finally, the minimal inhibitory concentration (MIC) of novel benzodiazole antitubercular agents is determined by using the resazurin microtiter assay (REMA) against four different types of *Mycobacterium tuberculosis* that are susceptible to Isoniazid, Rifampicin, Pyrazinamide and lead compound, respectively

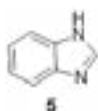
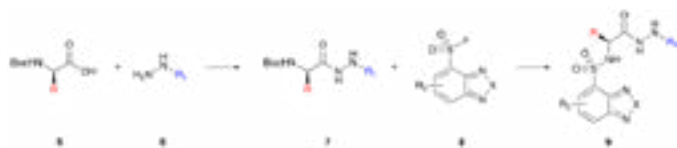


Figure 2: Benzimidazole moiety

Project Aim: The aim of this study focuses on the continued synthesis of the novel benzodiazole antibacterial agents to undertake a SAR study. Synthesis of a series of benzodiazole antibacterial agents: This will be achieved in two steps beginning with peptide bond coupling to give rise to hydrazide 7. Subsequent deprotection of 7 and coupling with benzodiazole 8 provides the final benzodiazole compounds 9 for biological screening. Additionally the hydrazides 7 will also be screened (Figure 3).



Microbiological testing will be undertaken using a resazurin microtiter assay (REMA) or a Microtitre alama blue assay (MABA) to produce minimum inhibitory concentration values (MIC) for 7 and 9

Biography

Jon Sellars is a lecturer in medicinal chemistry at the school of pharmacy and the institute of cellular medicine at Newcastle University. He gained a PhD with Patrick Steel at Durham University investigating the utility of silacyclohex-4-enes in organic synthesis. subsequent employment at sanofi-aventis in alwnick working on radio labelling active pharmaceutical ingredients was followed by a return to Durham University, to undertake a post doctoral position with Patrick Steel and Robert Edwards investigating multiple herbicide resistance in black grass (supported by syngenta). in 2010, he was awarded an epsrc life sciences interface fellowship to develop novel proteomic probes to study cytochrome p450's. after completion, he undertook a teaching fellowship at Durham University where in 2015 was appointed to a lectureship in medicinal chemistry at the school of pharmacy. in august 2017 the school was transferred to Newcastle University resulting in the creation of the school of pharmacy.

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