SYNTHESIS OF DIARYLAMINES IN THE BENZO[b]THIOPHENE SERIES BY PALLADIUM-CATALYZED AMINATION AND STRUCTURE-ACTIVITY RELATIONSHIP AS ANTIBACTERIAL AGENTS

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The palladium-catalyzed amination of arylhalides has become an important method for the synthesis of arylamines found in pharmaceuticals. Using this methodology we were able to synthesize several diarylamines in the benzo[b]thiophene series. Here we report the synthesis of differently substituted diarylamines derivatives of 6-bromo or 6-amino-2,3,5-trimethylbenzo[b]thiophene in good to high yields (50-90%) (Scheme). The amino precursor was prepared from the bromo compound using also a C-N palladium-catalyzed cross-coupling with benzophenone imine, followed by acidic hydrolysis in a 60% overall yield (Scheme).

The new diarylamines obtained were fully characterized and were submitted to a screening of antibacterial activity using two Gram positive (Bacillus cereus, Bacillus subtilis) and two Gram negative (Pseudomonas aeruginosa, Escherichia coli) bacteria. The results of the in vitro assays were evaluated by measuring the diameter of the halos of growth inhibition at different concentrations in DMSO (1mg/l, 0.5mg/l, 0.2mg/l and 0.1mg/l) allowing the determination of the minimal inhibitory concentration for each case. Very interesting results were obtained and it was possible to establish a structure-activity relationship that will be presented and discussed.

References: