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Program and Abstracts

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

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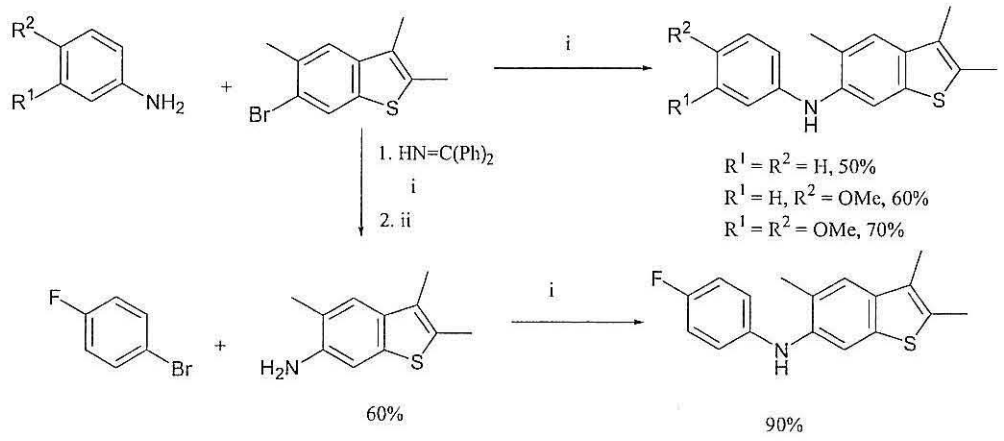
The palladium-catalyzed amination of arylhalides has become an important method for the synthesis of arylamines found in pharmaceuticals. Using this methodology we were able to synthesize several diarylamines in the benzo[*b*]thiophene series.[1]
Here we report the synthesis of differently substituted 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).



i) $Pd(OAc)_2$ (3mol%), Cs_2CO_3 (1.4equiv.), BINAP (4mol%), toluene, 100 °C, Ar
ii) HCl 2M/THF

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:

1- Isabel C. F.R.Ferreira, Maria-João R. P. Queiroz, Gilbert Kirsch *Tetrahedron*, **2003**, *59*, 975-981.