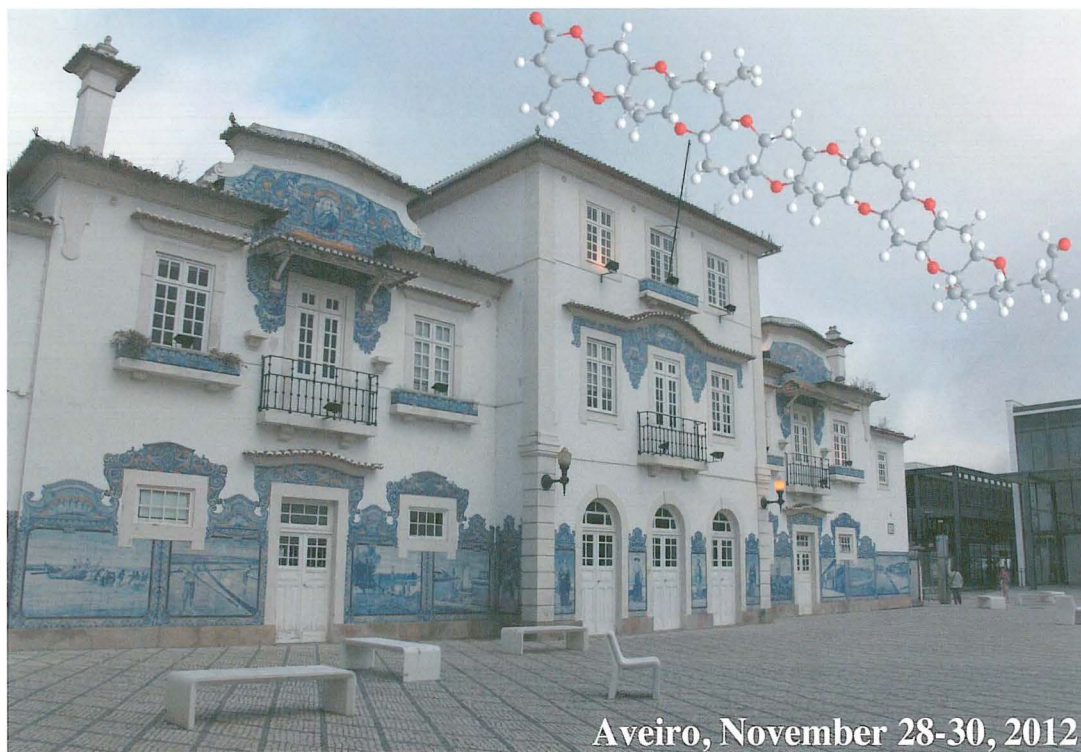


3º Encontro Nacional de Química Terapêutica



Aveiro, November 28-30, 2012

3rd Portuguese Meeting on Medicinal Chemistry
1st Portuguese-Spanish-Brazilian Meeting on Medicinal Chemistry.



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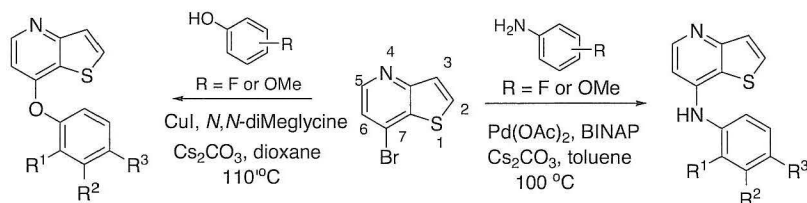
Synthesis, growth inhibitory activity on human tumor cell lines and evaluation of the hepatotoxicity of di(hetero)arylethers and di(hetero)arylamines in the thieno[3,2-*b*]pyridine series

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Thienopyridine skeleton has been reported as having interesting biological activity, namely antitumor^[1] and antiangiogenic^[2] activities.

Herein we describe the synthesis of di(hetero)arylethers **1a-f** and di(hetero)arylamines **2a-f** functionalizing the 7-position of the thieno[3,2-*b*]pyridine in good to high yields, using copper (C-O) or palladium (C-N) catalyzed couplings, like presented below.



1a R¹ = F, R² = R³ = H; 69%

1b R¹ = R³ = H; R² = F; 63%

1c R¹ = R² = H; R³ = F; 65%

1d R¹ = OMe, R² = R³ = H; 45%

1e R¹ = R³ = H; R² = OMe; 50%

1f R¹ = R² = H; R³ = OMe; 45%

2a R¹ = F, R² = R³ = H; 75%

2b R¹ = R³ = H; R² = F; 70%

2c R¹ = R² = H; R³ = F; 73%

2d R¹ = OMe, R² = R³ = H; 80%

2e R¹ = R³ = H; R² = OMe; 83%

2f R¹ = R² = H; R³ = OMe; 54%

The growth inhibitory activity of the di(hetero)arylethers **1a-f** and di(hetero)arylamines **2a-f** was evaluated against five human tumor cell lines (breast- MCF-7, non-small cell lung- NCI-H460, colon- HCT15- hepatocellular- HepG2 and cervical- HeLa carcinomas), using the sulforhodamine B assay. Furthermore, the hepatotoxicity of compounds was studied using a porcine liver primary cell culture (PLP2). The most promising compounds were shown to be the methoxy derivatives **1e** and **2e**, presenting GI₅₀ values comparable with ellipticine (control) without hepatotoxicity. For these compounds more studies are needed to find out their mechanisms of action.

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