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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 thiou[3,2-b]pyridine series

Ricardo C. Calhelha, a,b Daniela Peixoto, a Pedro Soares, a,c Isabel C. F. R. Ferreira, a Rui M. V. Abreu, a Maria João R. P. Queiroz a

a Centro de Química, Univ. do Minho, Campus de Gualtar 4710-057 Braga, Portugal; b CIMO/ESA, I.P. Bragança, Campus de Sta Apolónia, Apt. 1172, 5301-855 Bragança, Portugal; c CIQ/Dept. de Química e Bioquímica, Fac. Ciências, Univ. do Porto, 4169-007 Porto, Portugal.

Thiopyridine 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 functionailizing the 7-position of the thiou[3,2-b]pyridine in good to high yields, using copper (C-O) or palladium (C-N) catalyzed couplings, like presented below.

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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