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P049

Thieno[3,2-*b*]pyridine Arylethers: Synthesis and Growth Inhibitory Activity on Human Tumor Cell Lines

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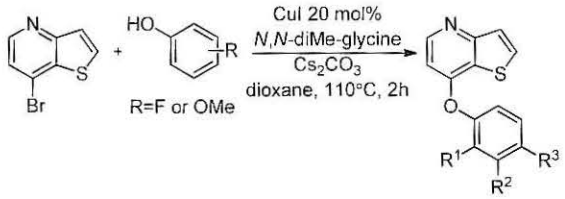
Thienopyridine skeleton has been reported as having interesting biological activity, namely antitumor[1] and antiangiogenic[2] activities. Herein, we describe the synthesis of thienopyridine arylethers **1a–f** in moderate to good yields by a copper-catalyzed C–O coupling, using *N,N*-dimethylglycine as a ligand, of the 7-bromothieno[3,2-*b*]pyridine, also prepared with substituted phenols (see scheme).



1a, R^1=F, R^2=R^3=H 63%
1b, R^1=R^3=H, R^2=F 61%
1c, R^1=R^2=H, R^3=F 66%
1d, R^1=OMe, R^2=R^3=H 40%
1e, R^1=R^3=H, R^2=OMe 50%
1f, R^1=R^2=H, R^3=OMe 45%

The growth inhibitory activity of the di(hetero)arylethers **1a–f** was evaluated against four human tumor cell lines (MCF-7, NCI-H460, HepG2 and HeLa), using the sulforhodamine B assay. Furthermore, the hepatotoxicity of compounds was studied using a porcine liver primary cell culture (PLP1). The most promising compound was shown to be the methoxy derivative (**1e**) presenting GI_{50} values in the range of 1.5 to 6.5 μM. For this compound, more studies are needed to find its mechanism(s) of action.

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P050

Non-anionic Aldose Reductase Inhibitors. Design, Synthesis, Biological Evaluation and In Silico Studies

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Aldose reductase's (ALR2) involvement on the onset and progression of diabetes secondary complications has attracted attention over the years.[1] Furthermore, recent evidence point towards ALR2's implication in inflammatory pathologies.[2] As such, ALR2 comprises a compelling target for medicinal chemistry.

In the plethora of aldose reductase inhibitors (ARIs) synthesized so far, two categories are the most studied, namely that of cyclic imides and carboxylic acid derivatives. However, a number of cyclic imide derivatives emerged with acute side effects and carboxylic acids presented with poor membrane penetration.

In our previous work and in order to overcome the limitations of the two classic categories of ARIs, we have presented a successful bioisosteric replacement of a carboxylic acid moiety with that of a 2,6-difluorophenol.[3,4] 2,6-Difluorophenol has a pK_a value of 7.12, therefore its derivatives could diffuse through membranes more adequately than their carboxylate counterparts. In the present work, we investigated the synthetic feasibility and ARI activity of aroylpyrroles bearing groups that are non-anionic in physiological pH such as the phenol, 2-fluorophenol, salicylaldoxime, nitroaldoxime, and 3,4-di-