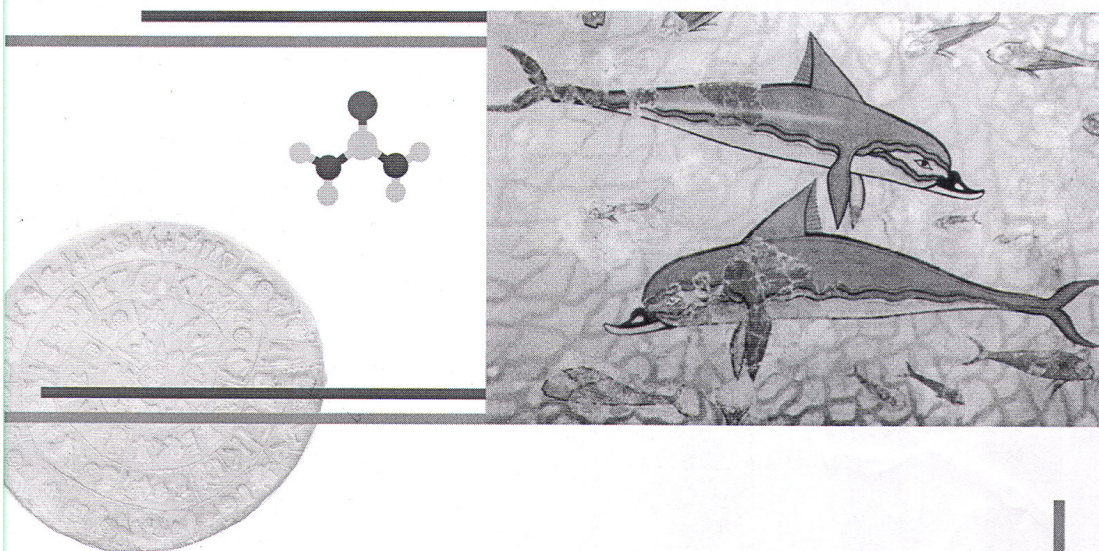




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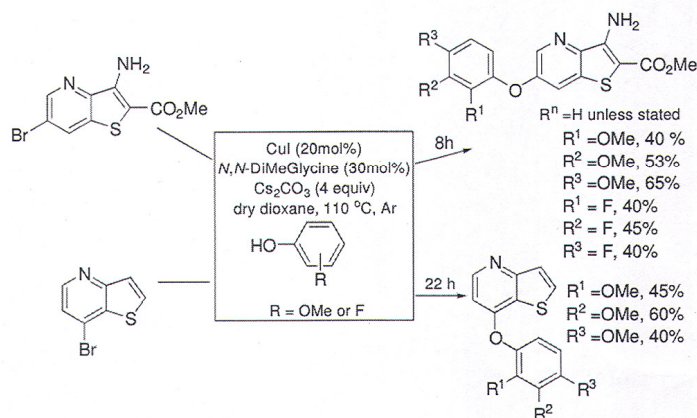
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SYNTHESIS OF DI(HETERO)ARYLEthers IN THE THIENO[3,2-*b*]PYRIDINE SERIES BY COPPER/*N,N*-DIMETHYLGLYCINE CATALYZED C-O COUPLING

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Di(hetero)arylether derivatives of the thieno[3,2-*b*]pyridine scaffold were shown to be tyrosine kinase (TK) inhibitors of the VEGFR (vascular endothelial growth factor receptor) and of the c-Met (receptor for the hepatocyte growth factor/scatter factor). Molecules that potentially inhibit both c-Met and VEGFR may have advantages over selective ones, since they can synergistically cooperate as antitumorals and anti-angiogenics.¹

Here we present the synthesis of several di(hetero)arylethers by Cu-catalyzed C-O coupling using *N,N*-dimethylglycine as a ligand and Cs₂CO₃ as a base in good yields, from the methyl 3-amino-6-bromothieno[3,2-*b*]pyridine-2-carboxylate² or the 7-bromothieno[3,2-*b*]pyridine, also prepared by us, and methoxy or fluorophenols (Scheme). The possible reaction mechanisms will be discussed.



Scheme

The compounds prepared were fully characterized and will be submitted to antitumoral activity studies using human tumor cell lines and also to TK inhibition assays using the receptors referred above.

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