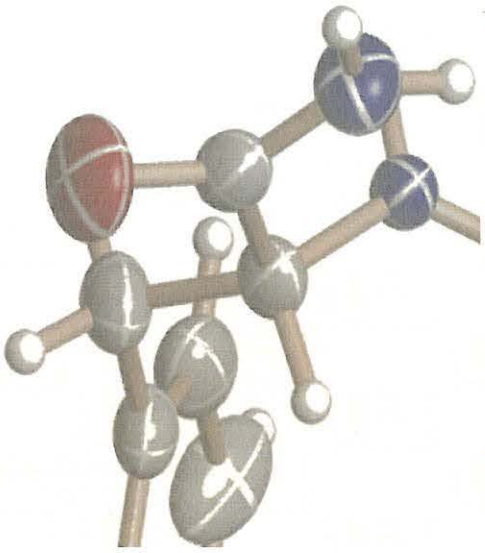

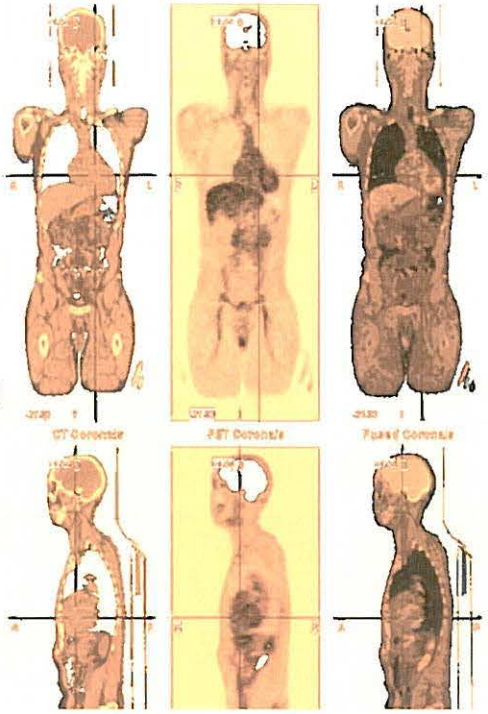

# 1st Symposium on MEDICINAL CHEMISTRY of University

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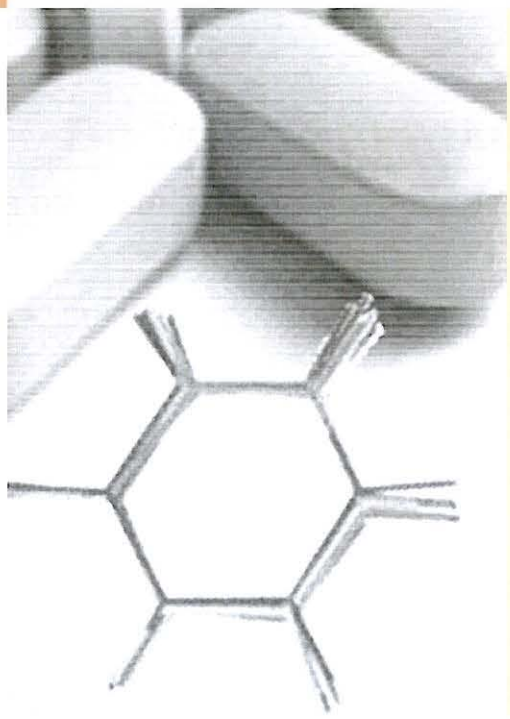

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# Synthesis of new *N*-[3-(thieno[3,2-*b*]pyridine-7-ylthio)phenyl]benzamides as potential inhibitors the tyrosine kinase domain of VEGFR2

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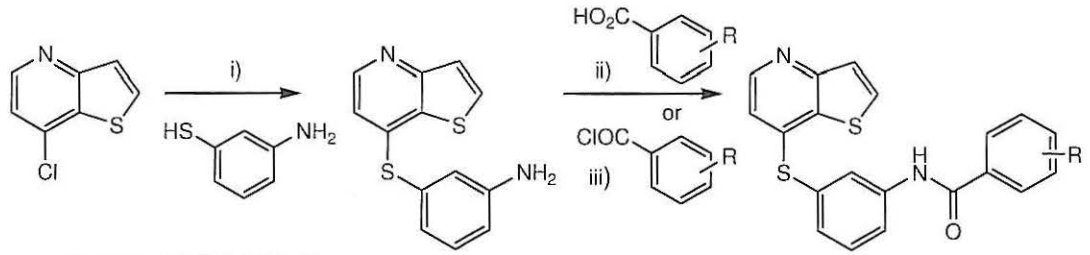
Angiogenesis, the growth of new vessels from preexisting vasculature, is a critical step in tumor progression [1]. The tyrosine kinase Vascular Endothelial Growth Factor Receptor 2 (VEGFR2) is a crucial mediator in angiogenesis since the VEGF, excreted by the tumor cells, binds to it activating several signaling pathways involved in cell survival and proliferation [2]. Recently thienopyridine derivatives showed to be promising inhibitors of the tyrosine kinase domain of VEGFR2 [3,4]. In this work new *N*-[3-(thieno[3,2-*b*]pyridine-7-ylthio)phenyl]benzamides were prepared as potential VEGFR2 inhibitors suggested by rational design, as presented below.




i) $K_2CO_3$, DMF, 140ºC, 4h
ii) HBTU, DIPEA, $CH_2Cl_2$, r.t.
iii) NMP, r.t.

R= *m* or *p* - F, Me

The inhibition of the tyrosine kinase domain of the VEGFR2 will be evaluated either by enzymatic or cellular and biomolecular assays using VEGF-stimulated Human Umbilical Vein Endothelial Cells (HUVECs).

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*References:*

[1] Bergers G, Benjamin LE, *Nat. Rev Cancer*, **2003**, 3, 401–410.[2] Hicklin DJ, Ellis LM, *J Clin Oncol*, **2005**, 23, 1011–1027. [3] Munchhof, M.J, *et al.*, *Bioorg. Med. Chem. Lett.*, **2004**, 14, 21-24. [4] Claridge, S. *et al.*, *Bioorg. Med. Chem. Lett.*,**2008**, 18, 2793-2798