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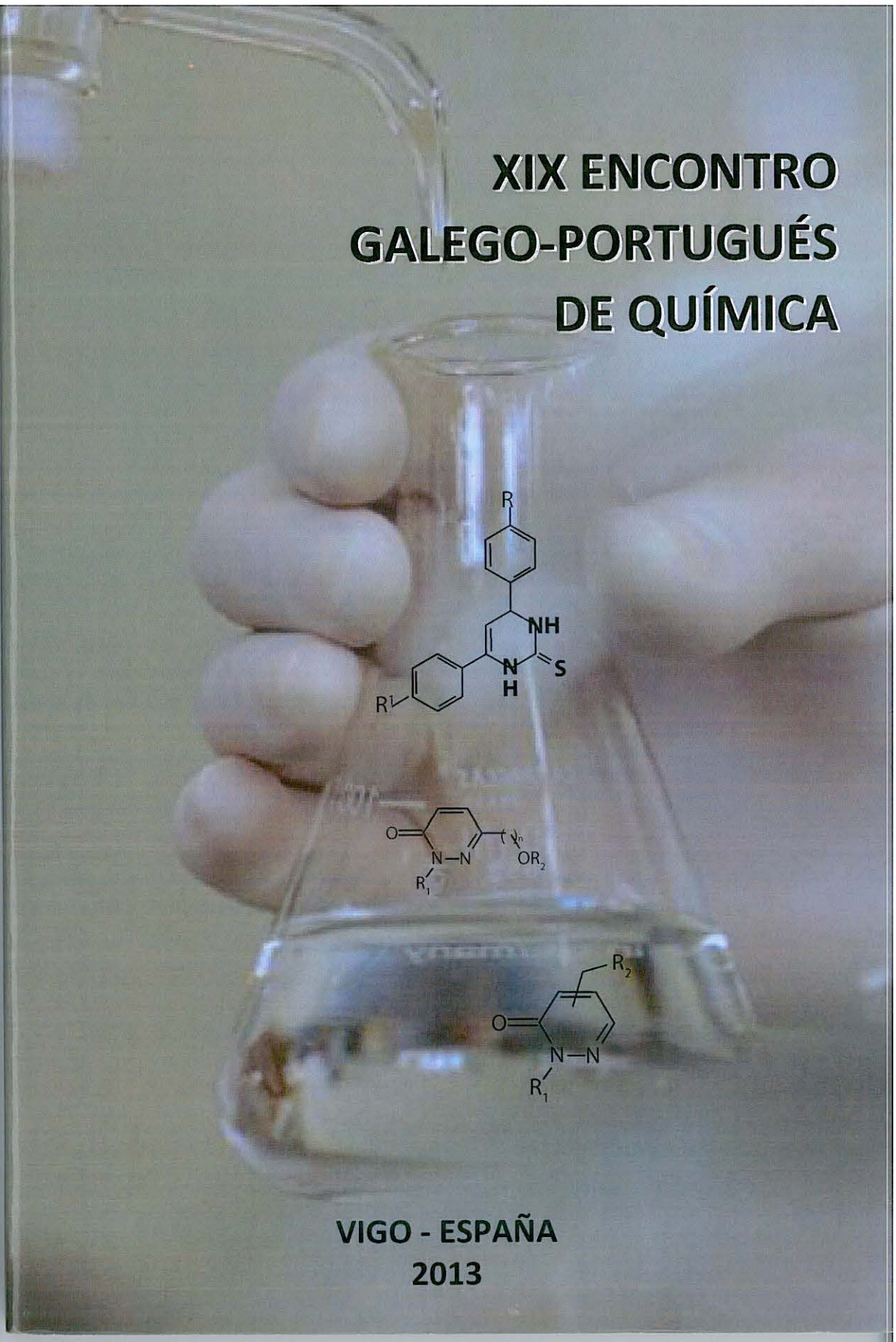

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Virtual screening of thieno[3,2-b]pyridine arylthioether (hetero)aryltriazole derivatives as potential tyrosine kinase VEGFR2 inhibitors

Ricardo C. Calhelha[1,2], Agathe Begouin[2], Joana F. Campos[2], Isabel C.F.R. Ferreira[1], Maria-João R.P. Queiroz[2], Rui M.V. Abreu[1]

1) Centro de Investigação de Montanha (CIMO), ESA, Instituto Politécnico de Bragança, Campus de Sta. Apolónia, Apartado 1172, 5301-855 Bragança, Portugal
2) Centro de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal

Recently we presented a series of thieno[3,2-d]pyrimidine ether 1,3-diaryl ureas with potent VEGFR2 inhibition activity. The binding mode was analyzed and the compounds showed a type-II tyrosine kinase inhibition mode, with the thienopyrimidine moiety forming a Hydrogen Bond (H-bond) with CYS919 residue and the urea moiety forming H-bonds with key residues GLU885 and ASP1046 of the kinase domain.[1]
In this study, the potential of changing the more widely used urea moiety to a triazole moiety now in thieno[3,2-b]pyridine arylthioethers, was analyzed. A number of 3D thieno[3,2-b]pyridine arylthioethers (hetero)aryltriazole derivatives (Figure 1) were designed and then molecular docking studies, using AutoDock4, were performed against a VEGFR2 crystal

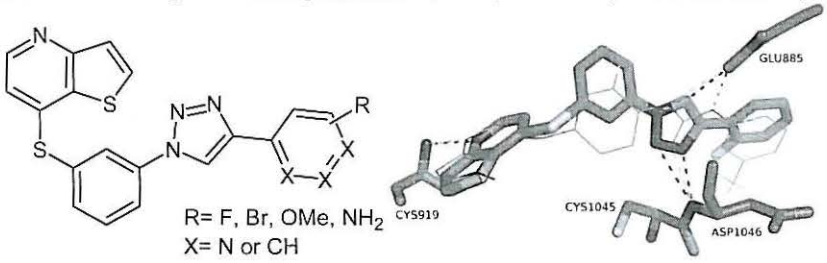

Figure 1. a) General structure of the thieno[3,2-*b*]pyridine thioether triazole derivatives designed in the present study; b) Docking binding mode of the most potent thieno[3,2-*b*]pyridine triazole derivative (cyan), with the predicted H-bond shown in red. For comparison, the co-crystallized inhibitor of the VEGFR2 structure (PDB:3VHE) is presented (green lines), with the respective H-bonds in yellow.

The structures and docking poses obtained for thieno[3,2-*b*]pyridine thioether triazole derivatives are present. Results show that the triazole moiety may be able to replace the urea moiety and form similar H-bonds. The thieno[3,2-*b*]pyridine thioether aryltriazole derivatives with F or Br in the *para* position, respectively, present the lowest predicted binding energy (ΔG). Due to the potential to inhibit VEGFR2, these compounds were synthesized and then tested in enzymatic, cellular and biomolecular assays.

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Reference

(1) M.-J. Queiroz, *et al. BioMed Res. Int.* **2013**, *2013*, 1-9.

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D. Ricardo C. Calhelha, ha participado en el *XIX Encontro Galego-Portugués de Química* celebrado, en el Salón de Actos del Museo do Mar de Galicia (Vigo - España), del 13 al 15 de noviembre de 2013, presentando la comunicación *"Virtual screening of thieno[3,2-b]pyridine arylthioether (hetero)aryltriazole derivatives as potential tyrosine kinase VEGFR2 inhibitors"*

En Vigo, a 13 de noviembre de 2013

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