2013

Book of Abstracts of the1st International Symposium on Profiling

2nd - 4th
September 2013
Caparica - Portugal

Book of Abstracts of the 1st International Symposium on Profiling 2013

ISPROF 2013 - 1st

Caparica - Almada, Portugal

2nd – 4th SEPTEMBER 2013

Book of Abstracts of the 1st International Symposium on Profiling 2013
ISPROF 2013 - 1st

Cover design: Hugo Santos

Organization of the Book of Abstracts: José Luís Capelo, Mário Diniz, Carlos Lodeiro, Hugo Santos, Elisabete Oliveira, Eduardo Araujo

ISBN: 978-989-98415-5-0 (pdf version)
ISBN: 978-989-98415-4-3 (paper version)

Printed by Proteomass (Portugal)

Printage: 200 copies (CD-ROM); 30 copies (paper)

Caparica, Portugal, 2013

Table of contents

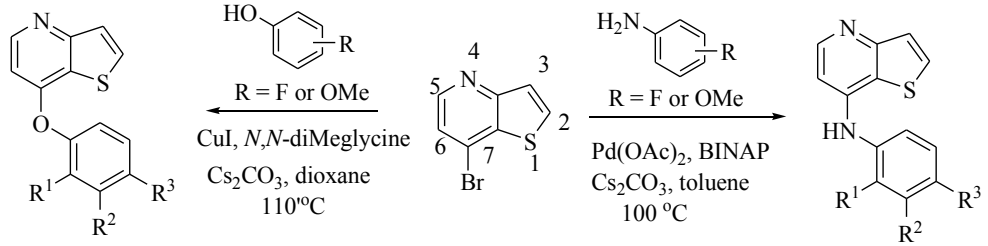
P12. Epidermal growth factor receptor inhibitory activity of new potential antitumor di(hetero)arylethers and di(hetero)arylamines in the thieno[3,2-*b*]pyridine series.

Ricardo C. Calhelha[1,2], Daniela Peixoto[1], Pedro Soares[1,3], Isabel C.F.R. Ferreira[2], Rui M.V. Abreu[2], Maria João R.P. Queiroz[1]

(1) Centro de Química, Univ. do Minho, Campus de Gualtar 4710-057 Braga, Portugal
(2) CIMO/ESA, I.P. Bragança Campus de Sta Apolónia, Apt. 1172, 5301-855 Bragança, Portugal.
(3) CIQ/Dept. de Química e Bioquímica, Fac. Ciências, Univ. do Porto, 4169-007 Porto, Portugal.
calhelha@ipb.pt

Abstract

Thienopyridine skeleton has been reported as having interesting biological activity, namely as antitumorals [1] and antiangiogenics [2]. The Epidermal Growth Factor Receptor (EGFR) exists in the cell surface and is activated by binding its specific ligands. The inhibition of its intracellular tyrosine kinase domain prevents the signaling pathways of cellular proliferation [3]. In our research group we have prepared the di(hetero)arylethers **1a-f** and the di(hetero)arylamines **2a-f** functionalizing the 7-position of the thieno[3,2-b]pyridine in good to high yields, using copper (C-O) or palladium (C-N) catalyzed couplings, like presented below.



1a R^1 = F, R^2 = R^3 = H; 69%
1b R^1 = R^3 = H; R^2 = F; 63%
1c R^1 = R^2 H; R^3 = F; 65%
1d R^1 = OMe, R^2 = R^3 = H; 45%
1e R^1 = R^3 = H; R^2 = OMe; 50%
1f R^1 = R^2 H; R^3 = OMe; 45%

2a R^1 = F, R^2 = R^3 =H; 75%
2b R^1 = R^3 = H; R^2 = F; 70%
2c R^1 = R^2 = H; R^3 = F; 73%
2d R^1 = OMe, R^2 = R^3 = H; 80%
2e R^1 = R^3 = H; R^2 =OMe ; 83%
2f R^1 = R^2 = H; R^3 = OMe; 54%

The di(hetero)arylethers **1a-f** and di(hetero)arylamines **2a-f** series were evaluated **for** EGFR tyrosine kinase inhibition activity. Compounds for series **1** presented practically no or very weak inhibition activity while compounds **2** presented good inhibition activity, with the most potent compounds **2e** presenting a IC50 value of 40 nM. These compounds can be view as good starting points for the synthesis of even more potent EGFR inhibitors.

References

[1] Queiroz, M.J.R.P., *et al.* (2011) *Eur. J. Med. Chem*. *46*, 236–240.
[2] Munchhof, M.J. *et al.* (2004) *Bioorg. Med. Chem. Lett.*, *14*, 21–24.
[3] Giamas, G., Yik *et al* (2010). *Cellular Signalling* 22, 984–1002.

Acknowledgments

To the Foundation for the Science and Technology (FCT–Portugal) for financial support through the Portuguese NMR network (Bruker 400 Avance III-Univ Minho). To FCT and FEDER-COMPETE/QREN/EU for financial support through the research unities PEst-C/QUI/UI686/2011 and PEst-OE/AGR/UI0690/2011, the research project PTDC/QUI-QUI/111060/2009 and the post-Doctoral grant attributed to R.C.C. (SFRH/BPD/68344/2010) also financed by POPH and FSE.