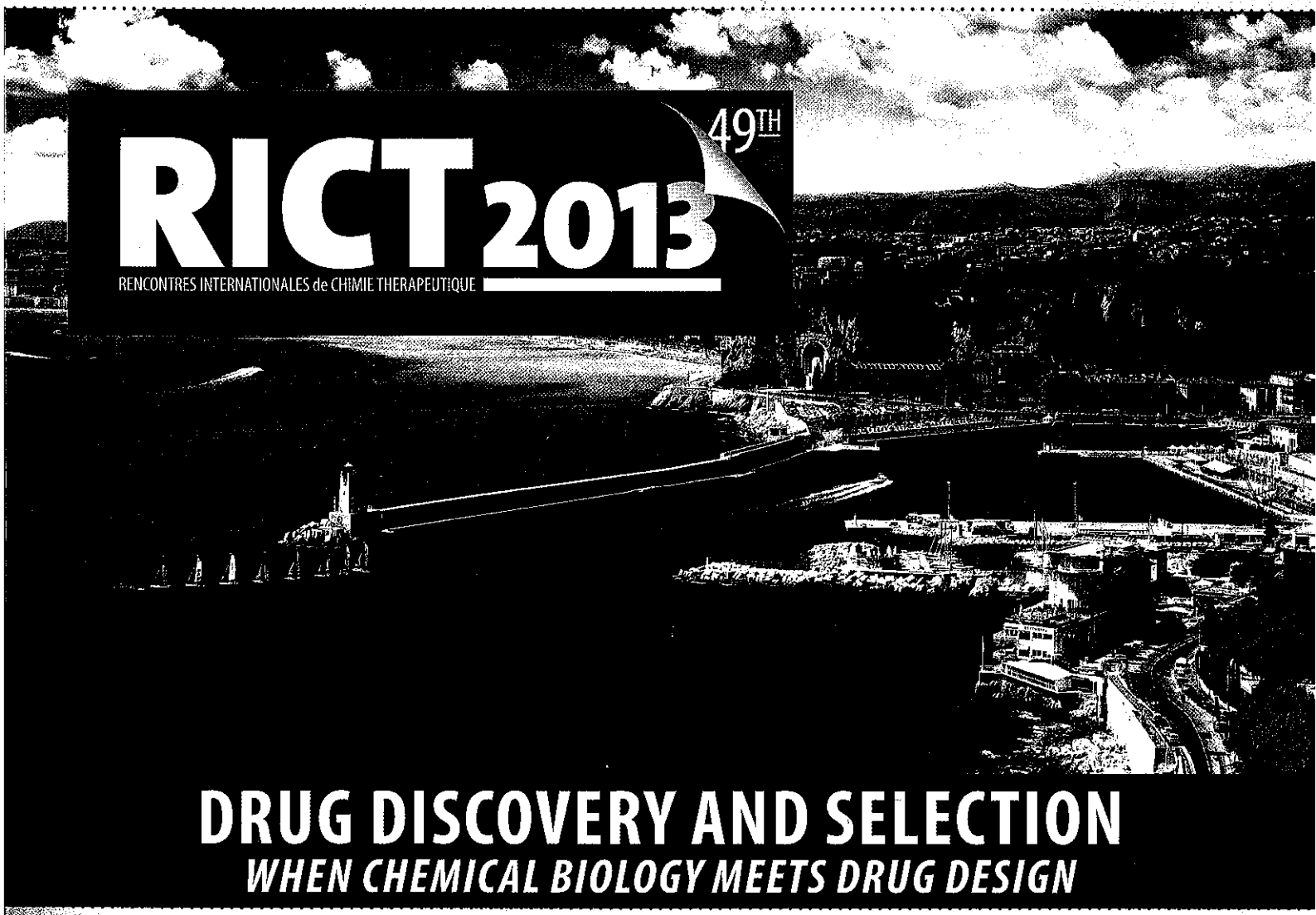
INTERNATIONAL CONFERENCE ON MEDICINAL CHEMISTRY



DRUG DISCOVERY AND SELECTION

WHEN CHEMICAL BIOLOGY MEETS DRUG DESIGN

JULY 3-5, 2013 | NICE, FRANCE

RICT

sct

SOCIÉTÉ DE CHIMIE THÉRAPEUTIQUE (SCT)

Université Nice Sophia Antipolis

UNIVERSITY OF NICE SOPHIA ANTIPOLIS

WWW.MEDCHEM.FR WWW.RICT2013.ORG

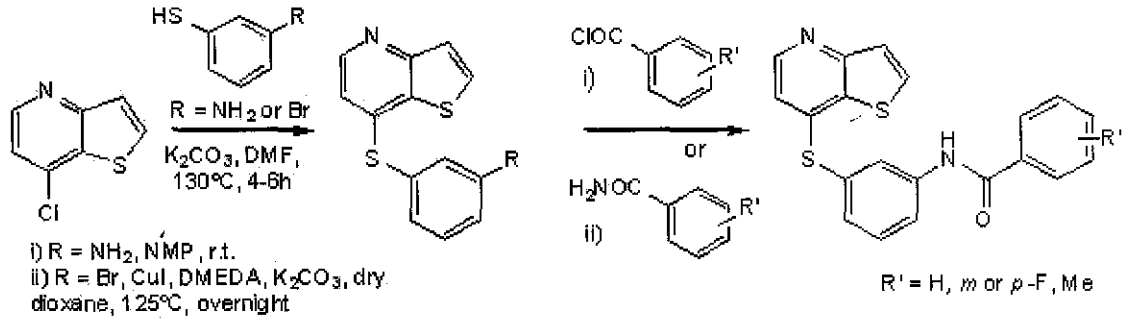
SYNTHESIS OF NEW N-[3-(THIENO[3,2-b]PYRIDINE-7-YLTHIO)PHENYL]BENZAMIDES AS POTENTIAL INHIBITORS OF VEGFR2 USING RATIONAL DESIGN

Maria-João R.P. Queiroz (1), Agathe Begouin (1), Joana F. Campos (1), Daniela Peixoto (1), Hugo J. C. Froufe (2), Ricardo C. Calhelha (1,2), Rui M. V. Abreu (2), Isabel C.F.R. Ferreira (2)

1) Centro de Química, Escola de Ciências Universidade do Minho, Campus de Gualtar 4710-057 Braga, Portugal mjrpq@quimica.uminho.pt
2) Centro de Investigação de Montanha(CIMO), Escola Superior Agrária, Instituto Politécnico de Bragança Campus de Santa Apolónia, apartado 1172, 5301-855 Bragança, Portugal

Vascular Endothelial Growth Factor Receptor 2 (VEGFR2) is the major receptor of the angiogenic effects when linked to VEGF released by tumors. It has a well known role as a transmembrane receptor activating multiple signaling pathways of proliferation and migration of endothelial cells [1], thus leading to the formation and the expansion of new blood vessels (vasculogenesis and angiogenesis) towards the tumor [2]. Therefore, several approaches have been developed to inhibit VEGFR activation and signaling [3].

Some thienopyridine derivatives have already been shown to be inhibitors of the tyrosine kinase domain of VEGFR2 preventing its activation [4]. Herein, we describe the synthesis of new *N*-[3-(thieno[3,2-*b*]pyridine-7-ylthio)phenyl]benzamides, suggested by rational design as potential inhibitors of this domain, either through a Cu-catalyzed C-N coupling of a brominated di(hetero)arylthioether thieno[3,2-*b*]pyridine with benzamides, or through a reaction of an aminated di(hetero)arylthioether thieno[3,2-*b*]pyridine with benzoyl chlorides, as presented below.



i) R = NH_2, NMP, r.t.
ii) R = Br, CuI, DMEDA, K_2CO_3, dry dioxane, 125°C, overnight

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

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

Acknowledgments: To FCT–Portugal for financial support through the NMR Portuguese network (Bruker 400 Avance III-Univ Minho). FCT and FEDER-COMPETE-QREN-EU for financial support through the research unities PEst-C/QUI/UI686/2011, PEst-OE/AGR/UI0690/2011, the research project PTDC/QUI-QUI/111060/2009 and the post-Doctoral grants attributed to A.B.(SFRH/BPD/36753/2007) and R.C.C (SFRH/BPD/68344 /2010), also financed by POPH and FSE.

References

1) M. J. Cross, J. Dixelius, T. Matsumoto, L. Claesson-Welsh, Trends Biochem. Sci. 2003, 28, 488–494.
2) (a) T. P. D. Fan; R. Jaggar; R. Bicknell, Trends Pharmacol. Sci. 1995, 16, 57–66. (b) J. Folkman, Nat. Med. 1995, 1, 27–31. (c) T. Veikkola, K. Alitalo, Semin Cancer Biol 1999, 9, 211–220.
3) L. M. Ellis, D. J. Hicklin, Clin. Cancer. Res. 2008, 14, 6371–6375.
4) (a) M. J. Munchhof, et al., Bioorg. Med. Chem. Lett., 2004, 14, 21-24. (b) Claridge, S. et al., Bioorg. Med. Chem. Lett., 2008, 18, 2793-2798.

PROGRAMME AT A GLANCE

WEDNESDAY JULY 03, 2013	
10:00	Registration
11:30	Reaxys Workshop
14:00	Introductive Remarks
	SESSION 1: Paul Ehrlich Prize-Lecture *Sponsored by Janssen-Cilag*
14:15	**L01** - M. Lazdunski
	SESSION 2: Ion Channels
15:00	**L02** - R. Owen
15:45	**L03** - H. Schirok
16:30	Coffee Break and Exhibition
	SESSION 3: Synergies between Medicinal Chemistry and Biotechnology *Sponsored by Pierre Fabre Reserach Institute*
17:30	**L04** - A. Beck
18:30	Welcome Reception

THURSDAY JULY 04, 2013		
	SESSION 4: Case Study, Immunology & Inflammation	**SESSION 5:** Fragment-based Drug Design
08:45	**L05** - L. Sanière	**L07** - C. Dalvit
09:30	**L06** - W. Haap	**L08** - J. Murray
10:15	Coffee Break, Poster Session (even numbers) and Exhibition	
	SESSION 6: Druggability	**SESSION 7:** ChemoGenomic
10:45	**L09** - P. Leeson	**L11** - S. Helliwell
11:30	**L10** - R. Law	**L12** - J. Brown
12:15	Lunch, Poster Session (even numbers) and Exhibition	
14:00 - 15:30	**CAREER SESSION**	
	SESSION 8: Molecular Networks	
14:15	**L13** - G. Superti-Furga	
	SESSION 9: Case Studies, Anti-infective Agents 1	**SESSION 10:** ChemBioTools
15:00	**L14** - K.H. Altmann	**L16** - M.Morris
15:45	**L15** - J.P. - Surivet	**L17** - D. Bonnaffé
16:30	Coffee Break and Exhibition	
	SESSION 11: Case Studies: Anti-Infective Agents *Sponsored by GlaxoSmithKline*	**SESSION 12:** GPCR
17:00	**L18** - J. Mottram	**L20** - M. Congreve
17:45	**L19** - P. Wyatt	**L21** - N. Tschammer
20:00	Symposium banquet	

FRIDAY JULY 05, 2013	
	SESSION 13: Breaking News
08:30	**L22** - C. Bouix-Peter
09:15	**L23** - I. Lewis
10:00	Coffee Break, Poster Session (odd numbers) and Exhibition
	SESSION 14: Antibody Drug Conjugates *Sponsored by Pierre Fabre Research Institute*
10:30	**L24** - R. Chari
11:15	**L25** - J. Junutula
	SESSION 15: European Lead Factory *Sponsored by ELF Chemistry SMEs: Edelris, Mercachem, Sygnature, Syncom, Taros*
12:00	**L26** - J. Hueser
12:35	Lunch *Sponsored by ELF Chemistry SMEs* Poster Session (odd numbers) and Exhibition
	SESSION 16: Case Studies, Pain & Cancer
14:05	**L27** - R. Foglesong
14:50	**L28** - E. Lingueglia
15:25	**L29** - F. Halley
16:10	Poster Prizes and Conclusive Remarks

SECRETARIAT RICT 2013
LD ORGANISATION | Scientific Conference Producers | Tel: +32 10 45 47 77 | Fax: +32 10 45 97 19 | secretariat@LDOrganisation.com