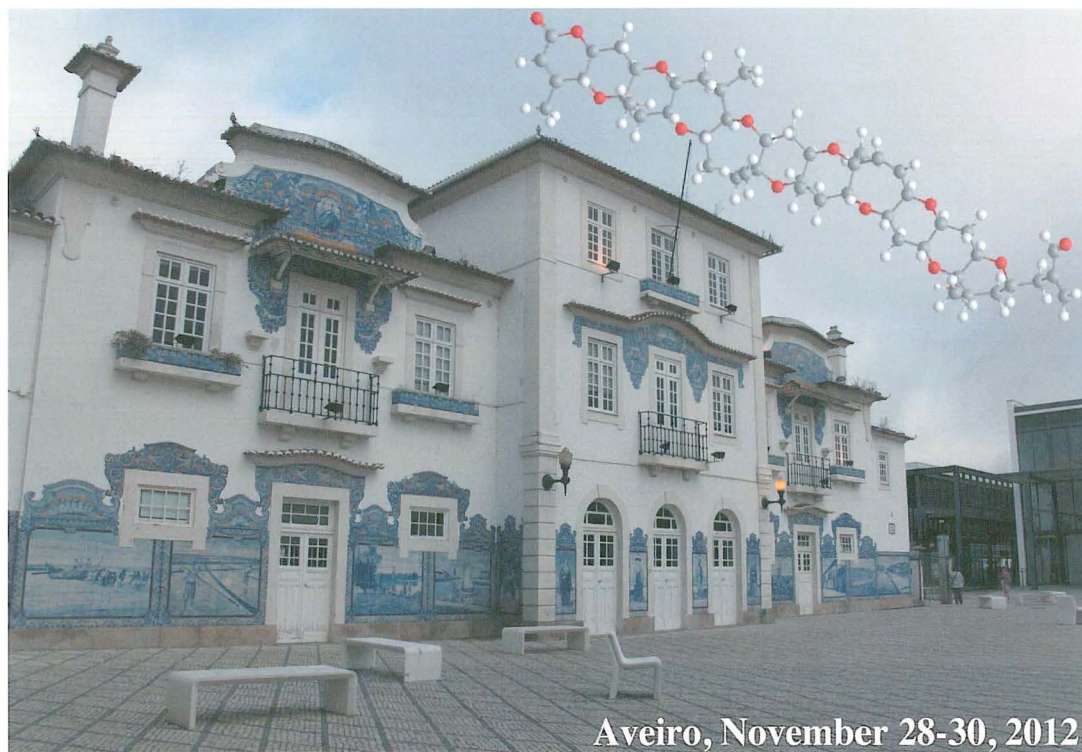


3º Encontro Nacional de Química Terapêutica



Aveiro, November 28-30, 2012

3rd Portuguese Meeting on Medicinal Chemistry
1st Portuguese-Spanish-Brazilian Meeting on Medicinal Chemistry.



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3rd Portuguese Meeting on Medicinal Chemistry

1st Portuguese-Spanish-Brazilian Meeting on Medicinal Chemistry

Supported by The Portuguese Society of Chemistry and the University of Aveiro

Scientific Committee

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Fernanda Proença	Department of Chemistry, School of Science, University of Minho
Hans Peter Wessel	F. Hoffmann-La Roche Ltd, Pharma Research & Early Development (pRED), Basel, Switzerland & Department of Chemistry, University of Aveiro
Madalena Pinto	Faculty of Pharmacy, University of Porto
Maria Luísa Sá e Melo	Faculty of Pharmacy, University of Coimbra
Patrício Soares da Silva	Bial - Portela & C. ^a , S.A.
Rui Moreira	Faculty of Pharmacy, University of Lisboa
William Heggie	Hovionne, Loures, Portugal

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Aurora Fernandes (Dep. Chem., Univ. Aveiro)

Scientific program

Wednesday, November 28th

09:00-10:50 Registration
10:50-11:15 Opening ceremony

Chairperson Artur Silva

11:15-12:00 PL1 – Gerhard Ecker
Department of Medicinal Chemistry, University of Vienna
The medicinal chemistry of drug transport – knowledge driven ligand design

12:00-12:30 IL1 – Maria M. M. Santos
Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon
Design of novel compounds to modulate apoptosis

12:30-13:00 IL2 – Ana Peixoto Gomes
Department of Chemistry & QOPNA, University of Aveiro
Synthesis of biologically active porphyrin derivatives in photodynamic Therapy

13:00-14:30 Lunch

Chairperson Sérgio Simões

14:30-15:15 PL2 – Mathias Montenarh
Medical Faculty, University of Saarland
Protein kinase CK2 as a pharmacological target in different cellular processes

15:15-15:45 IL3 – José Alberto Martins
Department of Chemistry, University of Minho
Gold nanoparticles functionalised with Gd³⁺ chelates as contrast agents for magnetic resonance imaging: fool's gold?

15:45-17:00 Posters discussion and coffee break

Chairperson Luísa Sá e Melo

17:00-17:15 OC1 – Patrícia M. R. Pereira
Department of Chemistry, University of Aveiro
Albumin and monoclonal antibody conjugated porphyrin: synthesis, characterization and biological potential against human bladder cancer cell line

17:15-17:30 OC2 – Gonçalo N. Costa
Luzitin, SA, Edifício Blupharma, São Martinho do Bispo, Coimbra
Synthesis of stable meso-aryl bacteriochlorin photosensitisers: 3rd generation compounds for photodynamic therapy

- 17:30-17:45 OC3 – Paula Gomes
Centro de Investigação em Química da Universidade do Porto, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade do Porto
Old drugs with new faces: boosting the antiparasitic activity of "antimalarial classics"
- 17:45-18:00 OC4 – M. Manuel Cruz Silva
CNC-Centre for Neuroscience and cell Biology and Faculdade de Farmácia, Universidade de Coimbra
Cytotoxic oxysterols: combining chemical and enzymatic approaches to obtain new derivatives with improved activity
- 18:00-18:15 OC5 – Ana Sofia Leal
Grupo de Química Farmacêutica, Faculdade de Farmácia da Universidade de Coimbra, Pólo das Ciências da Saúde, Coimbra, Portugal and Centro de Neurociências e Biologia Celular, Universidade de Coimbra, Coimbra, Portugal and Department of Medicine, Mount Sinai School of Medicine, New York, NY USA
Novel ursolic acid derivatives with potent anticancer activity
- 18:15-18:30 OC6 – Inês Martins
Centro de Química Estrutural, Instituto Superior Técnico, UTL, Lisboa, Portugal and Faculdade de Ciências e Tecnologia, UNL, Lisboa
New co-crystal forms and molecular salts of azelaic acid and nadidixic acid with potential medicinal application
- 19:00 Welcome reception

Thursday, November 29th

Chairperson Hans Peter Wessel

- 09:00-09:45 PL3 – Torsten Hoffmann
F. Hoffmann-La Roche Ltd, Pharma Research & Early Development (pRED), Basel, Switzerland
Future role of medicinal chemistry and its maturation to chemical biology
- 09:45-10:15 IL4 – Claus Jacob
Bioorganic Chemistry, School of Pharmacy, Saarland State University, Saarbruecken, GERMANY
Redox signaling via the cellular thiolstat – the special relationship in group 16
- 10:15-10:45 IL5 – Gonçalo Bernardes
Institute of Pharmaceutical Sciences, (ETH), Zürich, Switzerland
Traceless antibody-drug conjugates for cancer therapy
- 10:45-11:15 Coffee break

Chairperson Fernanda Proença

- 11:15-11:30 OC7 – Vasco Cachatra
Universidade de Lisboa, Faculdade de Ciências, Departamento de Química e Bioquímica/Centro de Química e Bioquímica, Carbohydrate Chemistry Group, Lisboa, Portugal
Synthetic studies on miharamycins sugar moiety and analogues

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- 11:30-11:45 OC8 – Raquel G. Soengas
Department of Chemistry & QOPNA, University of Aveiro, Portugal
Novel domino reaction of iodo glycosides: formal synthesis of aminocyclopentitols
- 11:45-12:00 OC9 – Daniela Ribeiro
REQUIMTE, Department of Chemical Sciences, Faculty of Pharmacy, University of Oporto, Oporto, Portugal
Flavonoids and inflammation: a structure-activity relationship study
- 12:00-12:15 OC10 – Maria do Carmo Barreto
CIRN/DCTD, Universidade dos Açores, Ponta Delgada, Portugal
Synthesis, biological evaluation and docking studies of oxygen heterocyclic compounds as acetylcholinesterase inhibitors
- 12:15-14:00 Lunch

Chairperson William Heggie

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- 14:00-14:45 PL4 – Rob Leurs
Amsterdam Institute of Molecules, Medicines and Systems, Division of Medicinal Chemistry, VU, University of Amsterdam
Parasite-specific cyclic nucleotide phosphodiesterase inhibitors to target Trypanosoma brucei
- 14:45-15:15 IL6 – João Nuno Moreira
Faculty of Pharmacy and Center for Neurosciences and Cell Biology (CNC), University of Coimbra
Tumor targeting with nanoparticles: making novel therapeutics from "old" drugs
- 15:15-15:30 OC11 – Francisco Peixoto
Department of Chemistry and CQ-VR, UTAD, Vila Real, Portugal
Toxicological evaluation of new tacrine analogues from 4-amino-1H-pyrrole-3-carbonitrile
- 15:30-15:45 OC12 – Daniel J. V. A. Dos Santos
Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon, Lisbon, Portugal
A unified view on P-glycoprotein efflux: blending experimental, pharmaphore, molecular dynamics and molecular docking results
- 15:45-17:00 Posters discussion and coffee break

Chairperson Madalena Pinto

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- 17:00-17:15 OC13 – Maria João R. P. Queiroz
Centro de Química, Univ. do Minho, Braga, Portugal
Synthesis, docking, enzymatic and celular assays of thienof[3,2-b]pyridine-thioether-1,3-diaryltureas as VEGFR2 inhibitors
- 17:15-17:30 OC14 – Tiago Rodrigues
Swiss Federal Institute of Technology (ETH Zürich), Institute of Pharmaceutical Sciences, Zürich, Switzerland
Ligand-based de novo design of kinase lead structure candidates

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- 17:30-17:45 OC15 – Susana D. Lucas
Research Institute for Medicines and Pharmaceutical Sciences (iMed.UL), Faculty of Pharmacy, University of Lisbon, Lisboa, Portugal
In silico approach toward lead generation for COPD drug discovery
- 17:45-18:00 OC16 – M. Manuel B. Marques
REQUIMTE - Departamento de Química, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, Portugal
Unveiling the role of a peptidoglycan involved in cellular recognition
- 18:00-18:15 OC17 – Mariana Leão
REQUIMTE, Department of Biological Sciences, Laboratory of Microbiology, Faculty of Pharmacy, University of Porto, Porto, Portugal
A new small-molecule inhibitor of p53-MDM2 interaction discovered using a yeast cell-based screening assay
- 18:15-18:30 OC18 – Ana Isabel Tomaz
Centro de Ciências Moleculares e Materiais, DQB, Faculty of Sciences, Lisbon University, Lisbon, Portugal
Promising organometallic ruthenium metallodrugs: [RuII(η⁵-Cp)(bpy)(PPh₃)⁺ a large spectrum antitumor agent
- 18:40- ... Meeting of the Medicinal Chemistry Group (SPQ)
- 19:30- ... Congress dinner

Friday, November 30th

1st Portuguese-Spanish-Brazilian Meeting on Medicinal Chemistry

Chairperson Artur Silva

- 09:00-09:35 PL1-PSB – Carlos Montanari
Institute of Chemistry of São Carlos, University of São Paulo, Brazil
“On the integration of in silico and in vitro assays for new trypanocidal agents discovery”
- 09:35-10:10 PL2-PSB – Antoni Torrens
President of the Spanish Society of Medicinal Chemistry (SEQT): ESTEVE, R & D, Barcelona, Spain
Discovery of new and selective 5-HT₇ agonists for the treatment of pain
- 10:10-11:30 Posters discussion and coffee break

Chairperson Fernanda Proença

- 11:30-12:05 PL3-PSB – João Rocha
CICECO, Department of Chemistry, University of Aveiro
Materials for medicinal chemistry: some case studies

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12:05-12:40	PL4-PSB – Andrei Leitão Institute of Chemistry of São Carlos, University of São Paulo, Brazil <i>Cell-based assays and cheminformatics approaches of novel anticancer compounds</i>
12:40-14:30	Lunch
Chairperson Rui Moreira	
14:30-14:40	Rui Moreira Faculty of Pharmacy, University of Lisbon, Portugal <i>International symposium on medicinal chemistry, Lisbon, 2014</i>
14:40-15:15	PL5-PSB – Madalena Pinto Faculty of Pharmacy, University of Porto <i>Chiral derivatives of xanthenes: bioactive small molecules and analytic tools</i>
15:15-15:50	PL6-PSB – María José Camarasa Instituto de Química Médica (CSIC), Madrid, Spain <i>A prodrug approach based on the DPPIV/CD-26 enzyme</i>
15:50-16:10	Closing ceremony

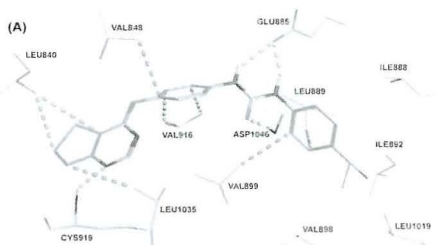
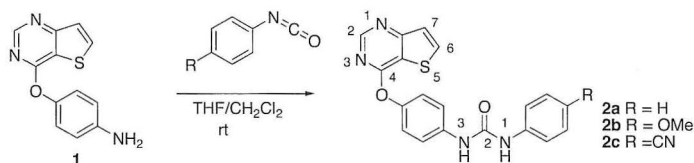
1-Aryl-3-[4-(thieno[3,2-*d*]pyrimidin-4-yloxy)phenyl]ureas as VEGFR2 inhibitors: synthesis, docking enzymatic and cellular assays

Daniela Peixoto,^a Ricardo C. Calhella,^{a,b} Pedro Soares,^{a,c} Rui M.V. Abreu,^b Hugo Froufe,^b Isabel C. F. R. Ferreira,^b Raquel Costa,^d Raquel Soares,^d Maria João R. P. Queiroz^a

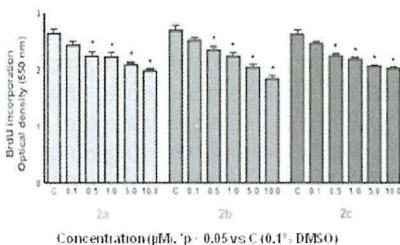
^aCentro de Química (UI686), Univ. do Minho, Campus de Gualtar 4710-057 Braga, Portugal; ^bCIMO (UI690)/ESA, I.P. Bragança Campus de Sta Apolónia, Apt. 1172, 5301-855 Bragança, Portugal; ^cCIQ/Dept. de Química e Bioquímica, Fac. Ciências, Univ. do Porto, 4169-007 Porto, Portugal; ^dCentro de Investigação Médica (UI38), Fac. Medicina, Univ. Porto, 4200-450 Porto Portugal

A number of thienopyrimidines derivatives have shown potent VEGFR2 (Vascular Endothelium Growth Factor Receptor2) tyrosine kinase inhibition activity.^[1] VEGF is a surrogate marker of angiogenesis that activates VEGFR2 in endothelial cells.

Here we present the synthesis of new 1-aryl-3-[4-(thieno[3,2-*d*]pyrimidin-4-yloxy)phenyl]ureas from the aminodi(hetero)arylether **1**, also prepared by us, which was reacted with arylisocyanates to give the corresponding 1,3-diarylureas **2a-c**.



(C) Superimposition of the docking poses at the VEGFR2 kinase domain for compounds **2a-c**.



(B) Proliferation of HUVECs with VEGF supplementat.

Compounds **2a-c** were evaluated for inhibition of VEGFR2 tyrosine kinase activity using enzymatic assays and showed good inhibition ability. The rationale for the inhibition is discussed using docking (A). To examine the activity of compounds **2a-c** in endothelial cells, HUVECs were cultured in M199 medium (supplemented with 2% FBS and 60 ng/mL of VEGF) in the absence (control) or presence of each compound at different concentrations. A reduction above 0.5 μM in the proliferation of HUVECs was observed, evaluated by the incorporation of BrdU in cell culture. These molecules are promising anti-angiogenic agents that may be used for therapeutic purposes.

Acknowledgments: To the FCT–Portugal for financial support through the PTNMR network. To FCT and COMPETE/QREN/EU for financial support through the research unities PEst-C/QUI/UI686/2011, PEst-OE/AGR/UI0690/2011, PEst-OE/SAU/UI0038/2011, 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.

References

[1] Dai, Y. *et al. J. Med.Chem.* **2005**, *48*, 6066–6083.