P28

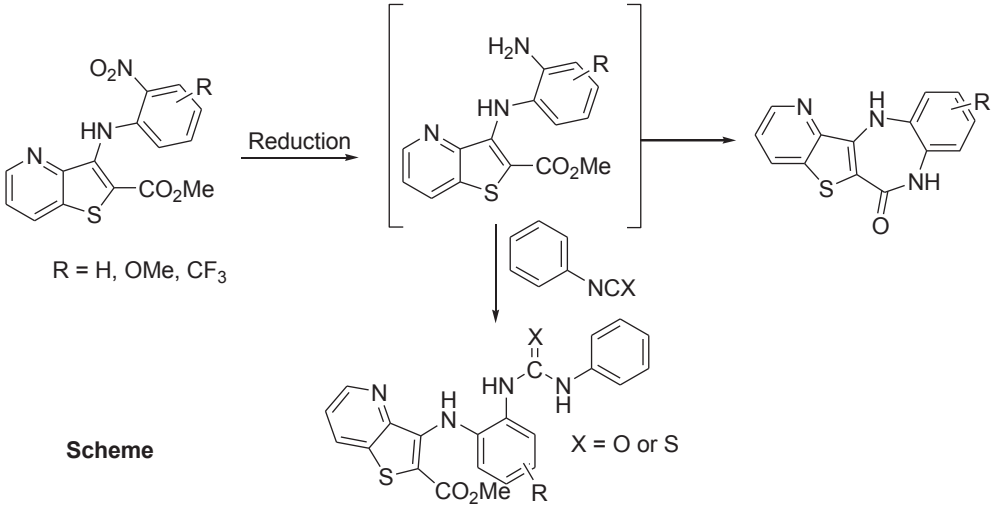
SYNTHESIS OF TETRACYCLIC SYSTEMS AND (THIO)UREAS FROM AMINODI(HETERO)ARYLAMINES IN THE THIENO[3,2-*b*]PYRIDINE SERIES

Maria-João R.P. Queiroz,[a] Daniela Peixoto,[a] Ricardo C. Calhelha[a,b]

[a] Departamento/Centro de Química, Universidade do Minho, Campus de Gualtar 4710-057 Braga, Portugal, email: mjrpq@quimica.uminho.pt
[b] CIMO-ESA, Inst. Politécnico de Bragança, Campus de Sta Apolónia, Apt. 1172, 5301-855 Bragança, Portugal.

Our research group has been interested in the synthesis of di(hetero)arylamines either in the pyridine or in the thiophene ring in the thieno[3,2-*b*]pyridine series and some of the compounds obtained have shown very low GI_{50} values in human tumor cell lines [1,2].

Here we present the synthesis of tetracyclic compounds and also urea and thiourea derivatives from aminodi(hetero)arylamines prepared by reduction of the corresponding nitro compounds which were obtained by Buchwald-Hartwig palladium-catalyzed C-N coupling [2]. If a longer reaction time in the reduction is used, the tetracyclic [1,4]diazepin-7-ones are formed (Scheme). From the aminodi(hetero)arylamines it was also possible to prepare ureas or thioureas by reaction with phenyliso(thio)cyanates (Scheme).



Scheme

The tetracyclic [1,4]diazepin-7-ones and the (thio)urea derivatives obtained will be submitted to biological activity studies as potential antitumor and/or anti-angiogenic compounds.

Acknowledgements: Foundation for the Science and Technology (FCT–Portugal) for financial support through the Portuguese NMR network (Bruker 400 Avance III-Univ Minho). FCT and FEDER (European Fund for Regional Development)-COMPETE/QREN/EU for financial support through the research centre PEst-C/QUI/UI686/2011, the research project PTDC/QUI-QUI/111060/2009 and the post-doctoral grant of R.C.C. SFRH/BPD/68344/2010.

[1] Queiroz, M.-J.R.P; Calhelha, R.C.; Vale-Silva, L.A.; Pinto, E.; Nascimento, M. São-José *Eur. J. Med. Chem.* **2010**, *45*, 5732-5738.
[2] Calhelha, R.C.; Ferreira, I.C.F.R.; Peixoto, D.; Abreu, R.M.V.; Vale-Silva, L. A.; Pinto, E.; Lima, R. T.; Alvelos, M. I.; Vasconcelos, M.H.; Queiroz, M.-J.R.P. *Molecules* **2012**, 17(4), 3834-3843.