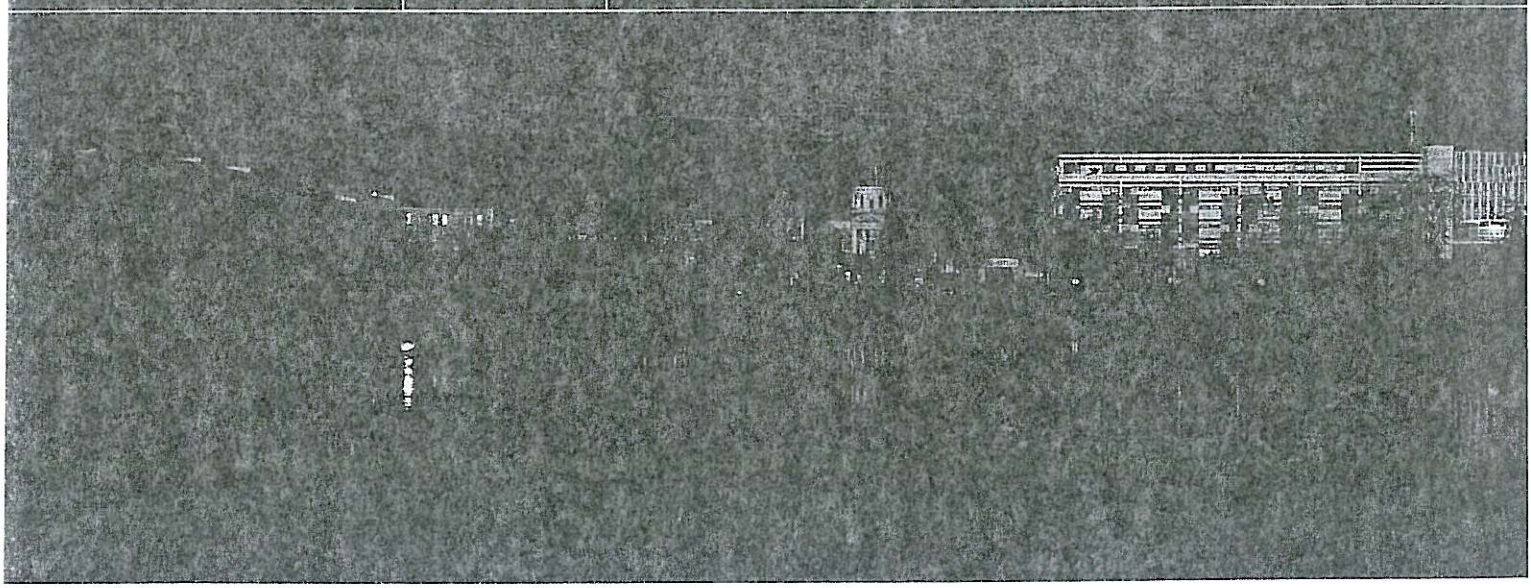
International Conference on Medicinal Chemistry

44èmes RICT

RENCONTRES INTERNATIONALES DE CHIMIE THERAPEUTIQUE

Organisées par la Société de Chimie Thérapeutique (SCT)



Interfacing Chemical Biology, Natural Products and Drug Discovery

July 2 - 4, 2008

Faculty of Pharmacy - Angers, France

www.medchem.fr

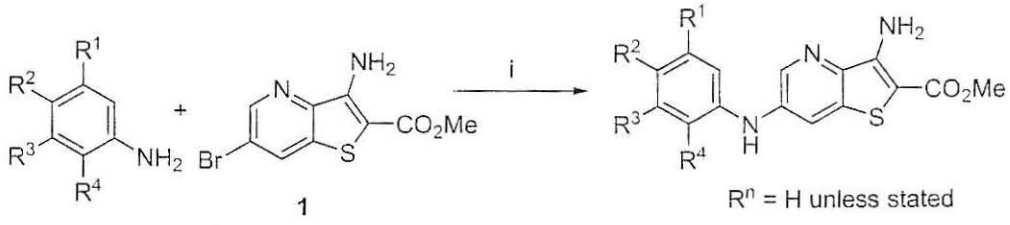
SYNTHESIS AND ANTIOXIDANT ACTIVITY OF NEW METHOXYLATED DI(HETERO)ARYLAMINES DERIVATIVES OF THIENO[3,2-*b*]PYRIDINES

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

[1]*Centro de Química, Universidade do Minho, Campus de Gualtar 4710-057 Braga, Portugal*
[2]*CIMO-ESAB, Instituto Politécnico de Bragança, Campus de Sta Apolónia, 1172, 5301-855 Bragança, Portugal*
[3] *Centro de Genética e Biotecnologia-IBB, UTAD, 5001-801 Vila Real, Portugal*

Due to their isosterism with pyrrolopyridines or quinolines, thieno[3,2-*b*]pyridines have attracted much attention because of their potential biological activity [1].

We have prepared the 6-bromothieno[3,2-*b*]pyridine **1**, following a known method used by us for benzo[*b*]thiophene compounds [2], as component for palladium-catalyzed Buchwald-Hartwig coupling with methoxylated anilines. The corresponding di(hetero)arylamines **2a-2d** were obtained in good yields and were fully characterized (Scheme 1).



1

R^n = H unless stated

2a R^2 = OMe, 21h, 50%
2b R^2 = R^4 = OMe, 4h, 60%
2c R^2 = R^3 = OMe, 6h, 60%
2d R^1 = R^3 = OMe, 27h, 40%

i) $Pd(OAc)_2$ (16 mol%) *rac*-BINAP (18 mol %), Cs_2CO_3 (1.8 equiv), toluene, 100 °C, under Ar

Scheme 1

The reducing properties of diarylamines make them very important as antioxidants, especially as radical scavengers [3]. In fact most representative examples of antioxidants are hindered phenols and diphenylamine derivatives [4].

Antioxidant assays as free radical scavenging activity on DPPH radicals, reducing power and lipid peroxidation inhibition using the beta-carotene linoleate system and the thiobarbituric acid reactive substances (TBARS) assay, have been performed on compound **1** and on the new diarylamines **2a-2d**, using alpha-tocopherol and ascorbic acid as standards. The results will be discussed in terms of EC_{50}. The best compound in all the methods studied is **2c** with two methoxy groups in *meta* and *para* positions. For the TBARS assay the EC_{50} results for compounds **2a-2c** are even better than for alpha-tocopherol (0.011 ± 0.001 mM). It was thus possible to establish some structure-antioxidant activity relationships depending on the number and position of the methoxy groups.

Acknowledgments:
FCT (Portugal) and FEDER for financial support through project POCI/QUI/59407/2004 and PhD grants to R.C.C. SFRH/BD/27294/2006 and R. M.V.A. SFRH/BD/27430/2006.

References

[1]- C. Comoy, E. Banaszak, Y. Fort *Tetrahedron* **2006**, *62*, 6036-6041 and references cited.
[2]- M.-J. R. P. Queiroz, R. C. Calhelha, G. Kirsch *Tetrahedron* **2007**, *63*, 13000-13005.
[3]- M. A. Esteves, N. Narender, M. J. Marcelo-Curto, B. Gigante *J. Nat. Prod.* **2001**, *64*, 761-766.
[4]- G. Scott *Bull. Chem. Soc. Jpn.* **1988**, *61*, 165-170.