10º Encontro Nacional de Química Orgânica

1° Simpósio Luso-Brasileiro de Química Orgânica

Book of abstracts

10ENQO - 1SLB
Faculty of Pharmacy
University of Lisbon
4-6 September 2013
PORTUGAL

Sociedade Portuguesa de Química

DQO Divisão de Química Orgânica SPQ

Faculdade de Farmácia Universidade de Lisboa

Sociedade Brasileira de Química

New Phosphonic Acids and Esters Derived from Indazole: Synthesis and Biological Activity Evaluation

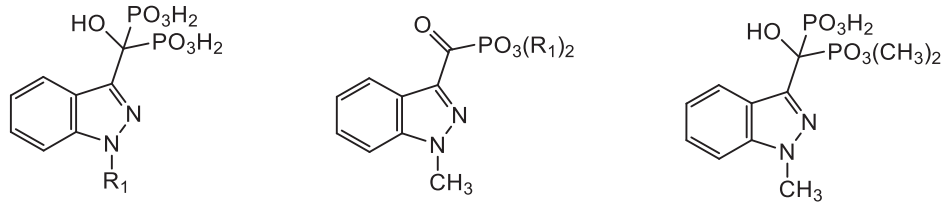
Silvânia S. Afonso,[a] António P. S. Teixeira,[a,b] M. Rosário Martins,[a,c] Fátima C. Teixeira[d]

[a]Departamento de Química, Escola de Ciências e Tecnologia, Universidade de Évora, R. Romão Ramalho, 59, 7000-671 Évora, Portugal; [b]Centro de Química de Évora, IIFA, Universidade de Évora, R. Romão Ramalho, 59, 7000-671 Évora, Portugal; [c]ICAAM, IIFA, Universidade de Évora - Pólo da Mitra, Apartado 94, 7002-554 Évora, Portugal; [d]LNEG,Estrada do Paço do Lumiar, 22, 1649-038 Lisboa, Portugal

apsteix@uevora.pt

Bisphosphonates (BPs) are a group of compounds derived from bisphosphonic acid and their salts, with a P-C-P structure which confers higher metabolic and chemical stability. They are an important class of drugs with therapeutic applications in the treatment of diseases of bone mineral metabolism such as osteoporosis and Paget's disease. These compounds have also shown activity in other areas, such as antitumor and antiparasitic activities.[1] The use of these compounds in therapy is affected by their low oral bioavailability due to low lipophilicity and the presence of charges at physiological pH. The improvement of their pharmacokinetic properties can be obtained by the use of ester derivatives as prodrugs.[2]

In this work, we present the synthesis and characterization of various phosphonic acids and esters derivatives of indazole (**Figure 1**). The biological activity of these compounds were evaluated including their toxicity, antioxidant and antimicrobial activities.[3] Bisphosphonic acid derivatives showed broad spectra with high activity against Gram – and Gram + pathogenic and commensal bacteria. These compounds also present antioxidant activity by the β-carotene/linoleic acid method.



R_1= H, CH_3

Figure 1: Structure of studied phosphonates derived from indazole.

Acknowledgements: We thank the Fundação para a Ciência e Tecnologia for financial support (POCI/QUI/55508/2004, PPCDT/QUI/55508/2004 and pluriannual CQE funding) and to the Portuguese NMR Network (IST-UTL).

References:

1. a) Fleisch H. *Bisphoshponates in Bone Disease: from the Lab to Patient*, 4th ed., Academic Press, San Diego, 2000. b) Bartl R., Frisch B., von Tresckow E., Bartl C.*Bisphosphonates in Medical Practice,* Springer-Verlag, Heidelberg, 2007. c) Zhang S., Gangal G., Uludağ H. *Chem. Soc. Rev.*, **2007**, *36*, 507.
2. Ezra A., Golomb G. *Adv. Drug Deliv. Rev.*, **2000**, *42*, 175.
3. NCCLS (2005), *Performance Standards for Antimicrobial Susceptibility Testing: Seventh Informational Supplement M100-S15*, National Committee for Clinical Laboratory Standards, Wayne, PA, USA.