Poster Session

11:30 - 14:30

Sala Ágora

	Title/Authors
1	***Structural Studies of Site Specific Mutants of p22HBP*** Susana S. Aveiro[1], Claudio H Santos1, J. Clayton[2], M.Camelo[2], G. C. Ferreira[2], A. L. Macedo[3], Brian J. Goodfellow[1] [1] CICECO, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal [2] Biochem. and Mol. Biol. Dept. , Col. of Med., USF, Tampa, FL 33612-4799, USA [3] REQUIMTE, Dept de Química, FCT-UNL, 2829-516 Caparica, Portugal
2	***Studying the Metabolic Profiling of Potencial Probiotic or Synbiotic Cheeses by NMR Spectroscopy*** Cláudio H. Santos[1], Dina Rodrigues[2], Ana C. Freitas[2], Brian J. Goodfellow[1] [1] Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal [2] ISEIT/Viseu, Instituto Piaget, 3515-776 Lordosa, Viseu, Portugal
3	***Metabonomics of Pregnancy: An NMR Study of Maternal Urine*** Sílvia O. Diaz[1], Gonçalo Graça[1], Joana Pinto[1], António S. Barros[2], Iola F. Duarte[1], Brian J. Goodfellow[1], Isabel M. Carreira[3], Eulália Galhano[4], M. Céu Almeida[4], Cristina Pita[4] and Ana M. Gil[1] [1] CICECO, Department of Chemistry, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal, [2] QOPNA, Department of Chemistry, University of Aveiro Campus Universitário de Santiago, 3810-193 Aveiro, Portugal [3] Cytogenetics and Genomics Laboratory, Faculty of Medicine, University of Coimbra, Portugal and CENCIFOR - Forensic Science Centre, Portugal, [4] Bissaya Barreto Maternity, Hospital Center of Coimbra, Portugal

	Title/Authors
7	**Structure Determination of Some Oxygen and Nitrogen Heterocyclic Compounds by NMR** Raquel S. G. R. Seixas,[1] Catia I. C. Esteves,[1] Cristela M. Brito,[1] Stéphanie B. Leal,[1] Diana C. G. A. Pinto,[1] Clementina M. M. Santos,[3] Ana M. L. Seca,[2] Artur M. S. Silva,[1] José A. S. Cavaleiro[1] [1] Department of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal [2] DCTD, University of Azores, 9501-801 Ponta Delgada, Açores; [3] Department of Vegetal Production and Technology, School of Agriculture, Campus de Santa Apolónia, 5301-855 Bragança, Portugal
8	**NMR Characterization of Novel Flavone-Nitrogen Heterocycle Conjugates** Regina M. S. Sousa[1], Diana C. G. A. Pinto[1], Artur M. S. Silva[1], Maria A. F. Faustino[1], Vanda Vaz Serra[1], Maria G. P. M. S. Neves[1], José A. S. Cavaleiro[1] [1] Department of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal
9	**NMR Crystallography of Amoxicillin Trihydrate** S. M. Santos[1], J. Rocha[1], L. Mafra[1] [1] Department of Chemistry, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal
10	**Solid-state NMR Techniques and Computational Methods Combined for the Assignment of Glutathione** Mariana Sardo[1], Renée Siegel[1], Sérgio M. Santos[1], João Rocha[1], José Richard B. Gomes[1] and Luis Mafra[1] [1] Department of Chemistry, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal
11	**Study of the Propylsulphonic Acid-functionalized PMO by High-resolution 1H Solid-State NMR Spectroscopy** R. Siegel[1], E. Domingues[2], R. De Sousa[3], F. Jérôme[3], C. M. Morais[3] N. Bion[3], P. Ferreira[2], L. Mafra[2] [1] Department of Chemistry, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal [2] Department of Ceramics and Glass Enginnering, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal [3] Laboratoire de Catalyse en Chimie Organique, University of Poitiers, 4 rue Michel Brunet, BP633 86022 Poitiers Cedex, France

2nd PTNMR Meeting
NMR in Portugal: an overview
3rd February 2012
Auditório da Biblioteca - FCT/UNL

university of aveiro
department of chemistry

Structure determination of some oxygen and nitrogen heterocyclic compounds by NMR

Raquel S. G. R. Seixas,[a] Cátia I. C. Esteves,[a] Cristela M. Brito,[a] Stéphanie B. Leal,[a] Diana C. G. A. Pinto,[a] Clementina M. M. Santos,[b] Ana M. L. Seca,[a,c] Artur M. S. Silva,[a] José A. S. Cavaleiro[a]

[a]*Department of Chemistry & QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal;* [b]*Department of Vegetal Production and Technology, School of Agriculture, Campus de Santa Apolónia, 5301-855 Bragança, Portugal;* [c]*DCTD, University of Azores, 9501-801 Ponta Delgada, Açores.*

Introduction

✓ Oxygen heterocyclic compounds are widely distributed in Nature, being chromone and xanthone derivatives some examples. For instance, the xanthone ring system is a structural motif prevalent in higher plants such as those of *Guttiferae* and *Gentianaceae* families.[1] Both natural and synthetic derivatives often endowed with interesting pharmacological properties, such as anti-inflammatory,[2] antitumour[3] and antioxidant activities.[4] Chromones and chromone derivatives play an important role in the normal human diet, due to their significant anti-inflammatory,[5] anti-cancer,[6] and antioxidant activities.[5]

✓ Nitrogen heterocyclic compounds are also widely distributed in Nature, being 4-quinolones a large group that can be found, mainly, in plants of the *Rutaceae* family.[7] However, a great number of the well-known derivatives are of synthetic origin and have been designed to be used as drugs, mainly for the treatment of tuberculosis.[8]

✓ In view of these important properties, we have dedicated our investigation in the establishment of new synthetic methods for these types of compounds[9] and also for the assessment of their biological properties.[10] Naturally, we devote special attention to the structural characterization, mainly by NMR experiments, not only to confirm the product structure but also to unequivocally establish their stereochemistry.

✓ The aim of this communication is to report some of our studies on the structural characterization of heterocyclic compounds by NMR spectroscopy.

Oxygen heterocyclic compounds

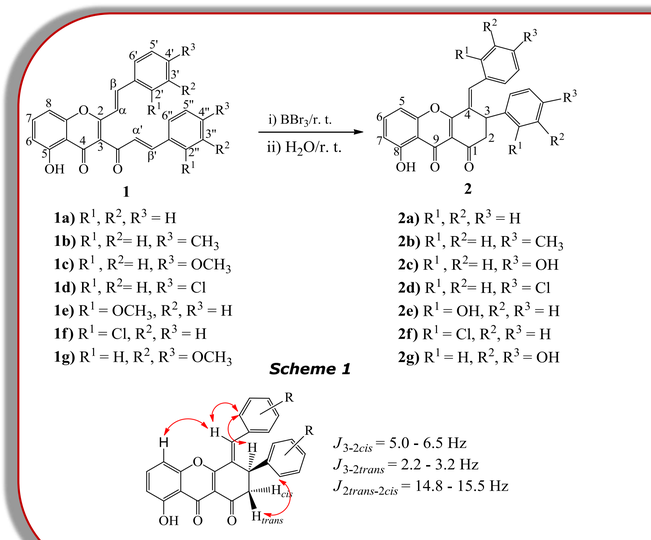
(*E*)-3-Aryl-4-benzyllidene-8-hydroxy-3,4-dihydro-1*H*-xanthene-1,9(2*H*)-diones

(*E*)-3-Aryl-4-benzylidene-8-hydroxy-3,4-dihydro-1*H*-xanthene-1,9(2*H*)-diones **2** were obtained by an efficient and concise synthetic route (Scheme 1).[11]

The structural elucidation of these compounds allowed to prove the formation of xanthone core, but also establish the stereochemistry of the exocyclic double bond.

The xanthone core formation was based mainly on HMBC spectral analysis although several evidences could be detected in the ^{1}H NMR spectra, such as a characteristic singlet at $\delta \sim 8$ ppm and signals due to the diastereotopic methylene protons attached to the stereocenter (Figure 1).

The stereochemical assignment was based on the ^{1}H-^{1}H coupling constants and NOESY spectra (Figure 2)



Scheme 1

$J_{3\text{-}2cis}$ = 5.0 - 6.5 Hz
$J_{3\text{-}2trans}$ = 2.2 - 3.2 Hz
$J_{2trans\text{-}2cis}$ = 14.8 - 15.5 Hz

Figure 2

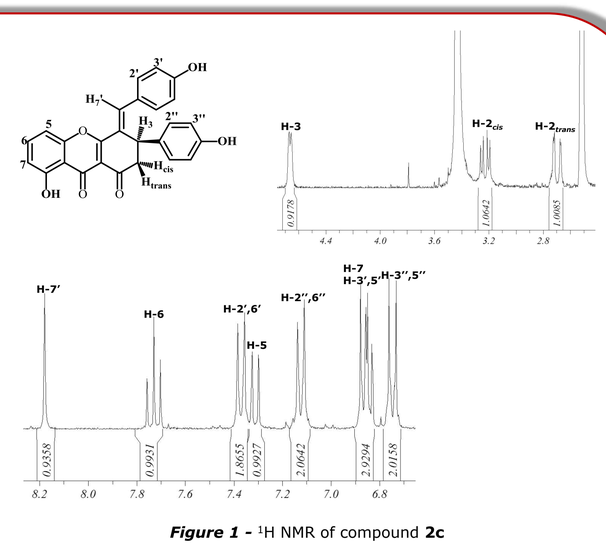


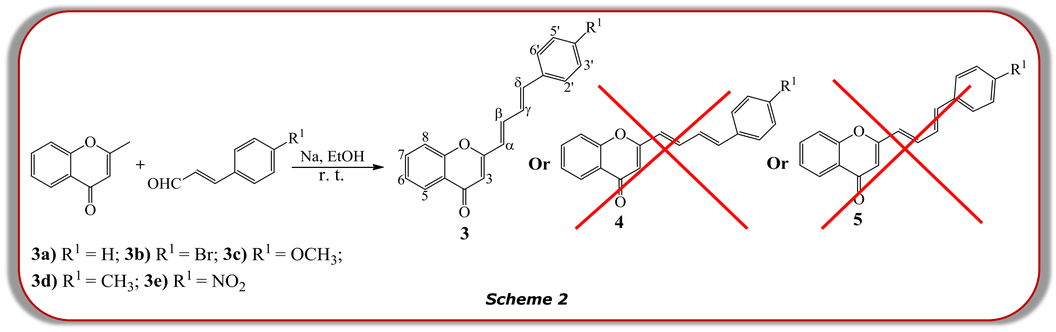
Figure 1 - ^{1}H NMR of compound **2c**

(*E,E*)-2-(4-Arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones

(*E,E*)-2-(4-Arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones **3** were obtained from the condensation of 2-methylchromone with cinnamaldehydes (Scheme 2).[12]

The most important aspect of the structural elucidation was the stereochemistry of the $\alpha,\beta,\gamma,\delta$-unsaturated system.

The (*E,E*)-configuration of the vinylic systems were established by the proton-proton coupling constants ($^3J_{H\alpha\text{-}H\beta}$ and $^3J_{H\gamma\text{-}H\delta} \sim$ 15-16 Hz) Figure 3). However, the (*E,E*)-configuration is consistent with structures **3**, **4** and **5** (Scheme 2).



Scheme 2

From the NOESY spectra it was possible to conclude on the close proximity between H-α and both H-3 and H-γ, and between H-β and H-δ (Figure 4). These findings unequivocally support the structure of (*E,E*)-2-(4-arylbuta-1,3-dien-1-yl)-4*H*-chromen-4-ones as it is depicted in scheme 2 and figure 4.

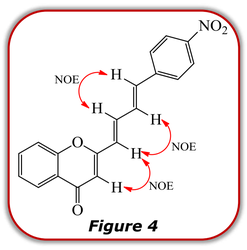


Figure 4

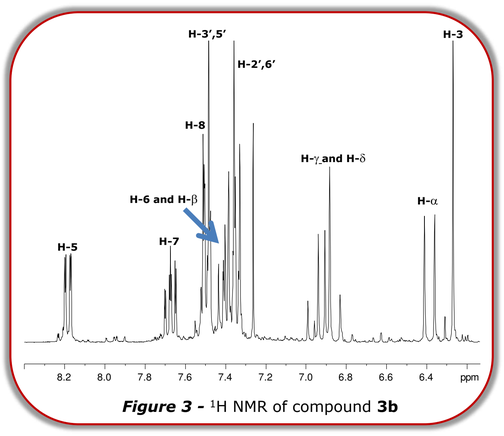


Figure 3 - ^{1}H NMR of compound **3b**

Nitrogen heterocyclic compounds

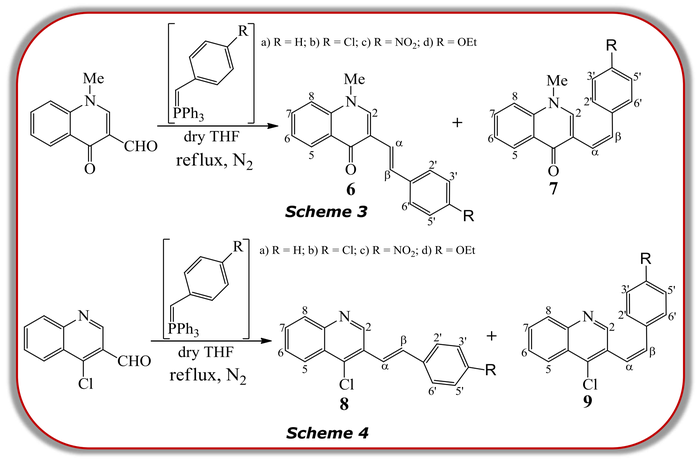
(*E*)/(*Z*)-3-Styrylquinolin-4(1*H*)-ones and (E)/(Z)-4-chloro-3-styrylquinolines

A diastereomeric mixture of (*E*)/(*Z*)-3-styrylquinolin-4(1*H*)-ones **6**/**7** was obtained from the Wittig reaction of quinolone-2-carbaldehydes with benzylidenetriphenylphosphoranes (Scheme 3).[13]

On the other hand, Wittig reaction of 4-chloroquinoline-3-carbaldehyde with benzylidenetriphenylphosphoranes led to the formation of a diastereomeric mixture of (*E*)/(*Z*)-4-chloro-3-styrylquinolines **8**/**9** (Scheme 4).[13]

The assignment of the stereochemistry of the α,β-unsaturated system was based on the coupling constant, $^3J \sim 16$ Hz for (*E*)-configuration and $^3J \sim 12$ Hz for (*Z*)-configuration (Figure 5), and also on the NOE cross peaks observed in the NOESY spectra (Figure 6).

DFT calculations on (*E*)- *vs.* (*Z*)-isomers and rotational isomerism of 1-methyl-3-styrylquinolin-4(1*H*)-one and of 4-chloro-3-styrylquinoline showed that the (*Z*)-isomers are always less stables. For the (*E*)-isomer, a *syn* conformation is more stable than the *anti* one in the case of 1-methyl-3-styrylquinolin-4(1*H*)-one, due to an IMHB between H-β and the carbonyl group, while in the case of 4-chloro-3-styrylquinoline the converse applies (Figure 6).



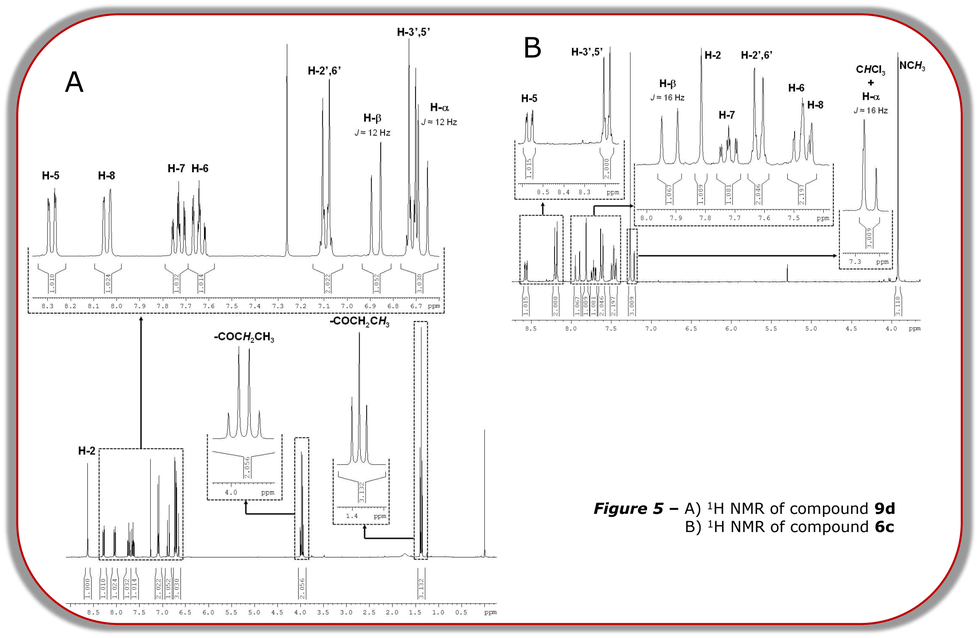


Figure 5 – A) ^{1}H NMR of compound **9d**
B) ^{1}H NMR of compound **6c**

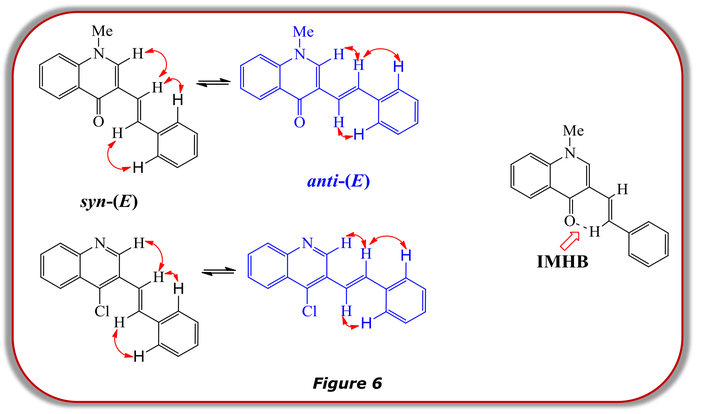


Figure 6

References

(1) Gales, L.; Damas, A. M. *Curr. Med. Chem.* **2005**, *12*, 2499.
(2) Park, H. H.; Park, Y.-D.; Han, J.-M.; Im, K.-R.; Lee, B. W.; Jeong, I. Y.; Jeong, T.-S.; Lee, W. S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5580.
(3) Ee, G. C. L.; Daud, S.; Izzaddin, S. A.; Rahmani, M. *J. Asian Nat. Prod. Res.* **2008**, *10*, 475.
(4) Suvarnakuta, P.; Chaweerungrat, C.; Devahastin, S. *Food Chem.* **2011**, *125*, 240.
(5) Yagi, A.; Kabash, A.; Okamura, N.; Haraguchi, H.; Moustafa, S. M.; Khalifa, T. I. *Planta Med.* **2002**, *68*, 957.
(6) Gamal-Eldeen, A. M.; Djemgou, P. C.; Tchuendem, M.; Ngadjui, B. T.; Tane, P.; Toshifumi, H. Z. *Naturforsch. C* **2007**, *62*, 331.
(7) Michael J. P. *Nat. Prod. Rep.* **2004**, *21*, 650.
(8) Janin Y. L. *Bioorg. Med. Chem.* **2007**, *15*, 2479.
(9) *e.g.* a) Rocha, D. H. A.; Pinto, D. C. G. A.; Silva, A. M. S.; Cavaleiro, J. A. S., Patonay, T. *Synlett* **2012**, *in press*; b) Almeida, A. I. S.; Silva, V. L. M.; Silva, A. M. S.; Pinto, D. C. G. A.; Cavaleiro, J. A. S. *Synlett* **2008**, 2593.
(10) *e.g.* Rocha-Pereira, J.; Cunha, R.; Pinto, D. C. G. A.; Silva, A. M. S.; Nascimento, M. S. J. *Bioorg. Med. Chem.* **2010**, *18*, 4195.
(11) Pinto, D. C. G. A.; Seca, A. M. L.; Leal, S. B.; Silva, A. M. S.; Cavaleiro, J. A. S. *Synlett* **2011**, 2005.
(12) Esteves, C. I. C.; Santos, C. M. M.; Brito, C. M.; Silva, A. M. S.; Cavaleiro, J. A. S. *Synlett* **2011**, 1406.
(13) Seixas, R. S. G. R.; Silva, A. M. S.; Alkorta, I.; Elguero, J. *Monatsh. Chem.* **2011**, *142*, 742.

Acknowledgments

We are grateful to the University of Aveiro, FCT and FEDER for their support to Organic Chemistry Research Unit (project PEst-C/QUI/UI0062/2011). We are also grateful to the Portuguese National NMR Network (RNRMN) supported with funds from FCT.
R. S. G. R. Seixas would also like to thank FCT for a PhD Grant (SFRH/BD/30734/2006) and C. I. C. Esteves is also grateful to FCT for her fellowship (SFRH/BI/51098/2010).

NMR in Portugal: an overview
2nd PTNMR Meeting - 2012