FA4-MS09-P01

The Structure of Rimonabant in the Solid State.
Laura Menéndez-Taboada[a],Santiago García-Granda[a], Mario Alvarado[b], Ibon Alkorta[b], Pilar Goya[b], Jose Elguero[b]. [a]*Department of Physical and Analytical Chemistry, University of Oviedo.* [b]*Medicinal Chemistry Institute,CSIC, Spain.*
E-mail: menendezlaura.uo@uniovi.es

Rimonabant is the first selective CB_1 receptor blocker used in patients of metabolic syndrome and related illness like diabetes and dyslipidaemia. There is a great interest on the polymorphism of Rimonabant and related compounds. The structures of Rimonabant [1] and three diarylazoles [2] (two pyrazoles and one 1,2,4-triazole) related to Rimonabant have been determined by X-ray diffraction. These studies will provide other researches in the active field of cannabinoid antagonist with the molecular properties of the reference compound. Data from Rimonabant were collected at 293K and at 150K in a Xcalibur Nova diffractometer. The structure of the methanol solvate of Rimonabant displays no noticeable modifications in crystal packing from RT to 150K. It is monoclinic and the space group is P21/c. The solvate molecule helps to the packing connecting two Rimonabant molecules throughout the –N-H…O-H…O- synthon, forming infinite chains propagating along the *b* crystallographic axis. Two additional C-H…O-weak interactions were better located in the low temperature experiment. In this work, we will show the crystal data and structure refinement of Rimonabant at both temperatures. Further details of the X-ray structural analysis will be given and exhaustive hydrogen bonding geometry study will be discussed. **Acknowledgments:** Financial support from Spanish Ministery of
Science and Technology (MAT2006-01997, CTQ2007-61901/BQU and 'Factoría de Cristalización' Consolider Ingenio 2010) and FEDER founding is acknowledged.

[1] Alkorta I., Alvarado M., Elguero J., García-Granda S., Goya P., Jimeno M.L., Menéndez-Taboada L. *Eur. J. Mol. Chem*. In press. [2] Alkorta I., Alvarado M., Elguero J., García-Granda S., Goya P., Torre-Fernández L., Menéndez-Taboada L. *J. Mol. Struct*. **2009**, 920, 8289.

Keywords: rimonabant; polymorphs; metabolic-syndrome; diarylazoles; cannabinoid-antagonist

FA4-MS09-P02

Crystallographic Study of Diarylazoles Related to Rimonabant.
Laura Torre-Fernández[a], Laura Menéndez-Taboada[a], Santiago García-Granda[a], Mario Alvarado[b], Ibon Alkorta[b], Pilar Goya[b], Jose Elguero[b]. [a]*Department of Physical and Analytical Chemistry, University of Oviedo.* [b]*Medicinal Chemistry Institute,CSIC, Spain.*
E-mail: torrelaura@uniovi.es

Rimonabant (1) is the first selective CB_1 receptor blocker used in many countries for patients with metabolic syndrome and related illnesses, like diabetes and dyslipidaemia. The unknown structure of 1 was recently determined by our research group [1]. It is worth mentioning the increasing interest on the polymorphs of 1 and related compounds.
A large series of compounds related to 1 was prepared and evaluated. Ethyl 5-(4-chlorophenyl)-1-phenylpyrazole-3-carboxylate (2), N-(1-hexadecyl)-1,5-bis(4-chlorophenyl)-1H-pyrazole-3-carboxamide (3) and methyl 1,5-bis(4-chlorophenyl)-1H-1,2,4-triazole-3-carboxilate (4) are three of these compounds. In this communication we deal with the structures of the three diarylazoles exhibing a very different secondary structure [2].
The crystal packing of compound 2 shows a helix type propagation along the c axis supported by a weak H-bond, involving nitrogen and carbon.
The molecular packing of compound 3 is made up of a network of hydrogen bonding interactions stabilizing hydrocarbon layers parallel to bc plane. Within the layers the aromatic rings are stacked.
The molecular structure of compound 4 contains two forms of hydrogen bonds: the O···H bonds along the chain and the O···H bonds between chains packing like a double chain. The double chain is packed by Van der Waals interactions. Chains are growing in the direction of the c axis.

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[1] Alkorta, I., Alvarado, M., Elguero, J., García-Granda, S., Goya, P., Jimeno, M. L., Menéndez-Taboada, *L. Eur. J. Med. Chem.*, in press. [2] Alkorta, I., Alvarado, M., Elguero, J., García-Granda, S., Goya, P., Torre-Fernández, L., Menéndez-Taboada, *L. J. Mol. Struc.*, **2009**, 920, 82-89.

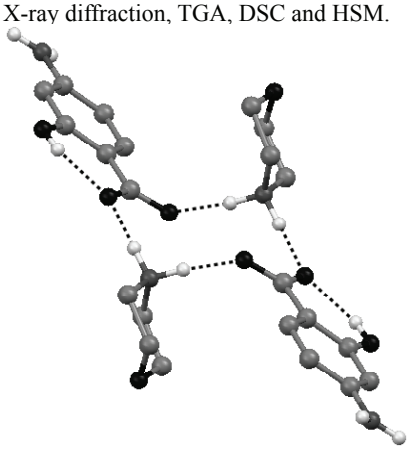
Keywords: rimonabant; polymorphs; metabolic-syndrome

FA4-MS09-P03

New Crystal Forms of the Antibiotic 4-aminosalicylic Acid.
Vânia André[a], Dario Braga[b], Fabrizia Grepioni[b], Maria Teresa Duarte[a]. [a]*Centro de Química Estrutural, DEQB, Instituto Superior Técnico, Av. Rovisco Pais 1, 1049-001 Lisbon, Portuga.* [b] *Dipartimento di Chimica "G. Ciamician", Universita di Bologna, Via Selmi 2, 40126 Bologna, Italy.*
E-mail: vaniandre@ist.utl.pt

4-aminosalicylic acid (ASA) is an antibiotic used in the treatment of tuberculosis. ASA has also been shown to be safe and effective in the treatment of inflammatory bowel diseases [1]. Solvates and salts of ASA have been obtained by using 6-membered non-aromatic rings [2], such as dioxane, morpholine (figure) and piperazine as crystal co-formers. With the latter, two different structures were obtained and these are the most promising forms as piperazine is pharmaceutically accepted in a drug dosage. Despite the similarities of the compounds interacting with ASA, the supramolecular arrangements of the new crystal forms are quite different. With the exception of the dioxane

solvate that loses the solvent and transforms into the original form of ASA, all the others are stable until melting point (>150ºC). Also 2 new forms with 4,4'-bipyridine (one anhydrous and one hydrated) and 3 hydrated new forms with DABCO were obtained [3]. All new solid species were obtained both by the traditional method of slow evaporation from solution and also by the "green" processes of grinding and/or kneading together the starting materials. Also slurries induce the formation of these crystal forms. All the species were characterized by single-crystal and powder X-ray diffraction, TGA, DSC and HSM.



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Keywords: solvates; salts; 4-aminosalicylic acid

FA4-MS09-P04

Crystal Structures and Theoretical Investigations on DPPH Radical-scavenging Mechanism of New Triazolymethyl Benzimidazole Derivatives. Arzu Karayel[a], Suheyla Ozbey[a], Gulgun Ayhan-Kilcigil[b], Cana Kus[b]. [a]*Physics Engineering Department, Hacettepe University, 06800 Ankara, Turkey.* [b]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ankara University, 06100 Ankara, Turkey.*
E-mail: akbas@hacettepe.edu.tr

Free radicals, including superoxide radical ($O_2^{\cdot-}$), nitric oxide ($NO^{\cdot}$), hydroxyl ($OH^{\cdot}$) and peroxyl ($RO_2^{\cdot}$) have been implicated in a number of disease processes, including atherosclerosis, rheumatoid arthritis and carcinogenesis [1]. It was also reported that pathogenesis and symptoms of inflammatory processes are accompanied and/or initiated by the production of reactive oxygen species (ROS) [2]. These ROS are produced as a normal consequence of biochemical processes in the body and as a result of increased exposure to environmental and dietary xenobiotics. Drugs possessing antioxidant and free radical scavenging properties are considered for preventing and/or treatment of such diseases which are directly related to the lack of the antioxidant capacity of the organisms.
In our previous study we described synthesis and antioxidant properties of compounds 5-(2-(p-chlorophenylbenzimidazol-1-yl-methyl)-4-(3-methylphenyl)-2,4-dihydro-[1,2,4]-triazole-3 thione (A) and 5-(2-(p-chlorophenylbenzimidazol-1-yl-methyl)-4-(2-methylphenyl)-2,4-dihydro-[1,2,4]-triazole-3 thione (B) [3]. According to the biological activity results compounds A and B were found to interact with DPPH strongly (78% and 76%, respectively) at 10^{-3} M concentration. The aim of this study was to determine the structures of compounds A and B by X-ray diffraction method and was to clarify the DPPH radical scavenging mechanisms. This mechanism will be helpful to elucidate the structure activity relationships for the novel antioxidants and to design novel compounds with better antioxidant properties. The elucidation of radical-scavenging mechanisms and structure-activity relationships (SAR) for these compounds were established by density functional theory (DFT) calculations using the B3LYP/6-311+G (2D, 2P) method.

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Keywords: antioxidants; density functional theory; pharmaceutical structure determination

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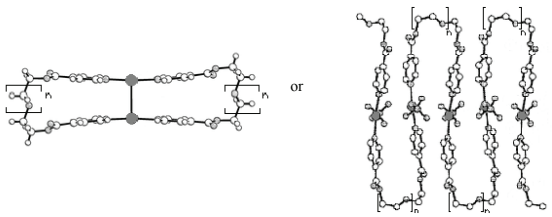
Synthesis of New Silver Compounds with Derivates of Nicotinate Acid. Chevrier Inès[a], Katharina M. Fromm[a]. [a]*Department of Chemistry, University of Fribourg . Fribourg, Switzerland.*
E-mail: ines.chevrier@unifr.ch

Silver ions have antibacterial properties, and complexes with this Ion have a great potential of applications in medical uses. Complexes of silver with several ligands derived from nicotinic acids and until three ethylene groups for spacer are already known. In our group we obtains metallacycles and in special conditions chain structures. We propose the development of complexes with longer spacers and to study the possible formation of solids, liquid crystals or polymers.



Keywords: silver compounds; coordination polymer; liquid crystals