

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 CB₁ 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 Ministry 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 CB₁ 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-carboxylate (4) are three of these compounds. In this communication we deal with the structures of the three diarylazoles exhibiting 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.

Financial support from Spanish Ministry 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. Med. 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, 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", Università 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