s13.m42.p15 **Conformations of the Antibiotic Azithromycin in Solution and Solid State. The Role of the Solvent.** Jose Montejo-Bernardo,[a] Santiago García-Granda,[a] Miguel Bayod[b], Luján Llavona[b], Isidro Llorente[b]. *Departamento Química-Física y Analítica. Universidad de Oviedo.Facultad de Química. 33006 Oviedo (Asturias), [a]Astur-Pharma, S.A. Departamento de Investigación y Desarrollo.33192 Silvota (Asturias), Spain. E-mail: jmmb@fq.uniovi.es*

Keywords: Azithromycin; Polarity; Pseudopolymorphs

The knowledge of the conformational structure of drugs in solution state, help us to understand its biological activity, prerequisite to desing new drugs and derivatives. Also, using different solvents and comparing with the conformation in solid state, usually crystalline, we can try to determine the influence of the solvent in the final product (*solvate* or *pseudopolymorph*).

For the azithromycin (an antibiotic of the family of the macrolides) two pseudopolymorphs are known, the monohydrate, with different alcohols as solvents of crystallization[1], and the dihydrate[2]. Studies in solutions of water, chloroform, ketone and ethanol, have been reported, concluding that the ***solvent polarity*** determines the drug conformation in solution, being *folded-out* conformation in polar solvents [3], and *folded-in* conformation in less polar solvents[4].

The present work analyzes the *solvent-pseudopolymorph* relationship for the azithromycin in three different alcohol solvents: ethanol, isopropanol and tert-butanol. The conformation in solution state is studied through ^{1}H and ^{13}C-NMR techniques, and in crystal state through single crystal X-ray diffraction. The concept of *polarity* itself is discussed too, concluding that it cannot be described by a single physical solvent parameter.

The results show a correspondence between the solvent polarity and the conformation of the azithromycin in solution, but does not seem to be a direct relation in the case of crystal state. Either there are more factors than polarity to determine the conformation of the drug in the final pseudopolymorph, or the concept of polarity is ambiguous and should be used with precaution. The molecular volume of the solvent does not seem to be one important factor.

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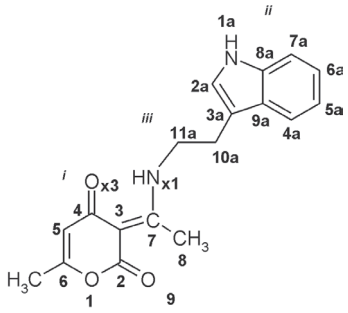
s13.m42.p16 **Synthesis and Characterization of Two Dehydroacetic Acid Derivatives and Molybdenum(V) Complexes: an NMR and Crystallographic Study.** Tanja Kajfez Novak[a], Marina Cindric[a], Visnja Vrdoljak[a], Manda Curic[b], Ana Brbot-Saranovic[c] and Boris Kamenar[a], *[a]Laboratory of General and Inorganic Chemistry, Chemistry Department, Faculty of Science, University of Zagreb, Ulica kralja Zvonimira 8, 10000 Zagreb, Croatia, [b]Rudjer Boskovic Institute, POB 1016, 10000 Zagreb, Croatia, [c]Department of Chemistry, Veterinary Faculty, University of Zagreb, Heinzelova 55 10000 Zagreb, Croatia. E-mail: tanja@chem.pmf.hr*

Keywords: Enaminones; Tryptamine; Dehydroacetic acid

Two enaminones (HL^1 and HL^2) have been prepared by the reactions of tryptamine with 2-hydroxy-4-(4-hydroxy)-6-methyl)-2H-pyrane-2-on-3-yl)-4-oxo-2butenoate (ehmpb) and dehydroacetic acid (dha) respectively. The NMR spectroscopy confirmed that both tautomeric forms of HL^1: *endo*-enol (tautomer A with hydroxyl group at position 4) and *exo*-enol form (tautomer B with hydroxyl group at position 7) are present in the solution. The molecular and crystal structures as well as the NMR data of HL^2 showed that the condensation of dha and tryptamine occurs at acetyl-carbonyl group. The molecular structure of HL^2 can be described as consisting of three structural fragments: (i) 2-pyrone ring; (ii) N-substituent consisting of 1H-indol ring and (iii) ethyl chain interconnecting parts (i) and (ii). In the crystalline state molecules of compound HL^2 are found as two symmetrically independent molecules. Molecules are also characterized by six membered pseudoaromatic chelate ring containing these NH-C=C-C=O (keto-amino tautomer) heterodienic moiety. Rings are formed by intramolecular hydrogen bonds enhanced by π-electron delocalization (resonance assisted hydrogen bond, RAHB; N11-H11...O13 = 2.578(1) Å; N21-H21...O23 = 2.570(1) Å) [1,2]



Scheme 1. Molecular structure of molecule HL^2 showing atom numbering scheme. (x=1 or 2)

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