

[o.m12.p15] Structural Study of 3,4-Dihydro-2(1H)pyridones and Isoxazolo[5,4-b]pyridin-6(7H)-ones. H. Novoa¹, N. Blaton¹, M. O. Peeters¹, C. De Ranter¹, M. Suárez², Y. Verdecia², E. Ochoa², E. Salfrán², L. Morán², N. Martín³, R. Martínez², M. Quintero³, C. Seoane³, J.L. Soto³. ¹Katholieke Universiteit Leuven. *Laboratorium voor Analytische Chemie en Medicinale Fysicochemie. Faculteit Farmaceutische Wetenschappen. 3000 Leuven, Belgium.* ²Laboratorio de Síntesis Orgánica. *Facultad de Química. Universidad de La Habana. 10400 Habana. Cuba.* ³Departamento de Química Orgánica I. *Facultad de Química. Universidad Complutense. E-28040 Madrid. Spain*

Keywords: calcium channel modulators, X-ray analysis, conformational study.

Along the last recent years, the synthesis and structural characterization of novel analogues of 1,4-dihydropyridine (DHP) calcium channels modulators has received particular attention due to the pharmacological properties they display.^{1,2,3} In this regard, crystallographic studies have played a very important role for determining receptor-ligand interactions in nifedipine and other related 1,4-DHPs.^{4,5} Bicyclic analogues have been synthesised to be used as geometrically well defined rigid structures which are of interest for unravelling the structure-activity relationship for this type of compounds. The absolute configuration at C-4 (R- versus S-enantiomer) of 1,4-DHPs is a critical factor for biological activity as antagonist or agonist of calcium ion.⁶ Thus, in order to evaluate the potential interest of novel molecules as calcium channel modulators, it is important to determine the geometrical parameters either in the solid state as well as in solution. We have recently reported a structural study of furo[3,4-b]-2(1H)pyridones⁷ and 2,5-dioxo-1,2,3,4,5,6,7,8-octahydroquinoline⁸ as potential calcium channel modulators. It is worthy to note that 1,4-DHPs fused to a second heterocyclic ring have been less studied in comparison with the crushing amount of studies carried out on differently substituted monocyclic 1,4-DHPs. A series of high stereochemically controlled isoxazolo[5,4-b]pyridin-6(7H)-ones (I) have been prepared from novel 3,4-dihydro-2(1H)pyridones (II) by reaction with hydroxylamine hydrochloride and subsequent 5-endo-trig cyclization. A structural study by X-ray analyses and theoretical calculations (AM1) of both heterocyclic systems (I and II) shows a favoured conformer with the aryl group on C4 in a pseudoaxial position. The same favoured conformation was found in solution according to ¹H-NMR NOE experiments and comparison of theoretical (AM1) and experimental coupling constants. Structural and conformational features of 1,4-DHPs have been mainly determined by X-ray analysis in the search of improving structure-activity relationship. The data reported in this work on 3,4-dihydropyridones (II) and, particularly on the less studied bicyclic systems (I), are of interest for a further study of receptor-ligand interactions.

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[o.m12.p16] Polymeric aqua-(hydrogen glutarato) glutarato lanthanum (III) monohydrate. B. Benmerad^a, A. Guehria-Laïdoudi^a, F. Balegronne^a, H. Birkedal^b, G. Chapuis^b. ^aLaboratoire de cristallographie appliquée, *Institut de Chimie, U.S.T.H.B., B.P. 32, El-Alia, 16111, Bab-Ezzouar, Alger, ALGERIE.* ^bInstitute of crystallography, *University of Lausanne, BSP, DORIGNY, CH-1015, Lausanne, SWITZERLAND.*

Keywords: glutarato lanthanum, polymeric structure, ten-fold coordination.

The structure of La (C₅H₇O₄) (C₅H₆O₄) (H₂O).1 H₂O consists of dense layers formed by chains of one-edge sharing La O₉ (H₂O) polyhedron linked together by glutarate ligand.

The three dimensional polymeric structure, built up from connection of these layers by the hydrogen glutarate ligand, exhibits cavities accommodating one guest water molecule. The lanthanum ion is ten-fold coordinated by four glutarates acting as bridging-chelating carboxylate groups, by three hydrogen glutarates three-time unidentate and by one water molecule.

Its coordination polyhedron is highly distorted and may be described as intermediate between a bi-capped dodecahedron and a tetra-capped trigonal prism. Hydrogen bonding links the two water molecules and the framework built up from this polynuclear coordination polymer. The protonated acid group is donating the hydrogen to a very short hydrogen bond to the carboxylate end of the group. This strong hydrogen bond is probably stabilizing the coordination geometry.

This structure is closely related to the two isostructural compounds Nd₂ (C₅H₆O₄)₃(H₂O)₂. 2H₂O⁽¹⁾ and Nd₂ (C₅H₆O₄)₃ (H₂O)₂. 4H₂O⁽²⁾.

The heavier lanthanide structures are all isostructural. In the Nd-structures, Nd is nine-fold coordinated and the solvent contained in cavities are truly open. The differences between the heavier lanthanides and the La-structure point to the importance of synthesis temperature and pH and consequently the number of water molecules of crystallization.

The importance of these factors is underlined by the fact that the glutarate of all lanthanoids have been previously obtained, except the glutarate of lanthanum.

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