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In order to make clear the structural function of C-terminal amide group of endomorphin-2(EM2:YPFF-NH_2) the conformations of EM2 and its C-terminal free acid (EM2OH:YPFF-OH) were analyzed by ^{1}H-NMR spectroscopy and X-ray crystal analysis.

The NMR spectra in trifluoroethanol(TFE) and water solvents indicated that both peptides were in equilibrium between the *cis*- and *trans*-rotamer around Tyr-Pro peptide bond, respectively. However they take almost trans rotmer in dodecylphosphocholine(DodPCho), micells, except for the EM2OH in water solvent at pH5.2. With the use of the proton-proton distance derived from ROESY cross peaks, possible fifty 3D structures are generated by dynamical simulated annealing method and were classified in four groups of two open and two fold conformers according to the folding of backbone structure.

On the other hand, two independent conformational isomers per asymmetric unit and seven water molecules were existed in the crystal structure of EM2OH. Both conformers were crystallized as neutral zwitterionic forms and took a folded-form with *cis*-configuration in around Tyr-Pro peptide bond.

Based on the conformational features of EM2 and EM2OH in solution and solid state, we would like to discuss the possible function of C-terminal amide group.

Keywords: NMR, X-ray conformation analysis, molecular conformation

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New Monocyclic and Acyclic hNK-2 Antagonists Retaining the β-turn Feature

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The human tachykinin NK-2 receptor is a promising target for important pathologies at respiratory, gastrointestinal and genitourinary level, where this receptor is mainly localized. Several peptidic and non-peptidic antagonists to this receptor are known, and a few of them are undergoing clinical studies. The bicyclic peptide MEN10627 [1] is one of the most potent antagonists for the neurokinin NK-2 receptor. However its low bioavailability prevents it to be used as a drug. We have already shown how, by selecting a proper part of its structure, i.e. that featuring the β-turn, it is possible to obtain simpler peptides still retaining their activity. The monocyclic series which originated was designed on the basis of theoretical assumptions with the support of modeling [2]. In the present contribution we show how subsequently that rationale has been experimentally validated through X-ray structure determination of a novel monocyclic hNK-2 antagonist (MEN13365). Moreover the same structural features have been retained in MEN15596, which belongs to a new non cyclic series of hNK-2 antagonists developed to circumvent the low oral bioavailability. Antagonists from this last series are presently undergoing preclinical development.

[1] Pavone V., Lombardi A., Nastri F., Saviano M., Maglio O., D'Auria G., Quartara L., Maggi C.A., Pedone C., *J. Chem. Soc. Perkin Trans. 2*, 1995, 987, *and references therein*. [2] Fedi V., Altamura M., Balacco G., Canfarini F., Criscuoli M., Giannotti D., Giolitti A., Giuliani S., Guidi A., Harmat N.J.S., Nannicini R., Pasqui F., Patacchini R., Perrotta E., Tramontana M., Triolo A., Maggi C.A., *J. Med. Chem.*, 2004, **47**, 6935, *and references therein*.

Keywords: molecular scaffold, β-turn, tachykinin

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Absolute Configuration of the κ-Agonist Salvinicin A

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Salvinorin A and B are potent κ selective opioid receptor agonists from *Salvia divinorum*. An infusion prepared from fresh or dried leaves is used by the Mazatec Indians to stop diarrhea, relieve headache and rheumatism, and is also used in traditional spiritual practices to produce "mystical" or hallucinogenic experiences.[1] Young adults and adolescents have begun to smoke the leaves and leaf extracts of the plants to induce powerful hallucinations.[2] The stereochemistry of Salvinorin has not previously been determined. In an effort to determine the sterochemistry of this opioid agonist a 3,4-dichlorobenzoyl derivative was prepared. Single crystal x-ray diffraction was able to unambiguously determine the absolute configuration of this dichloro derivative and by extension that of Salvinorin A.

[1] Valdes III L. J., Diaz, J. L., Paul A. G., *J. Ethnopharmacol.*, 1983, **7**, 287-312. [2] Hazelden Foundation, *www.research.hazelden.org* , 2004.

Keywords: κ-opioid receptor, structure, stereochemistry

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Crystal Structures of Cholesterol Derivatives

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We have undertaken a series of crystal structures of the esters, carbonates and ethers of cholesterol. These are cholesteryl formate, pentanoate, hexanoate, heptanoate, crotonate, isobutyrate, aniline, 2,4-dichlorobenzoate and hemisuccinate, cholesteryl phenyl acetate, methyl carbonate, ethyl carbonate, propyl carbonate, butyl carbonate, isobutyl carbonate, isopropyl carbonate, pentyl carbonate, hexyl carbonate, crotyl carbonate, cholesteryl ethyl ether, isopropyl ether and methyl ether.

Among these structures, (1) cholesteryl ethyl carbonate, propyl carbonate, crotyl carbonate, crotonate are isostructure each other, (2) cholesteryl pentyl carbonate, hexyl carbonate, hexanoate, heptanoate are also isostructural,

These structures are remarkable in forming layer structures in which the central region of the layers, composed largely of semi-rigid cholesteryl groups is closely packed and the packing of the flexible fatty acid or carbonate chains and the isoprenoid tail of the cholesterol form the interface region between layers. Some of the crystals show the liquid crystalline states. Typical packing modes will be discussed.

Keywords: cholesteryl ester, cholesteryl carbonate, cholesteryl ether

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Structure and Tautomerism of Mercapto-1,2,4-triazole Derivatives in the Solid State

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Molecular and crystal structures and tautomerism of new mercapto-1,2,4-triazole derivatives, which are structurally labile compounds capable to exist in different tautomeric forms, are discussed. X-Ray single crystal diffraction experiments show the existence of only 1*H*-triazole tautomer in crystal. As a result of our investigations it can be concluded, that for 3,5-substituted 1,2,4-triazoles usually crystallizes the tautomer, where hydrogen atom is bonded with the nitrogen (one of two neighbouring) situated near the electronodonor group, that is 3-R_A-5-R_D-1,2,4-(1*H*)-triazole. For 3-phenyl-5-mercap-to-1,2,4-triazole two thion-thiolic tautomers were found in one crystal: two molecules of four symmetrically independent ones are 3-phenyl-4,5-dihydro-(1*H*)-1,2,4-triazole-5-tion tautomers, and the rest are 3-phenyl-5-mercapto-(1*H*)-1,2,4-triazole. The asymmetric part of the unit cell of 3(5)-(2-hydroxyethyl)thio-1,2,4-triazolinium oxalate consists of two cation-anion pairs. The two cations are the endocyclic tautomers: one of them is 3-(2-hydroxyethyl)thio-(1*H*),(4*H*)-1,2,4-triazolinium cation and the other is 5-(2-hydroxyethyl)thio-(1*H*),(4*H*)-1,2,4-triazolinium cation. The