most of the amino acids in gramicidin A show a statistical preference for β conformation, that preference in tyrosine is highest and significantly greater than that of tryptophan. Apparently as a result of the tight coiling, the ψ,ϕ values of the L residues in the structures are in a sparsely populated region of the Ramachandran plot, while the D-residues are in the most densely populated region corresponding to β-sheet geometry. The properties of the gramicidin heterodimer may relate to analogous properties of prion. The enigmatic behavior of prions, the protein responsible for diseases such as *scrapie* in animals and kuru and Creutzfeldt-Jakob disease in humans, has been attributed to the presence of trace amounts of mutants that induce heterodimer formation or another type of aggregation.

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CNS Agents

PS05.03.01 CONFORMATIONAL ANALYSIS OF (*S*)-6-METHOXY-2-(DIPROPYLAMINO)-TETRALIN. Magnus Brisander,[a] Ingeborg Csöregh,[a] Johanna M. Jansen,[b] Anette M. Johansson[b] and Uli Hacksell.[b], [a]Department of Structural Chemistry, Arrhenius Laboratory, Stockholm University, S-106 91 Stockholm, Sweden, [b]Organic Pharmaceutical Chemistry, Uppsala Biomedical Center, Uppsala University, Box 574, S-751 23 Uppsala, Sweden.

The conformational behavior of (*S*)-6-methoxy-2-(dipropylamino)-tetralin·HCl (**1**) has been studied by X-ray crystallography, ^{1}H NMR spectroscopy and molecular mechanics calculations (MM2). The X-ray structure was determined using Cu Kα radiation at 20 °C, and the ^{1}H NMR spectral data was obtained at 400 MHz in CD_3OD at 30 °C.

The preferred conformations of **1** in the various states (solid, liquid and gas) were compared. In addition, the conformational preference of **1** was compared with recently published preferred conformations of 5-, 7-, and 8-OH-DPAT.[1]

(1) A. Karlén, A. Helander, A. M. Johansson, L. Kenne, S. Sundell, and U. Hacksell, *J. Chem. Research (M)*, 1993, 3028-3036.

PS05.03.02 STRUCTURE-ACTIVITY RELATIONSHIP INVESTIGATIONS OF 4-ANILINOPIPERIDINES H.A. Karapetyan, V.K. Jingozian, Mol. Struct. Research Center of Nat. Academy of Sciences of Armenia

The most potent narcotic analgesics, that are widely used in medicine are representatives of the 4-anilinopiperidines, the main prototype of which is Fentanyl [1-(2-ethylphenyl)-4-(N-propionylanilino)piperidine]. On the basis of comparison of X-ray single crystal[1] and conformational energy calculations data for isomers of 2,5- and 3,5-dimethyl and 5-Me (correctly this must be named 3-Me) derivatives of Fentanyl with their individual analgesic activities, we have concluded, that the productive conformation of the molecule is that, when N(amide)-C (carbon atom of Ph-ring of aniline) bond elapsed the C(3)-C(4) bond of piperidine cycle. Subsequent exposition of productive conformation of 4-anilinopiperidines let us suppose, that 2-Me group have a negative influence on analgesic properties of the molecule and this influence is minimum when 2-Me group has an axial orientation relative to piperidine ring.

[1]Karapetyan H.A., Struchkov Yu,T., Timofeeva T.V., Martirossian V.H., Vartanian R.S., Vartanian S.H. Structure and activity of phenaridine stereoisomers. Khimiko-Pharmatsevticheskii Zhurnal, 1989, V.23, No 5, P.565-572.

Antibiotics

PS05.04.01 CRYSTAL STRUCTURES OF VANCOMYCIN RELATED GLYCOPEPTIDE ANTIBIOTICS. Martina Schaefer, Thomas R. Schneider, George M. Sheldrick, Universität Göttingen, Germany

Glycopeptide antibiotics related to vancomycin have been of special clinical interest since 1956 when vancomycin itself was first discovered. Vancomycin is often the last hope in the treatment of infections caused by bacteria that have been developed resistance to other antibiotics, but unfortunately cases of vancomycin resistance are not unknown.

We direct our attention to these glycopeptide antibiotics for two reasons:

- With around 400 peptide atoms and 40-50% solvent content per asymetric unit crystals of glycopetide antibiotics have comparable diffraction properties to rubrodoxin, crambin and other small proteins. They should be good test structures for new ab initio approaches for the solution of the phase problem.
- With atomic resolution data (collected at EMBL-Hamburg with Synchrotron radiation) it is possible to obtain detailed structural information, for example in the region of the postulated binding pocket.

We will present new crystal structures of vancomycin related glycopeptide antibiotics that provide interesting details of the solvent structure, in particular in the region of the binding pocket.

PS05.04.02 THE CRYSTAL AND MOLECULAR STRUCTURE OF CHALCOMYCIN. J. Ronald Rubin, Peter W. K. Woo, Parke-Davis Pharmaceutical Research Division of Warner Lambert Comany 2800 Plymouth Road, Ann Arbor, MI. 48105

Chalcomycin ($C_{35}H_{56}O_{14}$, F.W.=700.8) is a macrolide antibiotic produced by *Streptomyces bikiniensis*. It is a member of the 16-membered macrolide ring antibiotic family and is unique in containing the sugars ß-chalcose and ß-mycinose. Colorless needles of the antibiotic were obtained from ethanol solutions. The unit cell parameters and x-ray diffraction data were measured on a CAD-4 diffractometer using CuKα radiation. The crystals are monoclinic, space group $P2_1$, with unit cell parameters, a=8.965(3),b=22.989(9), c=9.280(2) Å and ß=90.78(3) °. The unit cell of V=1913 Å^3 contains two molecules of the antibiotic. A total of 1557 unique reflections were measured using the omega scan technique. The structure was solved using direct methods using the SIR-92 programs and refined to an unweighted R-factor of 0.068. The conformation of the macrolide ring and the two glycosidic sugar residues is roughly planar. The molecule has opposing hydrophilic and hydrophobic surfaces. By extension from the known chirality of the sugar residues the configuation of all of the chiral centers was determined.