PS-04.04.04 X-ray crystal structure of conformationally constrained penta peptide Boc-Pro-dehydro Phe-Ala-dehydro Phe-Ala-OMe. Rajashankar K.R.(#), S.Ramakumar(#) and V.S.Chauhan(*). #Department of Physics, Indian Institute of Science, Bangalore-560012, India *International Center for Genetic Engineering and Biotechnology, Shaheed Jeet Singh Marg,NII Campus, New Delhi-11067, India

α,β-dehydro peptides are found to occur in many natural proteins and bioactive peptides (Noda et al, 1983, PEPTIDES, 5,285). The recent interest in these peptides in particular those containing α,β-dehydro phenylalanine (△Phe) residues is due to the conformation constraining property of △Phe (Rajashankar et al, J.Am. Chem.Soc.,1992,114 9225). As a part of our continuing research programme on α,β-dehydro peptides here we present the X-ray crystal structure of Boc-Pro-△Phe-Ala-△Phe-Ala-OMe, an α,β-dehydro penta peptide. Crystals grown from methanol/acetone are monoclinic, space group $P2_1$, a=14.365(2),b=9.931(2),c=25.787(2)Å β=104.03(1)°,V=3569.1Å^3, Z=4. Data was collected on a CAD-4 diffractometer (5205 reflections having $|F_o|>3\sigma(|F_o|)$, $\theta \leq 60°$). Structure solved by SHELXS86 and refined using SHELX400. The current agreement factors are: R=5.6% and RW=6.9%. The two independent molecules in the asymmetric unit are remarkably similar. Both of them are characterized by two non overlapping β-turns. Boc-Pro-△Phe-Ala lies in type I β-turn region while △Phe-Ala-△Phe-Ala lies in type II β-turn region with appropriate 4⟶1 hydrogen bonds. Structure solution, molecular conformation and crystal packing will be discussed in detail. Rajashankar thanks CSIR,India for a fellowship.

PS-04.04.05 STRUCTURE OF [Phe^1,Ala^9]ANTAMANIDE. By A.D.Vasiliev,Institute of Physics,Siberian Division of the Russian Acad.Sci.,Krasnoyarsk

The title compound (I) is a synthetic, symmetric and biologically active analog of the natural cyclic decapeptide antamanide (II). The structure of II had been solved by (I. L. Karle, T.Wieland,D.Schermer,H.C.J.Ottenheym,Proc.Nat Acad.Sci.USA, 1979, 76, 1532-1536). It forms complexes with alkali metal ions and acts as an antidote to the toxin phalloidin. The crystals were grown from a solution of I in a mixture of water and acetone (1:50). Intensities of 4389 independent X-ray reflections were collected with colorless and very stable in air spherical crystal of 0.4 mm in diameter. KM-4 diffractometer (Poland), θ-2θ scan mode, graphite monochromated Cu-radiation and two control reflections were used during the experiment. The space group is $P2_12_12_1$, with a=15.909(1), b=28.071(2), c=14.3672(5)Å, Z=4. The structure was solved by means of manual symbolic addition method and SHELX86 combination. 78 nonhydrogen atoms of the structure were located after 4 successive Fourier syntheses. Four atoms were not members of the peptide molecule and were identified as oxygen atoms of water molecules. The terminal phenyl atoms of the first and sixth residues were not located unambiguously and were refined as rigid groups starting from an averaged shape of the rings. The remaining atoms had been anisotropically refined in presence of H-atoms; R=0.078. Two intramolecular hydrogen bonds create the backbone shape with the following conformational angles:

	Phe 1	Pro 2	Pro 3	Ala 4	Phe 5	Phe 6	Pro 7	Pro 8	Ala 9	Phe 10
Φ	-76	-70	-88	-92	62	-74	-72	-93	-89	57
Ψ	142	165	-4	-26	33	151	160	-3	-28	38

These hydrogen bonds have N...O distances of 2.85Å. The shapes of the molecular backbone are almost identical to the conformation of II. Four water molecules are linked by H-bonds to each other with trans-arrangement, associated with the interior of a single peptide molecule, and also bonded to three carbonyl oxygens of the molecule above. This arrangement and H-bond is similar to II. The main difference between molecules of antamanide and our analogue is the degree of twisting of the molecules. Namely, the pseudotorsion angle O-C'...C'-O between the second and seventh residues is -97° in II and -77° in I. Since this angle is equal to -22° in the Li^+ complex of antamanide and -39° in the Na^+-complex of the Phe4, Val6-analog (I. L. Karle, J. Karle, Th. Wieland, W. Burgermeister, H. Faulstich, B. Witkop, Proc. Nat. Acad. Sci. USA, 1973, 70, 1836-1840) we conclude there is less stress in complexed molecule I in comparison with those mentioned above and, consequently, greater stability of alkali complexes of I. The fact was experimentally observed.

PS-04.04.06 THE CRYSTAL AND MOLECULAR STRUCTURE OF N^2-PHENYLSULPHONYL-L-GLUTAMINE. By Zhang Yan-ming, Zhang Shao-hui, Liu Zhi-lan, Zhuo Ren-xi Department of Chemistry, Wuhan University, Wuhan 430072, China, and Chen Liao-rong, The Center of Analysis and Measurement of Wuhan University, Wuhan 430072, China.

It has been reported (S. R. Burzynski, Drugs Fut., 1986, 11 (8), 679-688) that some L-glutamine and L-isoglutamine derivatives have anticancer activity. This work presents a continuation of our study of the conformational properties of glutamine analogs (Liu Zhi-lan, Zhuo Ren-xi, Zhang Yan-ming, Zhang Shao-hui, Chem. J. of Chines Universities, 1992, 13(5), 714-716). The title compound crystallizes in the orthorhombic space group $P2_12_12_1$ with four molecules in the unit cell of dimensions a=5.373(2), b=15.073(1),c=16.277(3) Å. The structure was determined by a combination of direct methods and Fourier techniques and refined by full matrix least-squares method to a final R value of 0.031 for 1622 reflections with $I \geq 3\sigma(I)$.

Table 1. Selected bond lengths(Å) and angles(°)

S-O(1)	1.438(2)	S-O(2)	1.434(2)	S-N(1)	1.606(2)
O(3)-C(2)	1.294(4)	O(5)-C(5)	1.245(4)	N(1)-C(1)	1.463(3)
O(4)-C(2)	1.218(4)	C(1)-C(2)	1.518(4)	C(1)-C(3)	1.533(4)
S-C(11)	1.771(3)	N(2)-C(5)	1.314(4)	C(3)-C(4)	1.523(4)
C(4)-C(5)	1.502(4)				

O(1)-S-O(2)	119.6(1)	O(1)-S-N(1)	105.2(1)
O(1)-S-C(11)	107.9(1)	O(2)-S-N(1)	107.5(1)
O(2)-S-C(11)	107.8(1)	N(1)-S-C(11)	108.4(1)
S-N(1)-C(1)	121.0(2)	N(1)-C(1)-C(2)	113.3(2)
N(1)-C(1)-C(3)	110.2(2)	C(2)-C(1)-C(3)	107.4(2)
O(3)-C(2)-O(4)	124.5(2)	O(3)-C(2)-C(1)	114.4(2)
O(4)-C(2)-C(1)	121.2(3)	C(1)-C(3)-C(4)	112.2(2)
C(3)-C(4)-C(5)	110.3(2)	O(5)-C(5)-N(2)	122.4(3)
O(5)-C(5)-C(4)	119.3(3)	N(2)-C(5)-C(4)	118.4(3)

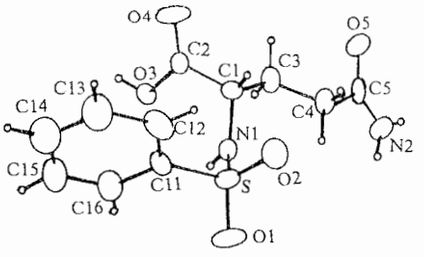

Table 2. Atomic Coordinates and thermal parameters

Atom	x	y	z	B_{eq}(Å^2)
S	0.8620(1)	0.44883(4)	0.46625(4)	2.405(9)
O(1)	1.1268(4)	0.4436(2)	0.4542(1)	3.56(4)
O(2)	0.7031(4)	0.3836(1)	0.4294(1)	3.34(4)
O(3)	0.6549(4)	0.5735(1)	0.6627(1)	3.77(4)
O(4)	0.2590(4)	0.5334(2)	0.6489(1)	3.91(5)
O(5)	0.4541(4)	0.1992(1)	0.7448(1)	3.61(4)
N(1)	0.8226(4)	0.4434(1)	0.5639(1)	2.09(4)
N(2)	0.8366(6)	0.1533(2)	0.7097(2)	3.58(5)
C(1)	0.5734(5)	0.4352(2)	0.5993(2)	2.13(4)
C(2)	0.4804(6)	0.5204(2)	0.6385(2)	2.56(5)
C(3)	0.5714(6)	0.3634(2)	0.6660(2)	2.85(5)
C(4)	0.6466(8)	0.2728(2)	0.6326(2)	3.53(6)
C(5)	0.6411(7)	0.2046(2)	0.6999(2)	2.90(5)
C(11)	0.7621(5)	0.5546(2)	0.4323(2)	2.71(5)
C(12)	0.5520(6)	0.5628(2)	0.3840(2)	3.73(6)
C(13)	0.4798(8)	0.6473(3)	0.3586(2)	4.62(8)
C(14)	0.6122(9)	0.7200(2)	0.3823(2)	4.66(8)
C(15)	0.8187(9)	0.7112(2)	0.4295(2)	4.79(9)
C(16)	0.8962(7)	0.6282(2)	0.4554(2)	4.00(7)

PS-04.04.07 HYDROGEN BONDING PATTERNS IN X-RAY DIFFRACTION STUDIES OF NEUROPEPTIDES, Judith. L. Flippen-Anderson and C. George and J. Deschamps, Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D. C. 20375-5341, USA

Hydrogen bonding is arguably the most important intra- and intermolecular cohesive force at work in determining the overall geometry, as well as the mode of recognition and association, of biological molecules. Polypeptides exhibit the same types of hydrogen bonding found in proteins: backbone - backbone, backbone - side-chain, side-chain - side chain, water - backbone, water - side-chain, and water-water. The X-Ray structures studied to date on Enkephalin and its analogs have contained from 0.5 to 6 co-crystallized water molecules per peptide molecule. The water molecules are an integral part of the overall peptide structure in that they not only fill structural cavities but they stabilize the geometry of the peptide itself. In fact, no unprotected neuropeptides have been crystallized without included solvent molecules, and there are even common patterns of solvation in their structures. In addition, some of our new structures have been found to contain internal clusters of water molecules which hydrogen-bond extensively within the cluster but have either minimal or only van der Waals interactions with the peptide molecules. While extensive studies have been performed on the hydrogen bonding patterns in nucleic acids and proteins few comparable studies have been made on linear and cyclic peptides. We have begun to compile this important information to aid in understanding the connection between molecular structure and biological activity in neuropeptides. Supported in part by ONR and NIDA.

04.05 – Conformation Analysis

PS-04.05.01 STRUCTURAL CHARACTERIZATION OF TWO POTENT ANTICONVULSANT 1,5-SUBSTITUTED-3-PYRAZOLIDONE COMPOUNDS. By Qing-chuan Yang*, Hui-juan Xu, Lu-hua Lai, You-qi Tang, Department of Chemistry, Peking university, Beijing 100871, China

Since 1-Alkyl-3-pyrazolidone was reported to be an inhibitor of γ-aminobutyrate-transaminase(White, H.J. et al.,J. Neurochem, 1982, 39: 271) , the 3 - pyrazolidone was expected to have anticonvulsant activity. 46 of 3 - pyrazolidone compounds with different substituents were studied (Lei, X. P. et al. , Acta Pharmaceutica Sinica, 1990, 25 : 684) . The pharmacological experiments showed that the anticonvulsant activity of 3 -pyrazolidones with a butyl group at 1-position of the ring were more potent.

The structural characterizations of 1-butyl-5-(p- fluophenyl) -3 -pyrazolidone (I) and 1-propyl-5-(p-methylphenyl))-3-pyrazolidone (II) were revealed by single-crystal X-ray diffraction methods.

Crystal data:

Compound I, $C_{13}H_{17}N_2OF$, triclinic, space group P $\bar{1}$, a 8.831(4), b 11.737(5), c 14.001(5) Å , α 113.19(3), β 91.77(3), γ 97.48(3)° , V 1317.2(9) Å^3 , Z=4.

Compound II, $C_{13}H_{18}N_2O$, monoclinic, space group P $2_1/c$, a 13.838(6), b 8.186(1), c 11.291(2) Å , β 104.52(3)° , V 1238.2(6) Å^3 , Z=4.

The conformations of the five membered rings of the two compounds are near to half-chair. The N(1) atoms at 1-position of the ring are sp^3-hybridized and the N(2) atoms at 2-position of the ring are sp^2-hybridized. The lone pairs of electrons on N(1) atom are clearly protophilic. There are conjugated systems consisted of carbonyl group and N(2) atom in the five membered rings. The C- N bonds between the carbonyl group and N(2) atom are partial double bonds. Therefore, the electron - withdrawing capability of 1- position substituted group might affect the electron distribution on the carbonyl O atom which is suspected to be a center of biological activity.

PS-04.05.02 CONFORMATIONAL ANALYSIS OF PYRAZOLIDONE-3-TYPE COMPOUNDS AND 3D-QSAR STUDY. By H.J. Xu*, L.H. Lai, Q.C. Yang, X.J. Xu, Department of Chemistry, Peking University, Beijing 100871, China.

Pyrazolidone-3-type compounds showed anticonvulsant activity. A series of 1,5-substituted-3-pyrazolidones were synthesized and their anticonvulsant activities were tested.

Single crystals of four compounds were obtained and their crystal structures were determined based on the X-ray diffraction data. Coordinates for 22 test compounds were generated by adding appropriate substituents to the crystal structure of 3-pyrazolidone ring with MMP2. The electronic properties of these compounds were analyzed with MNDO.

A comparative molecular field analysis (CoMFA) method was conducted to correlate the anticonvulsant activities with their structural features. The atomic charges were calculated by the method of Gast-Huck and the molecules were aligned by superimposing the 3-pyrazolidone ring. Results from a CoMFA analysis of 22 compounds correlate well with cross-validated r^2=0.757.