04-Crystallography of Biological Small Molecules

PS-04.04.04  X-ray crystal structure of conformationally constrained penta peptide Boc-Pro-dehydro Phe-Ala-dehydro Phe-Ala-Cme. Rajeshshanker A.R.1,2,3, S.Ramakumar1 and V.G.Chauhan4, 1Department of Physics, Indian Institute of Science, Bangalore-560012, India *International Center for Genetic Engineering and Biotechnology, Shaeed Jeet Singh Marg,NIIT Campus, New Delhi-110067, India

a,β-dehydro peptides are found to occur in many natural proteins and peptidomimetics (Henderson et al., 1993, PEPTIDES, 5, 285). The recent interest in these peptides is due to their roles containing a,β-dehydro phenylalanine (Phe) residues is due to the conformational constraint property of Phe (Rajeshshanker et al., J. Am. Chem. Soc., 11992, 114925). As a part of our continuing research programme on a,β-dehydro peptides here we present the x-ray crystal structure of Boc-Pro-dehydro Phe-Ala-dehydro Phe-Ala-Cme, an a,β-dehydro penta peptide. Crystals grown from ethanol/methanol are monoclinic, space group P21, a=146.75, b=9.804(3), c=27.670(3) Å, V=3369.14 Å^3, Z=4. Data was collected by a Nonius Kappa diffractometer (5200 reflections having 15<β<150, ψ<10). The Structure solved by SHELX86 and refined using SHELX90. The current agreement factors are: R=5.5% and Rw=5.9%. The two independent molecules in the asymmetric unit are remarkably similar. Both of them are characterized by two non overlapping α-turns. Boc-Pro-α-dehydro Phe-Ala lies in type 1 α-turn region while Phe-Ala-α-dehydro Phe lies in type 11 α-turn region with appropriate 4→1 hydrogen bonds. Structure solution, molecular conformation and crystal packing will be discussed in detail. Rajeshshanker thanks CSIR, India for a fellowship.

H--H atoms: R=0.078. Two intramolecular hydrogen bonds create the backbone shape with the following conformational angles:

| Phenyl | Pro | Ala | Phe | Phe | Pro | Pro | Ala | Phe |
|--------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|        | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   | 9   |
| 142    | 165 | -4  | -26 | 33  | 151 | 160 | -3  | -28 | 29  |

These hydrogen bonds have H...H distances of 2.85 Å. 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 oxygen 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 pseudorotation angle 0→C7 is between the second and seventh residues is -5° in II and -7° in I. Since this angle is equal to -22° in the 21 complex of antamanide and -32° in the 21 complex of the Phαe, Val6-analog (T. L. Karle, J. Karle, Th. Wieland, W. Burgermeister, H. Faulstich, H. Willkopp, 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-04.04.05  STRUCTURE OF Phe-Ale-IANTAMANIDE. By A.S. Vais, Institute of Physiology, Siberian Division of the Russian Acad.Sci.,Krasnoyarsk

The title compound (I) is a synthetic, symmetrical and biologically active analog of the natural cyclic decapeptide antamanide (II). The structure of II has been solved by (T. L. Karle, T. Wieland, Slichter, H.V. Ottkenhuyz, Proc. Nat. Acad. Sci. USA, 1979, 76, 1532-1536). It forms precipitates with alkali metal ions and acts as an antibiotic to the toxin phallolidin. The crystals were grown from a solution of I in a mixture of water and acetone (1:50). Intensities of 2390 independent X-ray reflections were collected with colorless and very stable in air spherical crystal of 0.4 mm in diameter. RU-4 diffractometer (F sociedad, 1980, 28, 1967-1968). The structure was solved by means of isometric symbolic addition method and SHELX86 combination. The 78 nonhydrogen atoms of the structure were located on a 4 successive Fourier synthesis. Four atoms were not members of the peptide molecule and were identified as oxygen atoms of water molecules. The terminal phenyl group 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

N atoms: R=0.078. Two intramolecular hydrogen bonds create the backbone shape with the following conformational angles:

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<th>Phe</th>
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