# 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-OMe.
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$\alpha,\beta$-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 $\alpha,\beta$-dehydro phenylalanine ($\Delta$Phe) residues is due to the conformation constraining property of $\Delta$Phe (Rajashankar et al, J.Am. Chem.Soc.,1992,114 9225). As a part of our continuing research programme on $\alpha,\beta$-dehydro peptides here we present the X-ray crystal structure of Boc-Pro-$\Delta$Phe-Ala-$\Delta$Phe-Ala-OMe, an $\alpha,\beta$-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 $\beta$=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 $\beta$-turns. Boc-Pro-$\Delta$Phe-Ala lies in type I $\beta$-turn region while $\Delta$Phe-Ala-$\Delta$Phe-Ala lies in type II $\beta$-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.
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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), $\theta$-2$\theta$ 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 |
|---|---|---|---|---|---|---|---|---|---|---|
| $\Phi$ | -76 | -70 | -88 | -92 | 62 | -74 | -72 | -93 | -89 | 57 |
| $\Psi$ | 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.
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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) |

  