03. CRYSTALLOGRAPHY IN BIOCHEMISTRY AND PHARMACOLOGY

03.2-6 CONFORMATIONAL ANALYSIS OF ANGIOTENSINOGEN FRAGMENTS. By S. Precigoux, M. Benachouche, M. Cotrait, G. Precigoux, Lab. Crystallography, University of Bordeaux I, France.

The (6-13) equine angiotensinogen octapeptide (his-pro-phe-his-leu-val-tyr) is described as the minimum endogenous substance sequence needed for efficient renin activity. We have studied the conformations of several fragments or analogs, in order to determine the most probable conformation in the neighbourhood of the "leu-val" acidic bond.

\[ \text{HIS-PRO-PHE-HIS-LEU-VALELY} \]

I Ac-PRO-PHE-LEU
II Ac-PHE-HIS-LEU-VAL-Tyr (OMe)
III Ac-PHE-HIS-IV
IV GOCHEC-LEU-PHE (OMe)
V HIS-730-PHE-IV
VI HIS-730-PHE-IV (OMe)

The I, II, III, IV, VI oligopeptides have been crystallized in a form suitable for X-Ray analysis. We have observed:

- the (G-W) β-terminal part presents a type I β-sheet at pro-phe with intramolecular hydrogen bond between O(αC) and N(H) of pro-phe. A theoretical conformational analysis of T confirms this type of β turn.
- the C-terminal part observed in the crystals of I, IV, VI is in β-sheet pleated conformation with the side chains alternatingly situated on the left and right of the main chain.

03.2-7 Structural Study of Novel ACE Inhibitors K26, K1821, K1827, and K1826. By G. Precigoux, M. Kasai, K. Shirahata, Tokyo Research Laboratories, Kyowa Hakko Kogyo Co. Ltd., 3-6-6 Asshimachi, Machida, Tokyo 194, JAPAN.

K26 (N-acetyl-I-L-leu-L-Tyr-(−)-1-smino-2-(4-hydroxyphenyl)ethylphosphonic acid) was isolated from the culture broth of Actinomyces, and shows potent inhibitory activity to angiotensin I converting enzyme (ACE). The X-ray analysis of a diethyl ester of K26 was undertaken to establish the absolute conformation of 1-smino-2-(4-hydroxyphenyl)ethylphosphonic acid nolety(Tyr-P) and the conformation.

The crystal data are as follows: C₂₅H₂₉O₂₄P₂, a=25.666(9), b=9.590(8), c=13.557(2), β=91.65(2), Z=4. The structure was solved by MULTAN75 and refined by full-matrix least-squares to a final R=0.092 for 1444 independent reflections.

The absolute configuration was determined to be (R).

Although the tripeptide backbone takes rather extended conformation, the side chain of Ile is located near the phenyl ring of Tyr-P(C9=C6=C7=C8=1.g.A.). The χ1 and χ2 of Tyr-P are 29° and 139° respectively. There is an intramolecular environment similar to that of captopril. Interactions between ACE-like proteins and K26 will be discussed.