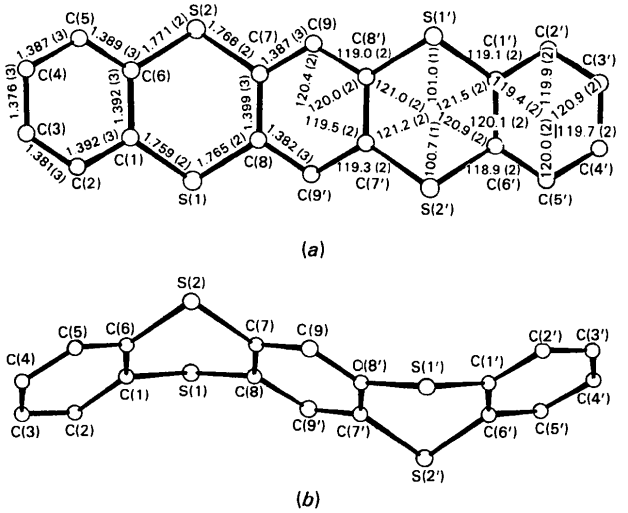

Fig. 1. The structure of molecule (II). (*a*) Bond lengths (Å) and angles (°). (*b*) General conformation of the molecule.

The pentacyclic centrosymmetric molecule (II) has a general chair-shaped conformation, previously suggested on the basis of spectral data (Ziegler & Rode, 1976). There are three approximately planar moieties in (II): *A* and *A'*, *i.e.* terminal phenylene rings with bonded S atoms [atomic deviations from the *A* and *A'* mean planes not exceeding 0·053 (2) Å], and *B*, *i.e.* a central tetrasubstituted benzene ring with bonded S atoms [atomic deviations from the mean plane not exceeding 0·036 (2) Å]. The dihedral angle between the *A* and *B* planes is 131·5 (2)°. The S(1) and S(2) atoms are displaced by 0·129 (1) and 0·101 (1) Å out of C(1)···C(6), and 0·050 (1) and 0·085 (1) Å out of C(7)···C(8) benzene planes, respectively. The heterocycles have boat conformations, the S(1) and S(2) atoms [and also S(1') and S(2')] bending out of the plane of the remaining four atoms of the ring by 0·651 (1) and 0·665 (1) Å respectively. The heterocycles in (I) and 2,7-dimethylthianthrene (III) (Weakley, 1982) have the same conformation. The folding of the heterocycles along the S···S line in (II) is 128·4 (1)° and coincides with that found in (I) (128·1°) and (III) (130·2°).

Some asymmetry in the distribution of the S–C distances in (II) is unclear, the observed values of these distances [1·759–1·771 (2) Å] agreeing with values found in (I) [1·766–1·778 (10) Å], (III) [1·760–1·774 (7) Å] and with the standard value of the ordinary S–C(sp^2) bond length of 1·77 Å (Argay, Kálmán, Nahlovski & Ribár, 1975).

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Structure of *N*-Acetyl-L-prolyl-L-phenylalanyl-L-leucine Monohydrate

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Abstract. $C_{22}H_{31}N_3O_5.H_2O$, $M_r = 435·5$. The peptide, (Leu^9)-angiotensinogen(7–9), crystallizes as a water solvate in the monoclinic space group $P2_1$ with $a = 6·572$ (2), $b = 21·823$ (6), $c = 8·512$ (3) Å, $\beta = 100·49$ (3)°, $V = 1200·4$ Å^3, $Z = 2$, $D_x = 1·205$ g cm^{-3}, Cu $K\bar{\alpha}$, $\lambda = 1·5418$ Å, $\mu = 7·5$ cm^{-1}, $F(000) = 468$, $T = 293$ K, $R = 0·057$ for 565 observed reflections with $I > 2\sigma(I)$ and $2\theta < 120°$. The proline ring has a type *A* conformation. The phenylalanine and leucine side chains are in the most commonly occurring conformations. The basic conformation of the peptide is a type I β-turn with Pro-Phe at the corner and an

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intramolecular hydrogen bond between NH of Leu and CO of the acetyl group. The molecules are stacked in layers perpendicular to the *b* axis.

Introduction. This work is part of a more general study on the crystalline conformations of renin substrates and renin inhibitors. The rate-limiting step in the series of reactions leading to angiotensin II is the release by renin of angiotensin I from the N-terminal part of angiotensinogen. Human renin has a strict specificity for the Leu-Val bond and requires a minimum octapeptide size (Skeggs, Lentz, Khan & Hochstrasser, 1968) including a proline residue. The proposal of a relatively stable conformation (β-turn) (Oliveira, Juliano & Paiva, 1977) involving residues 6–9 (His-Pro-Phe-His) of angiotensinogen led to the suggestion that the conformation of this part of the substrate plays an important role in the renin activity.

The present paper is concerned with the crystal structure of the tripeptide acetyl-Pro-Phe-Leu.H_2O, (Leu^9)-angiotensinogen(7–9). Although this is necessarily static information in particular surroundings, X-ray diffraction can provide a three-dimensional basis for substrate binding.

Table 1. *Positional* ($\times 10^3$) *and thermal parameters of non-hydrogen atoms*

$B_{eq} = \frac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	B_{eq}(Å^2)
Acetyl				
C(1)	1072 (3)	−86 (1)	1183 (2)	7·3 (11)
C(2)	917 (3)	−32 (1)	1152 (2)	6·3 (9)
O	724 (2)	−38 (1)	1137 (1)	6·8 (6)
Prolyl				
N	991 (2)	24 (1)	1130 (2)	6·1 (7)
Cα	863 (3)	78 (1)	1107 (2)	5·8 (9)
C′	692 (3)	81 (1)	951 (2)	6·1 (9)
O	545 (2)	113 (1)	946 (2)	7·5 (7)
Cβ	1021 (3)	132 (1)	1120 (3)	8·5 (12)
Cγ	1215 (3)	104 (1)	1200 (3)	9·2 (13)
Cδ	1217 (3)	39 (1)	1151 (2)	7·4 (11)
Phenylalanyl				
N	736 (2)	44 (1)	835 (1)	5·0 (6)
Cα	600 (2)	44 (1)	681 (2)	5·0 (8)
C′	471 (2)	−13 (1)	648 (2)	5·0 (8)
O	366 (2)	−22 (1)	515 (1)	6·2 (6)
Cβ	726 (3)	57 (1)	547 (2)	6·3 (10)
Cγ	838 (3)	114 (1)	561 (2)	6·5 (9)
Cδ(1)	1046 (3)	116 (1)	634 (2)	7·1 (9)
Cδ(2)	743 (3)	168 (1)	514 (3)	8·5 (12)
Cε(1)	1150 (3)	172 (1)	644 (3)	8·6 (12)
Cε(2)	850 (3)	224 (1)	526 (3)	9·8 (13)
Cζ	1053 (3)	225 (1)	589 (3)	8·1 (11)
Leucine				
N	470 (2)	−51 (1)	774 (2)	5·5 (7)
Cα	347 (2)	−107 (1)	741 (2)	5·4 (9)
C′	104 (3)	−90 (1)	697 (2)	6·8 (9)
O′	18 (2)	−128 (1)	578 (2)	7·0 (6)
O″	32 (2)	−53 (1)	762 (2)	7·3 (7)
Cβ	391 (3)	−152 (1)	878 (2)	6·5 (9)
Cγ	594 (4)	−182 (1)	897 (2)	10.2 (15)
Cδ(1)	643 (4)	−221 (1)	1045 (3)	12·0 (17)
Cδ(2)	652 (4)	−219 (1)	757 (3)	12·0 (17)
Water				
O	645 (2)	−105 (1)	400 (1)	7·0 (7)

Table 2. *Bond lengths and valence angles, average standard deviations are* 0·02 Å *and* 1·5° *respectively, and torsion angles in accordance with the IUPAC–IUB Commission on Biochemical Nomenclature* (1970) ($\sigma = 3°$)

Acetyl			
C(1)–C(2)	1·54	C(1)–C(2)–N	118
C(2)–O	1·26	C(1)–C(2)–O	124
C(2)–N	1·35	O–C(2)–N	118
Prolyl			
N–Cα	1·43	C(2)–N–Cα	123
Cα–C′	1·58	C(2)–N–Cδ	124
C′–O	1·20	Cα–N–Cδ	113
C′–N	1·35	N–Cα–C′	117
Cα–Cβ	1·56	N–Cα–Cβ	104
Cβ–Cγ	1·47	C′–Cα–Cβ	113
Cγ–Cδ	1·47	Cα–C′–N	112
Cδ–N	1·50	Cα–C′–O	120
		N–C′–O	127
		Cα–Cβ–Cγ	103
		Cβ–Cγ–Cδ	109
		Cγ–Cδ–N	100
Phenylalanyl			
N–Cα	1·45	C′–N–Cα	119
Cα–C′	1·50	N–Cα–C′	114
C′–O	1·23	N–Cα–Cβ	110
C′–N	1·36	C′–Cα–Cβ	112
Cα–Cβ	1·55	Cα–C′–N	116
Cβ–Cγ	1·45	Cα–C′–N	120
Cγ–Cδ(1)	1·40	N–C′–O	123
Cγ–Cδ(2)	1·36	Cα–Cβ–Cγ	115
Cδ(1)–Cε(1)	1·40	Cβ–Cγ–Cδ(1)	120
Cδ(2)–Cε(2)	1·40	Cβ–Cγ–Cδ(2)	122
Cε(1)–Cζ	1·37	Cδ(1)–Cγ–Cδ(2)	118
Cε(2)–Cζ	1·35	Cγ–Cδ(1)–Cε(1)	118
		Cγ–Cδ(2)–Cε(2)	123
		Cδ(1)–Cε(1)–Cζ	122
		Cδ(1)–Cε(2)–Cζ	119
		Cε(1)–Cζ–Cε(2)	119
Leucine			
N–Cα	1·45	C′–N–Cα	116
C–C′	1·62	N–Cα–C′	110
C′–O′	1·34	N–Cα–Cβ	112
C′–O″	1·13	Cα–C′–O′	108
Cα–Cβ	1·51	Cα–C′–O″	122
Cβ–Cγ	1·47	O′–C′–O″	130
Cγ–Cδ(1)	1·50	Cα–Cβ–Cγ	115
Cγ–Cδ(2)	1·54	Cβ–Cγ–Cδ(1)	114
		Cβ–Cγ–Cδ(2)	119

Peptide-backbone angles	Side-chain angles
Prolyl	
φ = −65	N–Cα–Cβ–Cγ = −18
ψ = −22	Cα–Cβ–Cγ–Cδ = 33
ω = −177	Cβ–Cγ–Cδ–N = −33
	Cγ–Cδ–N–Cα = 20
	Cδ–N–Cα–Cβ = −1
Phenylalanyl	
φ = −108	N–Cα–Cβ–Cγ = −59
ψ = 11	Cα–Cβ–Cγ–Cδ(1) = 95
ω = −179	
Leucine	
φ = −67	N–Cα–Cβ–Cγ = −72
N–C–C′–O′ = 141	Cα–Cβ–Cγ–Cδ(1) = 173
	Cα–Cβ–Cγ–Cδ(2) = −57

Experimental. Synthesis according to Merrifield's solid-phase method (Merrifield, 1963). Automatic synthesizer apparatus. Protected amino acids from Bachem Company. Chloromethylated polystyrene–1% divinylbenzene as solid phase. Amino-acid chain elongation: 30% trifluoroacetic acid deprotection, neutralization by 10% *N,N*-diisopropylethylamide dissolved in dichloromethane and coupling with dicyclohexylcarbodiimide (Sheenan & Ness, 1955). Released from the resin by hydrogen fluoride in presence of anisole. Purification by gel permeation chromatography (Sephadex G 15) and reverse-phase high-pressure liquid chromatography with as mobile phase methanol–water–trifluoroacetic acid (50/50/0·1). Colorless crystals from methanol–water. Enraf–Nonius CAD-4 diffractometer, graphite monochromator; plate-shaped crystal 0·08 × 0·30 × 0·80 mm. 1815 non-independent measured reflections, $\omega/2\theta$ scan; $2 < \theta < 60°$; h: −6→6; k: 0→20; l: −7→7. Three reference reflections ($\sigma < 1\%$). Refined unit-cell parameters obtained by centering 24 reflections $4 < \theta < 21°$. Correction for Lorentz and polarization effects. 565 observed unique reflections with $I > 2\sigma(I)$. Structure solved by direct methods (*MULTAN*80; Main *et al.*, 1980). The set having the best psi-zero figure of merit gave interpretable outline of structure of 18 out of 30 non-H atoms. Refinement on F by block-diagonal least-squares technique with anisotropic thermal parameters (β_{ij}) for non-hydrogen atoms. Hydrogen atoms in geometrical positions, not refined. $R = 0{\cdot}057$, $wR = 0{\cdot}063$; max. $\Delta/\sigma = 0{\cdot}4$; $S = 1{\cdot}52$; $|\Delta\rho|_{max}$ in final difference Fourier map 0·64 e Å^{-3}. $w = 1$ if $|F_o| < p$ and $w = p/F_o$ if $|F_o| > p$ with $p = [F_o^2(\text{max.})/10]^{1/2}$. Scattering factors for non-H atoms from *International Tables for X-ray Crystallography* (1974) and for H from Stewart, Davidson & Simpson (1965); local programs: *CRISAFFI, CRISUTIL;* Mini-6·92 Bull computer.*

Positional and thermal parameters are given in Table 1, bond distances, bond angles and torsion angles in Table 2. Fig. 1 shows a view of the molecule and Fig. 2 the crystal structure viewed down **a**.

Discussion. Most of the bond lengths and angles are in good agreement with those of similar oligopeptides. At the C-terminal end of the peptide the C′ atom seems to be misplaced as indicated by the Cα–C′ and C′–O″ distances, respectively long and short, and the very wide O′–C′–O″ angle. The reason for this is not clear. This result might be due to the small amount of information compared with the number of parameters refined. The N–Cα–C′ angle of the Phe residue, 114°, is in accord with the classical value for such an angle when Pro is the second residue of a β-turn (type I) in cyclic or linear oligopeptides (Ashida, Tanaka, Shimonishi & Kakudo, 1977). From the observed dihedral angles, it is clear that the β-turn formed by the molecule is of type I (Venkatachalam, 1968). All the peptide units are planar. In the present structure, with Phe as the third residue, the intramolecular N–O distance

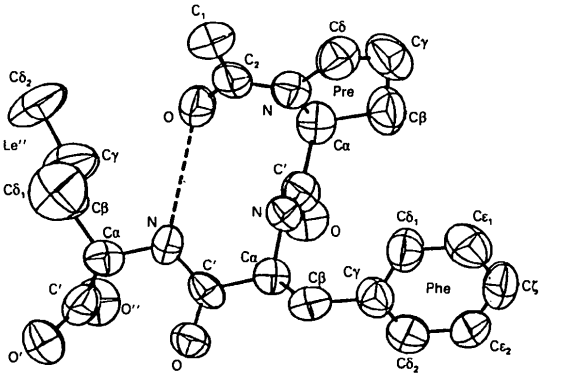

Fig. 1. Molecular structure of *N*-acetyl-Pro-Phe-Leu as viewed along the normal to the mean plane of the molecule. The internal hydrogen bond is indicated by the dashed line. The thermal ellipsoids are scaled to include 50% probability.

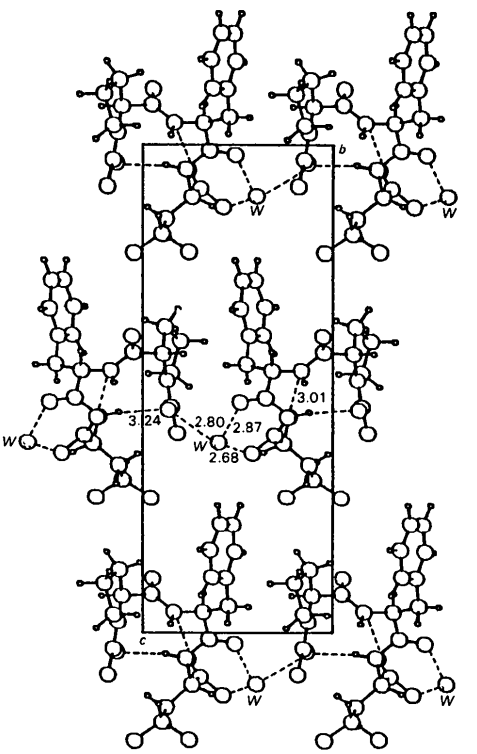

Fig. 2. The crystal structure of *N*-acetyl-Pro-Phe-Leu viewed along **a**. The hydrogen bonds are shown by dashed lines ($\sigma = 0{\cdot}03$ Å).

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42748 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

(hydrogen-bond like), 3·24 (3) Å, is longer than the values observed when Gly or Leu is the third residue (Tanaka, Ashida, Shimonishi & Kakudo, 1979; Ashida *et al.*, 1977).

The proline ring adopts a conformation of type *A* (Balasubramanian, Lakshminarayanan, Sabesan, Tegoni, Venkatesan & Ramachandran, 1971). The phenylalanine side chain is in the conformation that has the highest frequency of occurrence in peptides and proteins (Benedetti, Morelli, Nemethy & Scheraga, 1983) with $\chi1 = -59$ and $\chi2 = 95°$. This conformation leads to the most sterically favorable arrangement. The conformation of the leucine side chain corresponds to that most frequently occurring with ($\chi1$, $\chi2$, 1) ~ (−60, 180°).

The crystal structure can be described as consisting of layers of tripeptide molecules stacked perpendicular to the *b* axis. Each face of the layer is wholly hydrophobic, consisting of phenyl rings and leucine side chains which stabilize the structure by van der Waals interactions. A layer can be characterized by its hydrogen bonding. The two NH groups in the molecule give one proton each. The water molecule gives its protons to the oxygen atom of the acetyl group and to the carboxyl of the Phe residue and receives one proton from the OH group. The only oxygen atom without hydrogen interaction belongs to the carboxyl of Pro.

The Leu residue, which replaces His of angiotensinogen in order to make crystallization easier, seems to play an important role only in the packing of the molecule (interactions between hydrophobic side chains of neighboring peptides) and not at the molecular conformation level. So for the 6–9 tetrapeptide of angiotensinogen such a β-turn structure might be a favorable conformation in solution as proposed by Oliveira, Juliano & Paiva (1977).

The present study shows a preferred type I β-turn conformation for a peptide containing the Pro-Phe sequence. Such a conformation may be important for renin and the angiotensinogen converting enzyme. In order to study the possible role of the β-turn in angiotensinogen, it is of great interest to investigate analogous or longer peptides in which the leucine residue is replaced by histidine. Further studies of linear oligopeptides related to angiotensinogen are in progress.

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Structure of 4-Amino-5,7-dinitrobenz[1,2-*c*][1,2,5]oxadiazole 3-Oxide

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Abstract. $C_6H_3N_5O_6$, $M_r = 241·1$, monoclinic, $P2_1$, $a = 11·959$ (7), $b = 9·863$ (6), $c = 7·180$ (4) Å, $\beta = 98·131$ (1)°, $V = 838·4$ (9) Å^3, $Z = 4$, $D_x = 1·910$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 15·5$ cm^{-1}, $F(000) = 488$, $T = 293$ K, final $R = 0·079$ for 1208 unique observed intensities. The space group is close to $P2_1/a$; confirmation of $P2_1$ was obtained by two statistical tests and diffraction-vector rotation scans for three reflections that appeared to violate the *a*-glide systematic absences. Both of the molecules in the asymmetric unit are disordered, resulting in a structure that appears to contain two [1,2,5]oxadiazole rings,

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