Crystal Structures of Repeating Peptides of Elastin. 3. *N*-(*tert*-Butoxycarbonyl)-L-valyl-L-prolylglycyl-L-valine and Its Monohydrate Crystal

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Abstract: The structures of two crystalline forms of the title peptide, a part of a repeating peptide in elastin, have been established by X-ray methods. One form is in the orthorhombic space group $P2_12_12_1$ with a = 40.457 (11) Å, b = 9.658 (2) Å, c = 6.914 (2) Å, and Z = 4; R = 0.098 for 2208 nonzero reflections of $2\theta \leq 128°$. The other form crystallizes as a monohydrate in $P2_12_12_1$ with a = 30.071 (3) Å, b = 9.696 (1) Å, c = 9.476 (1) Å, and Z = 4; R = 0.066 for 2516 nonzero reflections of $2\theta \leq 128°$. The peptide molecules including all the side chains have essentially the same conformation in both crystalline forms. The main chains are in a type II β turn, which has been proposed by NMR studies as one of the most important conformations for the repeating peptides of the extensible regions in elastin. The Val residues at the first and the fourth sites, however, have an appreciable effect on the structure of the β turn, the 4→1 intramolecular hydrogen bond being significantly longer than usual. In the monohydrate crystal a water molecule makes a ten-membered ring with a peptide molecule via two hydrogen bonds, (Gly^3)N—H···O(water)—H···O=C(Val^4), that increase further the stability of the β-turn folding.

Introduction

In our previous reports in this series the crystal structures of Boc-Val-Pro-Gly-Val-Gly-OH[1] and Boc-Val-Pro-Gly-Gly-OBzl[2] have been reported. They are two of the three repeating peptides in an extensible region of tropoelastin, the other being Val-Ala-Pro-Gly-Val-Gly.[3,4] In the crystalline state, the central part of the pentapeptide takes a rather extended conformation and the molecules are arranged in an infinite antiparallel β sheet, while the tetrapeptide is folded at the Pro-Gly part into a type II β turn. On first inspection the difference in the conformations of the two peptides seems to be a result of the difference in the shapes and sizes of the fourth residues, Val and Gly.

On the other hand Urry and his collaborators[5-11] have proposed on the basis of NMR studies and conformational energy calculations that a type II β turn with Pro-Gly at the corner is the most important conformation for all three repeating peptides of tropoelastin.

The present paper deals with the structure of Boc-Val-Pro-Gly-Val-OH, which is a part of the pentapeptide. It is of interest to see whether the present peptide forms a β turn or not, since the large forked Val side chains have to be accommodated in both the first and the fourth sites, which are geometrically close to each other in the β turn. According to Chou and Fasman,[12] in globular proteins Val is one of the amino acid residues that have a low probability of occurring in the β turn. Meanwhile a type II β turn that has Val residues at both the first and the fourth sites was found in *cyclo*(Val-Pro-Gly-Val-Gly)$_3$, the cyclic trimer of the repeating pentapeptide.[13] The structure of this peptide, however, might have a significant constraint due to the presence of many Val and Pro residues in a small ring.

Table I. Crystal Data and Experimental Condition

	form A	form B
chemical formula	$C_{22}H_{38}N_4O_7$	$C_{22}H_{38}N_4O_7 \cdot H_2O$
space group	$P2_12_12_1$	$P2_12_12$
a, Å	40.457 (11)	30.071 (3)
b, Å	9.658 (2)	9.696 (1)
c, Å	6.914 (2)	9.476 (1)
Z	4	4
ρ(calcd), g cm^{-3}	1.157	1.174
ρ(obsd), g cm^{-3}	1.16	1.17
μ(Cu Kα), cm^{-1}	7.23	7.07
crystal size, mm	0.3 × 0.1 × 0.05	0.2 × 0.15 × 0.1
2θmax, deg	128	128
scan method	θ-2θ scan	θ-2θ scan
scan range, $\Delta\theta$, deg	1.5 + 0.142 tan θ	1.0 + 0.142 tan θ
scan speed, deg/min	5 (0°-80°)	10 (0°-100°)
(2θ range)	2 (80°-100°)	4 (100°-115°)
	0.5 (100°-128°)	2 (115°-128°)
background, s	3 (0°-80°)	3 (0°-100°)
	7.5 (80°-100°)	7.5 (100°-115°)
	30 (100°-128°)	15 (115°-128°)
number of reflections[a]	2607 (2208)	2645 (2516)

[a] Numbers of nonzero reflections are shown in the parentheses.

Experimental Section

Boc-Val^1-Pro^2-Gly^3-Val^4-OH was prepared by the DCC (*N,N'*-dicyclohexylcarbodiimide) coupling method. Two kinds of crystals were obtained by slow evaporation of an ethyl acetate solution at room temperature. Form A, which appeared first, was a very thin needle crystal, mp 171-172 °C; form B, which appeared later from the same batch, was a rod and included one water per peptide, mp 114-115.5 °C.

The X-ray diffraction measurements were done on a Rigaku four-circle diffractometer with graphite monochromatized Cu Kα radiation, the diffractometer being equipped with a rotating anode X-ray generator operated at 50 kV and 40 mA with a focus spot of 3 × 0.3 mm. Since the high-order reflections with large Bragg angles were so weak, they were measured with slower scan speed and longer background counting time than those for the low-order reflections. By this method the accuracy of the intensities of the high-order reflections was substantially improved. Intensities were corrected for Lorentz and polarization factors, but absorption correction was not made. The crystallographic data and the experimental details are summarized in Table I.

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Table II. Positional (×10⁴) and Thermal (×10) Parameters of Non-Hydrogen Atoms (Form A)

atom	*x*	*y*	*z*	B_{eq},[a] Å²
C(1)	5 060 (3)	1 219 (18)	5 238 (30)	89 (10)
C(2)	4 796 (4)	59 (20)	8 063 (29)	99 (11)
C(3)	4 835 (4)	−1 164 (17)	4 858 (34)	101 (11)
C(4)	4 791 (3)	227 (14)	5 886 (27)	74 (8)
C(5)	4 357 (3)	1 943 (14)	5 707 (24)	63 (7)
C(6)	3 885 (3)	3 433 (13)	4 749 (20)	54 (6)
C(7)	3 987 (3)	4 564 (13)	3 262 (23)	60 (7)
C(8)	4 312 (3)	5 248 (18)	3 846 (34)	96 (10)
C(9)	4 002 (4)	4 002 (19)	1 145 (25)	83 (9)
C(10)	3 529 (2)	2 979 (12)	4 386 (16)	43 (5)
C(11)	2 949 (2)	3 475 (12)	4 313 (17)	43 (5)
C(12)	2 753 (3)	4 784 (12)	4 925 (16)	46 (5)
C(13)	2 962 (3)	5 431 (13)	6 542 (16)	46 (5)
C(14)	3 312 (3)	5 143 (13)	6 003 (18)	50 (6)
C(15)	2 921 (2)	3 153 (11)	2 181 (17)	40 (5)
C(16)	2 686 (3)	1 618 (11)	−220 (20)	50 (6)
C(17)	2 880 (3)	322 (13)	−661 (19)	56 (6)
C(18)	3 329 (3)	−1 251 (11)	−15 (22)	58 (6)
C(19)	3 706 (4)	−1 128 (19)	636 (47)	136 (16)
C(20)	3 838 (6)	196 (26)	−433 (58)	170 (21)
C(21)	3 720 (5)	−1 233 (18)	2 995 (39)	116 (14)
C(22)	3 172 (3)	−2 508 (11)	796 (22)	53 (6)
N(1)	4 089 (2)	2 212 (10)	4 591 (19)	61 (6)
N(2)	3 290 (2)	3 854 (10)	4 873 (14)	45 (4)
N(3)	2 738 (2)	2 102 (8)	1 734 (13)	38 (4)
N(4)	3 137 (2)	12 (9)	437 (16)	50 (5)
O(1)	4 473 (2)	691 (10)	5 164 (17)	71 (5)
O(2)	4 463 (2)	2 699 (9)	6 960 (15)	68 (5)
O(3)	3 470 (2)	1 875 (8)	3 575 (13)	49 (4)
O(4)	3 055 (2)	3 900 (7)	981 (10)	42 (3)
O(5)	2 798 (2)	−395 (12)	−2 051 (17)	88 (6)
O(6)	2 913 (3)	−2 531 (11)	1 654 (22)	113 (8)
O(7)	3 334 (2)	−3 654 (8)	487 (13)	55 (4)

[a] Calculated from the anisotropic thermal parameters (deposited).

The structures were solved by the direct method with the program MULTAN78.[14] For form A the structure appeared rather easily. For form B it was necessary to make several trials based on the different sets of the reflections having different outer limits of 2θ, and one of the E map of the set with $2\theta < 110°$ gave an interpretable outline of the structure. All the remaining atoms were found on the successive difference Fourier maps. The positions of the hydrogen atoms were checked with the coordinates estimated geometrically from those of the non-hydrogen atoms.

The structures were refined with the block-diagonal least-squares program HBLS VI.[15] In form A the hydrogen atoms were included in the structure factor calculation but not refined, while in form B they refined but their temperature factors were set as equal to B_{eq} of their carrier atoms. The function minimized was $\sum w(|F_o| - |F_c|)^2$ with $w = [\sigma^2(F_o) + a|F_o| + b|F_o|^2]^{-1}$ for $F_o \neq 0$ and $w = c$ for $F_o = 0$. In form A $a = 0.129$, $b = 0.002$, $c = 0$, and $R = 0.098$ for all the nonzero reflections, and in form B $a = -0.034$, $b = 0.002$, $c = 0.288$, and $R = 0.073$ for all the reflections ($R = 0.066$ for the nonzero reflections). The atomic scattering factors were taken from International Tables for X-Ray Crystallography.[16] The atomic coordinates of the non-hydrogen atoms are given in Tables II and III.

Results and Discussion

The bond lengths and angles are shown in Figure 1. They are as a whole in good accordance with those observed in many other peptides.[17,18] The conformational angles are shown in Figure 2, and the ORTEP[19] drawings of the molecules are shown in Figure 3. Although the packing schemes are different in the two

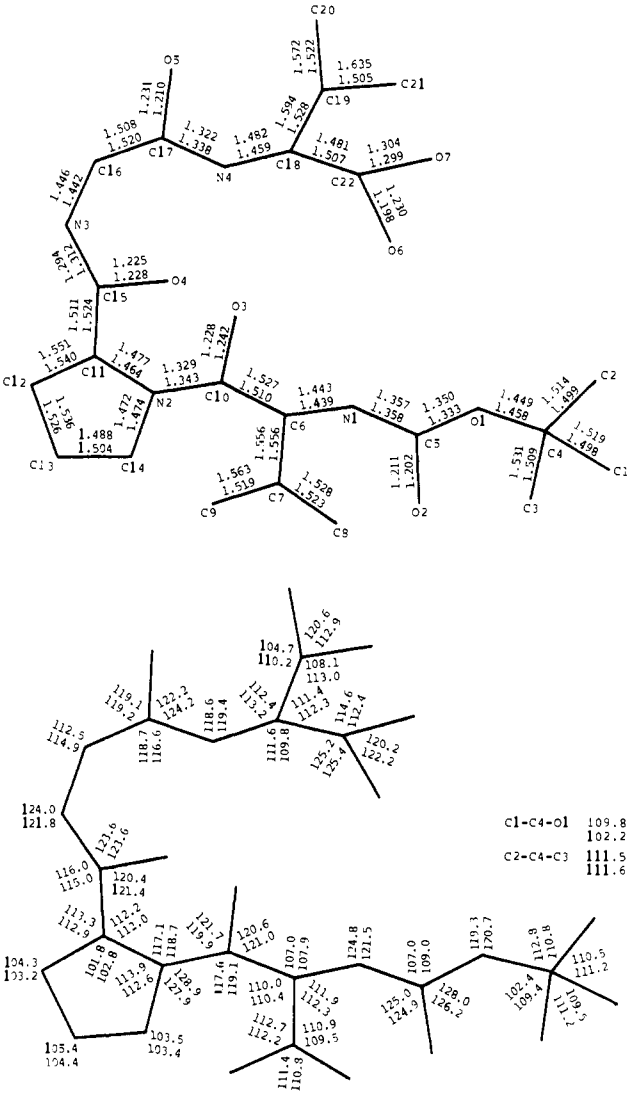

Figure 1. (Top) Bond lengths (Å) of form A (upper) and form B (lower). Esd's are 0.01–0.05 Å for form A and 0.005–0.014 Å for form B. (Bottom) Bond angles (deg) of form A (upper) and form B (lower). Esd's are 0.9–2.7° for form A and 0.3–0.8° for form B.

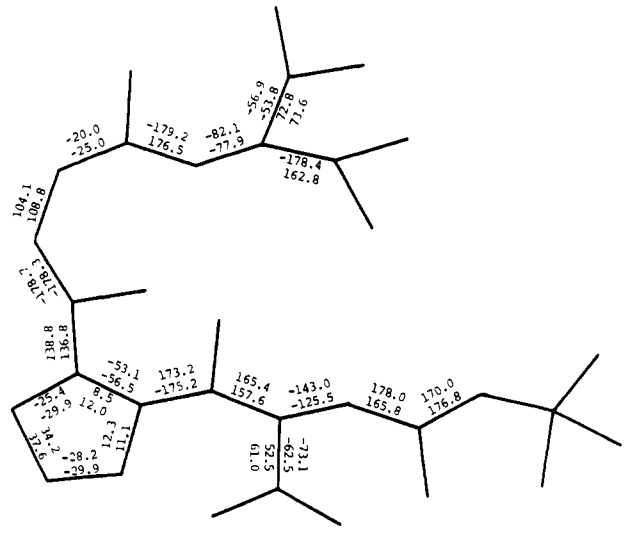

Figure 2. Conformational angles (deg) of form A (upper) and form B (lower). Esd's are 0.9–2.7° for form A and 0.3–0.6° for form B.

crystalline forms, the conformations of the peptide molecules including all the side chains are essentially the same in both forms A and B. Their similarity is excellent. The following discussions

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Table III. Positional (×10⁴) and Thermal (×10) Parameters of Non-Hydrogen Atoms (Form B)

atom	x	y	z	B_{eq},[a] Å²
C(1)	10 300 (3)	1 850 (12)	4 803 (11)	145 (7)
C(2)	10 620 (2)	3 772 (8)	3 421 (10)	94 (4)
C(3)	10 685 (3)	1 362 (9)	2 541 (13)	128 (6)
C(4)	10 405 (2)	2 379 (6)	3 355 (8)	75 (3)
C(5)	9 917 (1)	2 903 (5)	1 386 (6)	53 (2)
C(6)	9 310 (1)	3 502 (5)	−213 (5)	45 (2)
C(7)	9 156 (2)	2 458 (6)	−1 360 (5)	57 (2)
C(8)	8 782 (2)	1 533 (6)	−840 (8)	72 (3)
C(9)	9 551 (3)	1 604 (9)	−1 851 (9)	97 (5)
C(10)	8 928 (1)	4 411 (5)	234 (4)	40 (2)
C(11)	8 464 (1)	6 418 (4)	−91 (5)	44 (2)
C(12)	8 417 (2)	7 440 (5)	−1 326 (6)	59 (2)
C(13)	8 883 (2)	7 466 (6)	−1 965 (7)	69 (3)
C(14)	9 042 (2)	5 999 (5)	−1 853 (5)	53 (2)
C(15)	8 032 (1)	5 660 (4)	240 (4)	38 (2)
C(16)	7 431 (1)	5 402 (5)	1 895 (5)	46 (2)
C(17)	7 483 (1)	4 489 (4)	3 188 (4)	40 (2)
C(18)	7 965 (1)	3 127 (5)	4 673 (5)	46 (2)
C(19)	8 351 (2)	2 110 (6)	4 511 (7)	66 (3)
C(20)	8 280 (3)	1 212 (6)	3 213 (8)	81 (4)
C(21)	8 799 (2)	2 800 (8)	4 531 (7)	82 (4)
C(22)	8 024 (2)	4 065 (5)	5 927 (5)	51 (2)
N(1)	9 480 (1)	2 824 (4)	1 025 (4)	46 (2)
N(2)	8 811 (1)	5 479 (4)	−588 (4)	42 (1)
N(3)	7 836 (1)	6 044 (4)	1 411 (4)	41 (1)
N(4)	7 886 (1)	3 948 (4)	3 408 (4)	42 (1)
O(1)	9 965 (1)	2 471 (4)	2 713 (4)	64 (2)
O(2)	10 209 (1)	3 302 (5)	622 (5)	74 (2)
O(3)	8 720 (1)	4 176 (3)	1 340 (3)	46 (1)
O(4)	7 880 (1)	4 790 (4)	−566 (3)	51 (1)
O(5)	7 163 (1)	4 269 (4)	3 928 (4)	57 (2)
O(6)	8 108 (2)	5 272 (4)	5 871 (4)	83 (2)
O(7)	7 978 (1)	3 418 (4)	7 119 (3)	62 (2)
OW	6 812 (1)	2 438 (4)	6 103 (4)	59 (2)

[a] Calculated from the anisotropic thermal parameters (deposited).

on the molecular structure hold for both forms unless otherwise noted.

In both crystalline forms the peptide molecules have the same type II β turn with Pro²-Gly³ at the corner, the intramolecular 4→1 hydrogen bond being (Val⁴)N—H···O=C(Val¹). This is the structure that has been proposed by the NMR studies as the conformation of the repeating peptides of the extensible region of elastin in solution.[5-11] In the crystalline state the same type II β turn has been found in the tetrapeptide Boc-Val-Pro-Gly-Gly-OBzl[2] and cyclo(Val-Pro-Gly-Val-Gly)$_3$,[13] but not in the pentapeptide Boc-Val-Pro-Gly-Val-Gly-OH, which is in a rather extended conformation.[1] The present peptide is a part of the pentapeptide. Thus it is now clear that the pentapeptide also may make the same type II β turn in some other crystalline fields.

A comparison among the type II β turns of forms A and B and Boc-Val-Pro-Gly-Gly-OBzl was made; for each pair two models are superimposed by adjusting the relative positional and rotational parameters by the least-squares procedure with the program CMRL.[20] Nine non-hydrogen atoms in the ten-membered β turn loop and six non-hydrogen atoms bonded directly to the atoms in the loop were included in the calculation. The rms deviation is 0.07 Å between forms A and B, which is negligibly small, but 0.35 and 0.38 Å for forms A and B, respectively from Boc-Val-Pro-Gly-Gly-OBzl. The latter two deviations are significant, and brought about by the difference in the conformational angles (ϕ,ψ) of Gly³. The conformational angles in the β turn will be discussed later.

β Turn and Val. The large hydrophobic branched side chain of Val will severely affect the main chain conformation, but it is thus shown that type II β turn can accommodate two Val residues in both the first and the fourth sites at the same time.

(20) Itoh, H. "UNICS-NAGOYA"; Nagoya University: Nagoya, Japan, 1981; p 95.

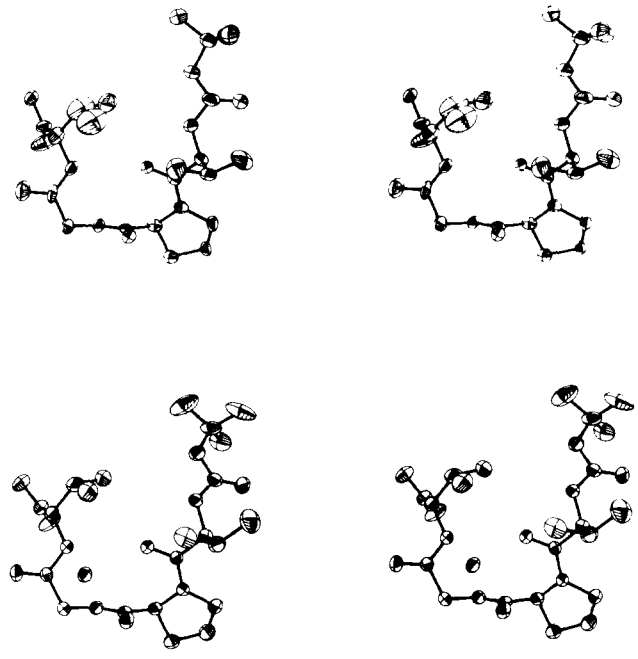

Figure 3. A stereodrawing of the peptide molecule. Thermal ellipsoids are drawn at the 30% probability level. (Top) Form A. (Bottom) Form B with the water molecule, which makes two hydrogen bonds with the peptide molecule.

According to Chou and Fasman[12] the potential for Val to appear in β turns in globular proteins is very low. The present study has shown that this tendency is merely a resultt of the hydrophobic nature but not of the geometry of the branched side chain of Val, since in globular proteins β turns are usually found at the surfaces of the molecules which are usually hydrophilic. Val has, however, not yet been found in the second or the third site of the β turn of the linear oligopeptides. These two sites have more severe geometrical restrictions than the first and the fourth sites.

4→1 Hydrogen Bond in β Turn. Usually the lengths of the intramolecular 4→1 hydrogen bonds in the β turns of the linear oligopeptides are 3.00–3.05 Å[21] and significantly longer than the other types of N–H···O bonds having the mean length of 2.90 Å in peptides and proteins.[17] Table IV shows, however, that the present peptides have even longer bonds of 3.12 and 3.19 Å. They are certainly much longer than usual, but their H···O distances, 2.13 and 2.18 Å, are significantly shorter than the sum 2.60 Å, of the van der Waals radii. The three atoms of N–H···O are roughly linearly located. Thus they are long but undoubtedly the intramolecular hydrogen bonds characteristic of the β turn. In addition there is a close contact of (Val⁴)C(21)–H···O(3) (Val¹), which may be a weak hydrogen bond and contribute to the stability of the β turn; the parameters also listed in Table IV.

A few rather short van der Waals contacts are found between Val¹ and Val⁴. They lengthen unusually the 4→1 hydrogen bonds. Of the two Val residues, Val⁴ especially seems to play an important role in this lengthening effect, since the bond length of 3.05 Å in Boc-Val-Pro-Gly-Gly-OBzl is quite normal, while the length of 3.28 Å in *cyclo*(Val-Pro-Gly-Val-Gly)$_3$[13] is longer than the present ones. This cyclic pentadecapeptide may have more direct contacts between two Val side chains at the first and the fourth sites.

Thus, although two Val residues can occupy the first and the fourth sites of the β turn at the same time, they lengthen unusually the 4→1 hydrogen bond.

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Table IV. Hydrogen Bonds and Hydrogen Bond Like C-H···O Interactions

donor (D)	hydrogen (H)	acceptor (A)	symmetry equivalent of acceptor	distance, Å D···A	distance, Å H···A	angle D-H···A, deg
			Form A			
N(3)	H(26)	O(5)	$^1/_2 - x, -y, ^1/_2 + z$	2.85 (2)	2.08	132
N(4)	H(29)	O(3)[a]	x, y, z	3.12 (1)	2.13	165
O(7)	H(38)	O(4)	$x, -1 + y, z$	2.64 (1)	1.77	145
C(12)	H(21)	O(6)	$x, 1 + y, z$	3.50 (2)	2.47	156
C(13)	H(22)	O(4)	$x, y, 1 + z$	3.43 (1)	2.42	152
C(21)	H(37)	O(3)	x, y, z	3.19 (3)	2.24	147
			Form B			
N(3)	H(26)	OW	$^3/_2 - x, ^1/_2 + y, 1 - z$	2.92 (1)	2.00 (5)	150 (4)
N(4)	H(29)	O(3)[a]	x, y, z	3.19 (1)	2.18 (6)	170 (5)
O(7)	H(38)	O(4)	$x, y, 1 + z$	2.58 (1)	1.59 (6)	161 (5)
OW	H(39)	O(5)	x, y, z	2.92 (1)	2.03 (6)	165 (6)
OW	H(40)	O(6)	$^3/_2 - x, -^1/_2 + y, 1 - z$	2.82 (1)	1.99 (7)	153 (6)
C(16)	H(28)	O(7)	$^3/_2 - x, ^1/_2 + y, 1 - z$	3.31 (1)	2.35 (6)	154 (5)
C(21)	H(37)	O(3)	x, y, z	3.31 (1)	2.33 (8)	151 (7)

[a] 4→1 hydrogen bond of β turn.

Table V. Type II β Turn: Conformational Angles (deg) and 4→1 Hydrogen Bond Distances (Å)

R1	R2	R3	R4	ϕ_2	ψ_2	ϕ_3	ψ_3	N···O distance	ref
Boc-Val-	Pro-	Gly-	Val-OH (form A)	−53	139	104	−20	3.12	this study
Boc-Val-	Pro-	Gly-	Val-OH (form B)	−57	137	109	−25	3.19	this study
Boc-Val-	Pro-	Gly-	Gly-OBzl	−62	136	75	3	3.05	2
Ibr-	Pro-	Ala-	NH-Ipr[a]	−59	136	66	14	3.05	22
Ibr-	Pro-D-	Ala-	NH-IPr	−62	137	84	3	3.10	22
cyclo(Val-	Pro-	Gly-	Val-Gly)$_3$	−53	140	84	−7	3.28	13
cyclo(Gly-	Pro-	Gly-D-	Ala-Pro)	−52	126	74	12	2.87	23
cyclo(Ser-	Ser-	Gly-	Orn-Orn-Orn)	−57	132	82	−1	2.98	24

[a] Ibr, $(CH_3)_2CHCO$–; Ipr, $-CH(CH_3)_2$.

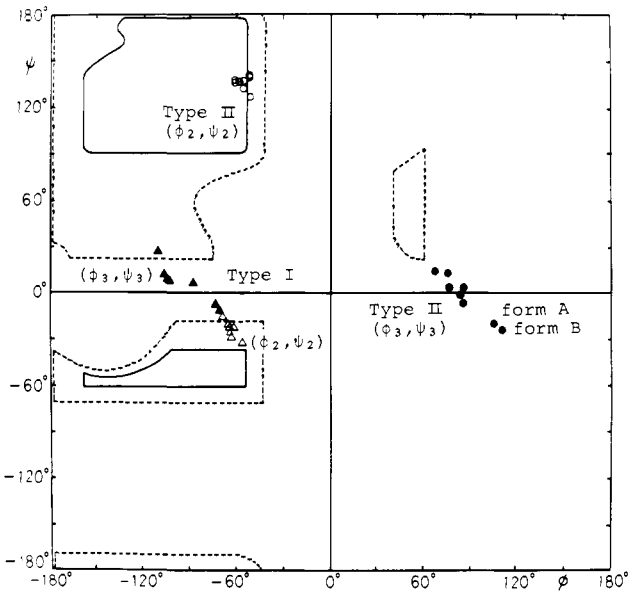

Figure 4. (ϕ_2,ψ_2) and (ϕ_3,ψ_3) of the type II β turn in oligopeptides that are listed in Table IV. Some of the type I β turn also are listed: Boc-Pro-Leu-Gly-OH,[25] Boc-Pro-Pro-Gly-NH_2,[26] Z(*p*-Br)-Gly-Pro-Leu-Gly-OH,[27] Z(*o*-Br)-Gly-Pro-Leu-Gly-Pro-OH,[28] (*S*-benzyl)Cys-Pro-Leu-Gly-NH_2,[29] Z-Gly-Pro-Leu-Gly-Pro-OH,[30] and cyclochlorotin.[31]

Conformational Angles in β Turn. Some of the conformational angles of the type II β turns are shown in Table V and Figure 4. Although (ϕ_2,ψ_2)'s concentrate in a narrow range, (ϕ_3,ψ_3)'s distribute in a fairly wider range. The (ϕ_3,ψ_3) values of the present peptide, (104°, −20°) for A and (109°, −25°) for B, are considerably different from the others listed in Table V, their mean values being (77°, 4°). This difference produces the significant deviations between the geometries of the β turns of the present peptide and Boc-Val-Pro-Gly-Gly-OBzl.[2] Between ϕ_3 and ψ_3 of the type II β turn there is a clear correlation shown approximately by $\psi_3 = -\phi_3 + 80°$. A similar correlation, $\psi_3 = -\phi_3 - 90°$, has been found for type I β turn.[26] By these correlation the 4→1 hydrogen bond is preserved even if ϕ_3 and ψ_3 deviate significantly from each other. The structural changes produced by a clockwise rotation of the N–C^α bond and an anticlockwise rotation of the C^α–C′ bond partly compensate for each other, and the geometry

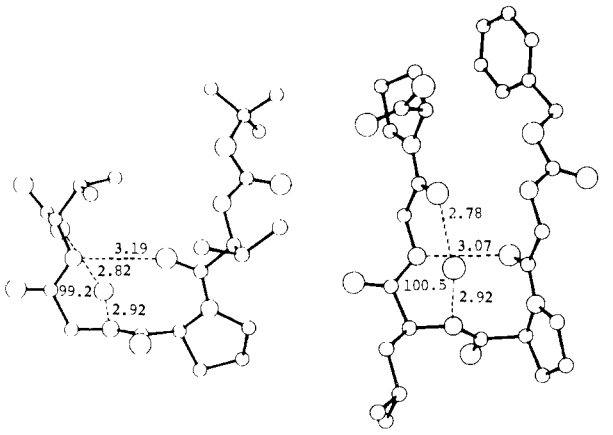

Figure 5. A ten-membered loop made by two hydrogen bonds between a water molecule and a peptide molecule. Hydrogen bonds are shown by broken lines with their lengths. The N–O (water)–O angles are also shown. (Left) Present molecule form B; (Right) Z-Gly-Pro-Leu-Gly-Pro-OH (type I).[30]

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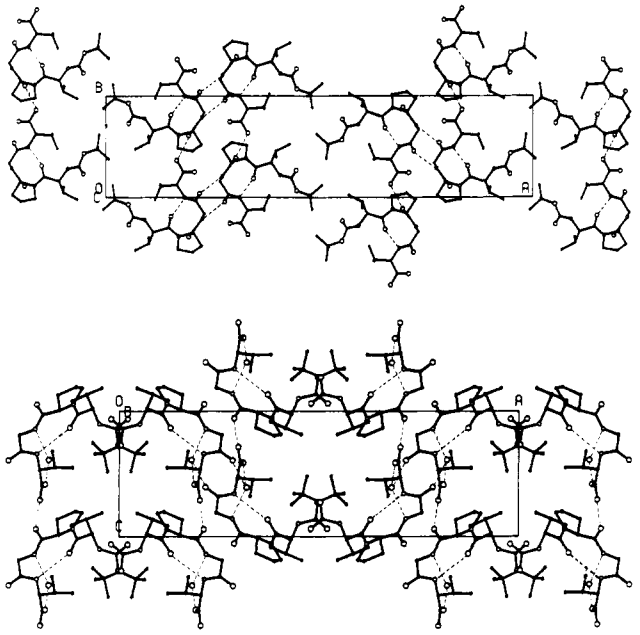

Figure 6. (Top) Form A, the crystal structure viewed along the c axis. (Bottom) Form B, the structure viewed along the b axis.

of the 4→1 hydrogen bond may not significantly be affected.

β Turn and Water. The hydrogen bond parameters in the crystals are shown in Table IV. In form B a water molecule makes three hydrogen bonds, of which two are "intramolecular" bonds made with one peptide molecule as (Gly^3)N—H···O—H-(water)···O=C(Val^4). Thus a ten-membered loop is made up (Figure 5). This loop also stabilizes further the β-turn folding. This same structure, or its mirror image in the strict sense, has been reported in Z-Gly-Pro-Leu-Gly-Pro-OH[30] and its Br derivative,[28] although both are folded in a type I β turn. Thus, the present hydrogen bond scheme looks like one of the important structures for the "hydrated β turn" and may frequently be found at the molecular surfaces of elastin as well as globular proteins.

Side Chains. The isopropyl side chain of Val^4 of form A has unusually large temperature factors and shows unusual bond lengths and angles. Such an anomaly would suggest a presence of some sort of disordered structure of the side chain, e.g., coexistence of two or three rotational isomers due to a rotation of the C^{α}–C^{β} bond, although definite evidence could not be found on the difference Fourier map. Among the three C atoms in the side chain, C(21), which has a C–H···O hydrogen bond, has the smallest temperature factor. The large R factor for form A may largely be a result of such an unusual appearance of the side chain.

The conformations of all the Val side chains are gauche II; that is, all the N–C^{α}–C^{β}–C^{γ} chains are in the G or $\bar{G}$ conformations. The conformations of the pyrrolidine rings are both C_2–C^{γ}-exo,[18] which supports the tendency that most pyrrolidine rings at the second site of the type II β turn are in a C^{γ}-exo conformation, which is characterized by a negative χ_1.[2]

Hydrogen Bonds. The crystal structures are shown in Figure 6. There are two types of intermolecular hydrogen bonds in form A and four in B. Besides, a few short C–H···O interactions are found. Their geometries shown in Table IV indicate that they seem to be weak hydrogen bonds. As mentioned before the intramolecular (Val^4)C(21)–H···O(3)(Val^1) contacts are found in both forms. The N–H of Val^1 is not involved in any hydrogen bonds, but it points to the Val^4 side chain. This contact also lengthens the 4→1 hydrogen bond. In Boc-Val-Pro-Gly-Gly-OBzl also N–H of Val^1 is not involved in a hydrogen bond, but it points to a hydrophobic solvent, ethyl acetate.[2]

In summary, Boc-Val-Pro-Gly-Val-OH is folded in type II β turn with Pro-Gly at the corner. Two Val residues significantly affect the length of the intramolecular 4→1 hydrogen bond. This study suggests that although Boc-Val-Pro-Gly-Val-Gly-OH, the repeating pentapeptide in elastin, has been found in an extended conformation in the crystal it may fold in the same type II β turn in some other environments. In the monohydrate crystal the β turn is "hydrated" by making a ten-membered loop by two hydrogen bonds, (Gly^3)N—H···O—H(water)···O=C(Val^4), which increase further the stability of the β turn folding.

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Registry No. Boc-Val-Pro-Gly-Val-OH, 84254-48-8; Boc-Val-Pro-Gly-Val-OH·H_2O, 84254-49-9.

Supplementary Material Available: Listing of thermal parameters of non-hydrogen atoms, positional and thermal parameters of hydrogen atoms, and structure factors (28 pages). Ordering information is given on any current masthead page.

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