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The Crystal Structure of Glycyl-phenylalanyl-glycine*

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The crystal structure of the tripeptide glycyl-phenylalanyl-glycine 'mono'-hydrate has been determined by analysis of three-dimensional intensity data from copper radiation. The crystals are orthorhombic with space group $P2_12_12_1$; the unit-cell dimensions, as reported previously by Dégeilh and Pickworth (1956), are:

$$a = 29.72, b = 9.98, c = 4.90 \text{ A}$$
.

The peptide chain is in an extended configuration and adjacent molecules are hydrogen-bonded together to form a parallel-chain pleated sheet. The benzene ring of the phenylalanine residue protrudes laterally from the pleated sheet and packs in an interlocking fashion with benzene rings of neighboring sheets.

Approximately 50% of a water molecule of crystallization is present for each molecule of tripeptide.

Introduction

As part of a continuing program of research on the structure of amino acids and peptides, Dégeilh and Pickworth (now Glusker) (1956) determined the unitcell dimensions, space groups and densities of six peptides. Of these, the tripeptide glycyl-phenylalanylglycine (GPG) was chosen as being the most advantageous subject for a complete structure determination.

Experimental

Dégeilh and Pickworth (1956) carried out preliminary crystallographic studies on GPG. They obtained crystals in the form of long, thin needles, elongated along c, by slow cooling of an aqueous solution of DL-glycyl-phenylalanyl-glycine, and reported the following unit-cell dimensions, space group, and density:

$$\begin{array}{c} a = 29 \cdot 72, \ b = 9 \cdot 98, \ c = 4 \cdot 90 \text{ Å} \\ (all \pm 0 \cdot 5 \%) \\ \varrho_{obs.} = 1 \cdot 334 \text{ g. cm.}^{-3} \\ \text{Space group, } P2_1 2_1 2_1 \ (D_2^4) \ . \end{array}$$

They reported the compound to be a monohydrate with four molecules of $GPG.H_2O$ in the unit cell.

The density calculated on the basis of four molecules of the monohydrate per unit cell is 1.36 ± 0.02 g. cm.⁻³, slightly larger than the observed value. During the course of the refinement of the structure it became evident that the actual amount of water of crystallization present corresponds to approximately 0.5 molecules per molecule of GPG, or two molecules per unit cell. On this basis the calculated density is 1.32 g. cm.⁻³, in somewhat better agreement with the observed value.

Since the space group $P2_12_12_1$ contains no symmetry operation of the second kind, resolution of the original DL-solution must have occurred during crystallization. We have not determined the absolute configurations of the molecules within the particular crystals we used; the parameters we have derived, when referred to a right-handed coordinate system, define the L configuration of the phenylalanine residue.

A preliminary set of multiple-film equi-inclination Weissenberg photographs about the c axis was prepared from a very thin crystal. The equator and first three layer lines were photographed with copper radiation and exposures of approximately 100 hours; even with exposures of this length, reflections could be observed only to $\sin \theta = 0.7$ (d = 1.1 Å). Later we were able to grow a somewhat larger crystal from which additional Weissenberg intensity photographs were prepared. The new hk0 and hk1 photographs were quite satisfactory and reflections were observed out to the edge of the film; the hk^2 photograph, however, was of poor quality due to partial decomposition of the crystal and no hk3 photograph was obtained. Subsequently it became impossible to grow any satisfactory crystals in this laboratory as the compound chose to crystallize in a different modification with the same space group and similar unit-cell dimensions but apparently containing two molecules of water of crystallization per molecule of tripeptide.*

$$a = 31 \cdot 49 \pm 0.04, \ b = 10 \cdot 15 \pm 0.02, \ c = 4 \cdot 838 \pm 0.007 \text{ A};$$

 $\rho_0 = 1.354 \pm 0.002 \text{ g.cm.}^{-3}.$

The density calculated on the basis of two water molecules per molecule of peptide is 1.353 ± 0.006 g.cm.⁻³.

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^{*} The unit-cell dimensions and density of this second modification, which was originally crystallized from ethanolwater solutions and later from aqueous solutions, were kindly measured by Dr E. L. Eichhorn. The values are:

Attempts to cleave the small crystals perpendicular to the needle axis were unsuccessful; nevertheless, some Weissenberg photographs were taken with needle crystals rotating about the b axis. Because of absorption effects—and, more important, because in certain orientations not all of the crystal was irradiated—the intensity data from these photographs were unreliable; they served mainly as an aid in correlating data obtained from the *c*-axis photographs.

Intensities were estimated visually and corrected for Lorentz and polarization effects. Altogether, 255 nonequivalent hk0 reflections were observed out of a total of 377 within the copper sphere, 314 hk1 reflections out of a possible 395, 190 hk2 reflections out of a possible 360, and 78 hk3 reflections out of a possible 314. In spite of these restrictions on the number of data available, it seemed worthwhile to pursue the structure determination of the compound.

Determination of the structure

A sharpened three-dimensional Patterson function, from which a spherical origin peak was subtracted, was calculated. The sharpening factor was modified by a function with a maximum at $\sin \theta = 0.5$ so that contributions from reflections with very high and low scattering angles were considerably reduced.

We first attempted a direct analysis of the Patterson map, concentrating particularly on vectors which might determine the positions of the benzene rings. The presence of a high peak along the line u=0, $v = \frac{1}{2}$ suggested that the benzene rings might be packed parallel to the b axis along the lines x=0 and $x=\frac{1}{2}$, and a large number of structures based on this principle were formulated and tested. Although some of the structures were quite close to the correct one, none could be refined. Attempts to determine the precise orientation of the benzene ring from the Patterson peaks near the origin were unsuccessful. Furthermore, the Harker section at $w = \frac{1}{2}$ could not be interpreted, as there were too many non-Harker peaks on or near this section. Finally, after many months of failure, attempts at a direct interpretation of the Patterson map were abandoned.

The key to the solution of the structure was the short c axis whose length of 4.9 Å is close to the value 4.85 Å predicted by Pauling and Corey (1953) for the distance between two polypeptide chains hydrogenbonded together in a parallel-chain pleated-sheet structure. As supporting evidence for a structure based on this configuration, there is a maximum in the Patterson function along the line u=v=0 which could be interpreted as the C-O interactions of the two carbonyl groups.

A model of GPG based on the parallel-chain pleatedsheet configuration was built with the backbone of the tripeptide chain extended in a direction perpendicular to c and with the planes of the two amide groups parallel to c. In such a configuration the length of the three amino-acid residues is nearly 10 Å (Pauling & Corey, 1953), which suggested that the molecule is extended in the *b* direction. The benzene ring of the phenylalanyl residue would then extend in the *a* direction.

These principles led to a satisfactory trial structure. Preliminary refinements of the x and y parameters were carried out on the basis of the hk0 data; approximate z parameters were derived from a consideration of the Patterson projection onto (010). An ambiguity concerning the orientation of the benzene ring was resolved and initial refinement of the z parameters was undertaken by a number of electron density projections onto (010). Attention was then turned to the three-dimensional data.

Refinement of the structure

All calculations were carried out on a Burroughs 205 digital computer, using a structure-factor least-squares

Table 1	1.	Calculated hydroger	n atom	coordinates
		$(B = 6 \text{ Å}^2)$		

		(= • • • • •		
Atom	Attached to	\boldsymbol{x}	\boldsymbol{y}	z
H_1	C ₂	0.1063	0.569	1.008
н,	$\tilde{C_2}$	0.1101	0.611	0.686
Н	Ň,	0.1254	0.786	1.118
$\mathbf{H}_{\mathbf{A}}$	C_{A}	0.1391	0.993	1.069
H_5	N ₂	0.1852	1.058	0.571
HÅ	C ₆	0.2768	1.133	0.804
Н,	C_{6}	0.2407	1.182	0.574
н	N_{2}	0.2708	1.364	0.745
н°	N_3	0.2663	1.320	1.030
H_{10}	N_3	0.2261	1.359	0.874
H_{11}	C ₇	0.1038	1.120	0.806
H_{19}	C_7	0.0976	1.062	0.557
H_{13}	C'a	0.0524	1.188	1.143
H_{14}	C_{10}	-0.0209	1.131	1.340
H_{15}^{11}	C11	-0.0601	0.945	1.178
H_{16}	C_{12}^{12}	-0.0299	0.814	0.822
H_{17}	$C_{13}^{}$	0.0446	0.868	0.631

 Table 2. Atomic coordinates

Atom	x	\boldsymbol{y}	z	$B~({ m \AA}^2)$
C,	0.1690	0.5447	0.850	4.7
C,	0.1254	0.6153	0.869	4.3
C ₃	0.1366	0.8492	0.755	4.4
C₄	0.1389	0.9941	0.866	$3 \cdot 8$
C_5	0.2100	1.1126	0.931	4.1
C ₆	0.2480	1.1810	0.772	$4 \cdot 2$
Č,	0.0989	1.0730	0.760	$4 \cdot 6$
C,	0.0543	1.0319	0.877	4.3
C	0.0353	1.1084	1.074	4.9
Cio	-0.0072	1.0757	1.191	$5 \cdot 8$
C11	-0.0300	0.9674	1.097	5.5
C_{10}	-0.0126	0.8940	0.892	5.4
C_{12}	0.0309	0.9236	0.779	$5 \cdot 2$
N,	0.1286	0.7560	0.946	$4 \cdot 0$
N,	0.1794	1.0553	0.752	4 ·0
N.	0.2532	1.3192	0.865	4.4
0,	0.2051	0.6071	0.881	$5 \cdot 0$
O,	0.1678	0.4228	0.787	6.1
0,	0.1432	0.8240	0.512	5.4
O₄	0.2064	1.1181	1.176	$6 \cdot 6$
0,	0.1276	0.3115	0.323	$7 \cdot 4$

Table 3. Observed and calculated structure factors

The five columns in each group contain the values, reading from left to right, of h, $10|F_0|$, $10|F_c|$, $10A_0$, and $10B_0$ Reflections indicated with an asterisk were given zero weight in the least-squares calculations

<u>b00</u>	<u>bł-0</u>		hol			<u>h7</u>	<u>n</u>	13 34	N 10 -38	116 174	193 -130 -	116 1		h92
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3 67 50 0 67 4 129 118 129 0 5 90 107 0 90	27 < 27 4 0 - 28 29 48 29 0 29 29 31 0 -20	5 < 25 9 0 6 40 51 -40 7 < 24 4 0	22 85 73 -2 85 23 89 76 69 -56 24 < 27 31 -	2 196 3 137 4 104	200 22 -194 163 -97 -97 101 9 104	7 54 59 8 26 21 9 36 46	-32 10 -14 -22	16 79 17 103 18 72	89 8 79 118 -94 -44 80 -44 57	6 57 7 < 47 8 < 47	66 33 33	-47	5 168 6 < 66 7 144	.69 -11 188 25 119 -10 -143
6 242 226 -242 0 7 213 203 0 -213 8 67 50 -67 0	30 47 50 47 0 31 23 28 0 23 32 <21 19 - 0	8 28 43 -28 9 27 35 0 2 10 70 71 -70	25 102 84 -63 81 26 35 41 -32 -16 27 58 51 31 49	5 74 6 81 7 95	68 45 59 77 78 20 72 -51 -80	10 35 36 11 32 34 12 <24 11	-28 22 -29 13	19 44 20 124 21 78	128 60 108 100 -6 -77	10 <48 11 116	31 - 95 -107		8 85 9 100 1 10 115 1	81 40 -75 107 6 100 129 -100 56
9 91 98 0 -91 10 146 128 146 0 11 < 20 0 0 -	33 23 28 0 -23 han	11 < 23 9 0 12 < 22 18 - 1 13 < 21 7 0	29 < 27 30 30 64 60 -36 53 31 28 31 -20 21	9 26	94 -94 -15 36 -23 -17 125 -39 -128	13 31 17 14 27 14 15 28 25	7 -24 -20 7 -26 15 -24	23 59	59 45 38 56 17 66	15 124 14 64 15 86	122 -102 41 37 84 82	69 -52 -28	11 91 1 12 75	.08 -50 76 26 -2 75
$12 \ 105 \ 102 \ 105 \ 0$ $13 < 21 \ 32 \ 0$ $14 \ 67 \ 50 \ -67 \ 0$	1 108 94 0 108	14 20 11 - 15 27 25 0 2 16 41 36 -41	32 39 35 28 -27 33 < 22 24 -	12 69 13 129	51 56 39 111 -74 -101	16 25 24 17 34 35 18 46 47	2 25 11 35 18 45	26 98 27 < 48	101 22 96	16 <48 17 48 18 <48	15 45 -28 16 -	-i-0	0 86	<u>h53</u> 50 0 -86
15 195 212 0 195 16 129 113 129 0 17 100 96 0 100 18 33 35 33 0	5 26 32 0 -26 4 129 114 -129 0 5 144 128 0 -144	17 24 15 0 -2 18 <15 6 - 19 <13 26 0	35 34 41 -31 -12 36 29 37 -28 8	15 150 16 39 17 81	100 -90 00 153 44 -145 26 7 -32 52 77 25	20 23 20 21 <16 16 22 26 16	-21 -10	20 11	b32		<u> 182</u>		1 141 1 2 113 1 3 101 1	.49 -57 -129 125 94 -62 143 99 -21
19 110 101 0 110 20 < 27 4 - 0 21 < 27 17 0 -	6 37 34 37 0 7 69 44 0 69 8 61 39 61 0	<u>h 12 0</u>	<u>h31</u>	18 39 19 <26 20 32	عراد 21 - 19 0ر ⊔- 62	<u>ь</u> п	1	0 293 1 189	293 0 -293 172 -187 -30	0 116 1 < 48	154 116 15 -	°,	4 113 1 5 146 1 6 < 74 7 < 74	55 80 80 48 55 155 51
22 < 28 14 - 0 23 84 82 0 84 24 98 91 -98 0	9 80 77 0 80 10 39 33 -39 0 11 83 77 0 -83	0 <20 16 - 1 <20 8 0 2 <20 0 -	1 193 196 193 0 2 92 113 91 9 3 219 198 199 190	21 104 22 112 23 70	85 26 -101 79 57 96 60 -70 3	0 <24 0	0 - -2 -38	2 169 3 175 4 230	160 20 168 151 23 -17 228 -219 72	3 42 4 < 48 5 99	45 41 42 - 118 -84	9	8 106 9 76 10 129 :	89 91 -55 32 76 -12 10 129 -6
26 < 30 26 - 0 27 77 54 0 77 28 54 55 54 0	13 122 117 0 -122 14 179 164 179 0 15 67 80 0 67	4 < 20 26 - 5 < 19 6 0	4 108 110 85 -68 5 307 318 -135 -276 6 359 354 352 -67	25 50 26 40 27 40	46 47 15 41 -38 -13 28 1 -39	3 < 24 7 4 < 23 6 5 < 23 20		6 110 7 128 8 202	158 5 110 117 -57 -115 176 -175 -100	6 < 48 7 < 48 8 42	10 - 44 - 42 7	42	ц 78 i	19 76 -18
29 < 28 10 0 - 30 < 27 11 - 0 31 43 34 0 -43	16 61 60 61 0 17 48 36 0 48 18 101 96 -101 0	7 21 32 0 -2 8 56 65 56 9 < 16 10 0	7 229 216 229 14 8 < 17 26 9 236 205 -133 -195	28 49 29 <21 30 <19	41 21 40 14	6 26 28 7 <22 8 8 25 24	-18 -18 -9 -24	9 165 10 370 11 132	166 -162 -32 395 -345 134 90 -102 -83	9 48 10 59 11 64	04 -13 72 13 54 64 54 40	47 -\$8 -1	0 95 1 ≼ 76	<u>nož</u> 74 -95 0
32 < 25 16 - 0 33 < 23 0 0 - 34 55 31 -35 0	19 < 30 9 0 - 20 < 29 21 - 0 21 < 29 31 0 -	10 26 25 -26 11 40 54 0 44 12 <14 16 - 0	10 50 59 50 -50 11 285 292 -217 -184 12 228 211 148 -173 13 265 258 36 269	31 36 32 × 15	19 19 31	9 <22 28 10 <21 19 11 <20 18		12 178 13 61 14 82	161 80 160 49 49 38 96 58 59	13 139 14 91 15 62	138 -138 96 -91 60 26	16 -2 57	2 164 1 3 < 78 4 78	.90 161 -31 71 75 -20
x x 16 19 - 0	23 < 27 14 0 -	1	14 116 105 -105 49	I		• LE 25 30		10 YU	ye -or -39	16 89	85 23	-86	5 < 78	22

program developed by Lavine and Rollett (1956) and a Fourier routine which calculates electron density at intervals of 1/38 or 1/76 of the unit cell. Four parameters for each atom-three positional coordinates and one isotropic temperature factor-were refined. Hydrogen parameters were calculated assuming tetrahedral or plane trigonal configurations and C-H and N-H distances of 1.0 and 0.9 Å, respectively; the hydrogen atoms of the terminal NH₃⁺ group were placed in a tetrahedral configuration such that the three N-H...O hydrogen bonds were, on the average, as linear as possible. The hydrogen atoms of the water molecule were not included. The calculated hydrogen parameters are listed in Table 1. These positions were checked on two- and three-dimensional maps and without exception fell on pronounced maxima.

During the course of refinement of the atomic parameters, approximately thirty cycles of structure-factor least-squares or structure-factor difference-map calculations were carried out, many of the cycles being based on data from only one or two layer lines. The primary reason for this inordinate number of cycles lay in the poor quality of the intensity photographs and especially in the lack of adequate data for reflections with high values of l; as a result, the rate of convergence of the z parameters was quite slow. An additional difficulty arose in the refinement of the parameters of the carbon and oxygen atoms of the two carbonyl groups; within each group the carbon and oxygen atoms have nearly the same x and yparameters and their z parameters differ by almost exactly $\frac{1}{4}$, and the coupling between the indicated parameter shifts of the two atoms in each pair was extensive. This difficulty, too, can be traced to the lack of satisfactory high-layer-line data.

A series of difference projections on to (001) calculated at an intermediate stage of the refinement indicated the presence of approximately one-half a water molecule per asymmetric unit; no further attempt was made to refine the compositional parameter of the water. The contributions of the hydrogen atoms were included at an early stage, but the hydrogen parameters were not adjusted by least-squares. The weighting function of Hughes (1941) was used for the least-squares adjustment of the positional and individual isotropic temperature factors of the heavy atoms; the hk3 data, as well as a few low-order reflections which were observed only on the hol Weissenberg photograph, were given an additional weight of $\frac{1}{2}$. Missing reflections were included in the least squares only if the calculated structure factor was greater than the minimum observable, in which case $\varDelta F$ was taken as the difference between the two quantities. Scale factors for the various layer lines were adjusted after every few cycles; since the data from the different layer lines were not well correlated, the individual scale factors undoubtedly compensate for thermal anisotropy in the c direction which, in view

of the geometry of the molecule, might be expected to be large.



Fig. 1. The final electron-density projection on (001). Contours are at intervals of 2 e.Å⁻²; the dashed line is the 1 e.Å⁻² contour.

The final positional and temperature-factor parameters for the twenty-one heavy atoms are given in Table 2; the observed and calculated structure factors are listed in Table 3. (The calculated values listed in Table 3 were obtained from the penultimate set of parameters which differed from the final ones by a maximum of 0.007 Å). An electron density projection on to (001), based on signs for the hk0 reflections calculated from the final parameters, is shown in Fig. 1.

Accuracy of the results

The R factors for the individual layer lines are listed in Table 4; the over-all factor for 885 reflections is 0·126. All observed reflections which were given nonzero weight in the least-squares treatment were included in the computation of the R factor; the unobserved reflections for which the calculated structure factor was greater than the threshold value were also included, the observed structure factor being set equal to the threshold value. The principal sources of error between calculated and observed structure factors are undoubtedly two-fold: (1) the poor quality of the data, particularly for the second and third layer lines; (2) the failure to compensate for anisotropic thermal effects.

Table 4.	Final	Rf	factors	for	the	individua	l layer	lines

l	R	ΣF_o	ΣF_{c}	n
0	0.112	3602	3658	276
1	0.119	3796	3901	331
2	0.123	2242	2241	196
3	0.202	942	917	82
All	0.126	10582	10717	885

The standard deviations in the positional parameters were calculated from the residuals and diagonal elements of the normal equations of the least-squares procedure; they range from 0.006 to 0.010 Å for the x and y parameters and from 0.013 to 0.022 Å for the z parameters of the atoms in the tripeptide molecule. The standard deviations in the x, y, and z parameters of the oxygen atom of the water molecule are 0.015, 0.016, and 0.033 Å, respectively. It seems appropriate, then, to quote standard deviations of about 0.02 Å in the bond distances and 1.5° in the bond angles; for reasons discussed earlier, it seems likely that the uncertainties in the distances involving the carbon and oxygen atoms of the carbonyl groups are somewhat larger.

The calculated standard deviations in the temperature-factor parameters *B* range from 0.14 to 0.24 Å² for the atoms in the main molecule; it is 0.42 Å² for the oxygen atom of the water molecule.

Discussion of the structure

(i) Bond distances and angles

The bond distances and angles calculated from the parameters in Table 2 are shown in Fig. 2 and listed in Table 5. The equations for the best planes of the carboxyl group, of the two peptide groups, and of the benzene ring are given in Table 6, together with the deviations of the individual atoms from these best planes. None of these deviations is significant.

In view of the relatively large uncertainties in the atomic parameters, it is probably not fruitful to undertake a detailed discussion of the individual bond distances and angles. In general, the values are in good agreement with those found in analogous compounds. The average of the five single-bond C-C distances is 1.51 Å, which is smaller than the value 1.54 usually assigned to a C-C single bond but close to the average values found in leucyl-prolyl-glycine (Leung & Marsh, 1958) and in various amino acids (see Donohue & Trueblood, 1952). The average C-C distance within the benzene ring is 1.38 Å, which is

Dista	nce	Angle	
C ₁ -C ₂	1·48 Å	0,-C,-O,	122°
C ₂ -C	1.55	$O_1 - C_1 - C_2$	120
$C_{5} - C_{e}$	1.53	$O_{9} - C_{1} - C_{9}$	117
C ₄ -C ₇	1.52	$C_{1} - C_{2} - N_{1}$	115
$C_7 - C_8$	1.50	$C_{2} - N_{1} - C_{3}$	120
		$N_1 - C_3 - O_3$	124
$C_{g}-C_{g}$	1.35	$N_1 - C_3 - C_4$	114
$C_{9} - C_{10}$	1.42	$O_3 - C_3 - C_4$	122
$C_{10} - \tilde{C}_{11}$	1.36	$C_3 - C_4 - C_7$	109
$C_{11} - C_{12}$	1.35	$C_{3} - C_{4} - N_{2}$	107
$C_{12}^{}-C_{13}^{}$	1.44	$C_7 - C_4 - N_2$	107
C ₁₃ -C ₈	1.37	$C_{4} - N_{2} - C_{5}$	118
		$N_{2} - C_{5} - O_{4}$	126
$C_2 - N_1$	1.46	$N_2 - C_5 - C_6$	110
$C_4 - N_2$	1.46	$O_4 - C_5 - C_6$	123
$C_6 - N_3$	1.46	$C_{5} - C_{6} - N_{3}$	110
		$C_4 - C_7 - C_8$	115
$N_1 - C_3$	1.34	$C_7 - C_8 - C_9$	119
$N_{2} - C_{5}$	1.39	$C_7 - C_8 - C_{13}$	122
		$C_{8} - C_{9} - C_{10}$	122
C ₁ -O ₁	1.25	$C_{9} - C_{10} - C_{11}$	119
$C_{1} - O_{2}$	1.26	$C_{10} - C_{11} - C_{12}$	120
-		$C_{11} - C_{12} - C_{13}$	121
C ₃ -O ₃	1.23	$C_{12} - C_{13} - C_{8}$	119
$\tilde{C_5}-O_4$	1.21	$C_{13} - C_8 - C_9$	119



Fig. 2. The bond distances (a) and bond angles (b).

close to the accepted value of 1.39 Å. With the exception of the N₂-C₅ distance, which appears to be about 0.07 Å longer than usual, the distances within the peptide and carboxyl groups are close to the expected values (Pauling & Corey, 1953); the surprising length of the N₂-C₅ bond is, we feel, an artifact associated with the difficulty discussed earlier in positioning the carbon and oxygen atoms of the peptide groups. Additional evidence that the parameters of the atoms in the N-terminal peptide group are especially poorly determined is furnished by the small value of the N₂-C₅-C₆ bond angle and the general lack of coplanarity of the five atoms (Table 6).

(ii) Intermolecular packing

The most important result of this structure inves-



Fig. 3. Drawings showing the pleated-sheet arrangement of GPG molecules. (a) Portions of three molecules viewed at an angle of 15° from the c axis. (b) A single molecule viewed down c. (c) Three molecules viewed along a.

tigation is, we feel, the observation that the parallelchain pleated sheet configuration of a polypeptide

Table 6. Best planes through various groups of atoms							
The equations of the planes are expressed in the form $A(a_0x) + B(b_0y) + C(c_0z) = D$, where D is the origin-to-plane distance							
Plane	Atom	Devia- tion	A	В	C	D	
Carboxyl group	$\begin{array}{c} \mathbf{C_1}\\ \mathbf{C_2}\\ \mathbf{O_1}\\ \mathbf{O_2} \end{array}$	$ \begin{array}{r} 0.020 \\ -0.006 \\ -0.007 \\ -0.007 \end{array} $	Å -0.032	-0.224	0.974	0.121	
Phe-gly peptide group	$\begin{smallmatrix} \mathbf{C_2} \\ \mathbf{C_3} \\ \mathbf{C_4} \\ \mathbf{N_1} \\ \mathbf{O_3} \end{smallmatrix}$	$ \begin{array}{c} -0.004 \\ -0.011 \\ 0.000 \\ 0.009 \\ 0.006 \end{array} $	0.980	-0.102	0.169	3.941	
Gly-phe peptide group	$\substack{\substack{\mathrm{C}_4\\\mathrm{C}_5\\\mathrm{C}_6\\\mathrm{N}_2\\\mathrm{O}_4}}$	$\begin{array}{c} 0{\cdot}025\\ -\ 0{\cdot}034\\ 0{\cdot}027\\ -\ 0{\cdot}025\\ 0{\cdot}006\end{array}$	0.503	0.863	-0.051	- 2.119	
Benzene ring	$C_{7} C_{8} C_{9} C_{10} C_{11} C_{12} C_{13}$	$\begin{array}{c} 0.011 \\ - 0.024 \\ 0.012 \\ - 0.002 \\ - 0.009 \\ 0.021 \\ - 0.010 \end{array}$	0.448	- 0.578	0.682	2.324	
						•	

chain occurs in crystals of a simple peptide. This configuration was first formulated by Pauling & Corey (1951), who later (Pauling & Corey, 1953) modified the atomic parameters and, on the basis of the close agreement between the predicted repeat distance along the polypeptide chain and the observed fiber-axis identity distances in the β -keratin proteins, suggested that it may be the basic structural feature of these proteins. In glycyl-phenylalanyl-glycine we now find direct evidence of the stability of this configuration.

Views of the pleated sheet structure of GPG are shown in Fig. 3. The dimensions of the two-residue fragment occurring in GPG differ somewhat from

those proposed by Pauling and Corey (1953) for the parallel-chain pleated sheet. The distance between C2 and C₆, which corresponds to the repeat distance in the pleated sheet configuration, is 6.74 Å compared with the proposed value of 6.50 Å; the distance between adjacent chains within the sheet (the c-axis identity distance) is 4.90 Å compared with the proposed value 4.85 Å, and the dihedral angle at C₄ between the chains of the two peptide groups is $126 \cdot 2^{\circ}$ compared with $117 \cdot 8^{\circ}$. Thus, the peptide chain in GPG is slightly more extended than in the parallelchain pleated sheet configuration; this extension, which causes some distortion of the N-H...O hydrogen bonds between chains, might easily be accounted for by considering other intermolecular forces, particularly those involving the terminal groups.

Besides the N-H ... O hydrogen bonds between peptide groups of adjacent molecules, there is a network of hydrogen bonds between the terminal NH₃+ group and the carboxylate ions of adjacent molecules; this network is shown in Fig. 4. The distances and angles involving the hydrogen bonds are listed in Table 7; these values are similar to those found in other peptides and amino acids (see, for example, Fuller, 1959).

The water molecule, when present, is surrounded

Table 7. Hydrogen-bond dis	stances ana	angies
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$N_1 \cdots O_3$	2·89 Å	$\substack{\mathbf{C_2-N_1}\cdots\mathbf{O_3}\\\mathbf{C_3-N_1}\cdots\mathbf{O_3}}$	119° 119
$N_2 \cdots O_4$	3 ·00	$\substack{\mathrm{C_4-N_2}\cdots\mathrm{O_4}\\\mathrm{C_5-N_2}\cdots\mathrm{O_4}}$	$\begin{array}{c} 132\\110\end{array}$
$\begin{array}{c} \mathrm{N}_3 \cdots \mathrm{O}_1 \\ \mathrm{N}_3 \cdots \mathrm{O}_1 \\ \mathrm{N}_3 \cdots \mathrm{O}_2 \end{array}$	2·78 2·91 2·77	$\begin{array}{c} C_6-N_3\cdots O_1\\ C_6-N_3\cdots O_1'\\ C_6-N_3\cdots O_2\\ O_1\cdots N_3\cdots O_1'\\ O_1\cdots N_3\cdots O_2\\ O_1'\cdots N_3\cdots O_2\\ O_1'\cdots N_3\cdots O_2 \end{array}$	124 92 102 119 101 115
$\begin{array}{c} \mathbf{O}_{w} \cdots \mathbf{O}_{2} \\ \mathbf{O}_{w} \cdots \mathbf{O}_{2}' \\ \mathbf{O}_{w} \cdots \mathbf{O}_{4} \end{array}$	2·80 3·09 3·12	$O_2 \cdots O_w \cdots O_2' O_2 \cdots O_w \cdots O_4 O_2' \cdots O_w \cdots O_4$	113 97 75



Fig. 4. A drawing of the structure viewed along the c axis.

by three oxygen atoms at distances of 3.12 Å or less. On the basis of the interatomic distances and angles in Table 7, there is little evidence for deciding which two of the three $H_2O \ldots O$ distances represent hydrogen bond interactions; nor did the difference maps, which contained background due to uncompensated temperature motions, decide the question. We believe that the negative charge on atom O_2 would tend to make it a significantly better hydrogen-bond acceptor than O_4 , and that accordingly the water molecule probably forms hydrogen bonds to the two neighboring O_2 atoms rather than to O_4 . As is the case in the crystal structure of leucyl-prolyl-glycine (Leung & Marsh, 1958), the principal role of the water molecules appears to be one of filling space. None of the $H_2O...O$ distances is very short and the water molecule is not important in hydrogen bonding the tripeptide molecules together. It is hardly surprising, then, that the structure is stable with only half the water sites occupied.

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