bonding interactions. The packing is spatially efficient, since there are five intermolecular contacts within the range 3·30–3·39 Å.

References

CHAMBERS, D. & DENNY, W. A. (1986). *J. Chem. Soc. Perkin Trans.* 1, pp. 1055–1060. (Note the acid 18a in this paper is incorrectly named as a 6-, and not a 7-nitroquinoxaline.)

DENNY, W. A. & WILSON, W. R. (1986). *J. Med. Chem.* **29**, 879–887.

Enraf–Nonius (1981). *Structure Determination Package* . Enraf–Nonius, Delft, The Netherlands.

International Tables for X-ray Crystallography (1974). Vol. IV, pp. 99, 149. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

SHELDRICK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1986). *SHELXS86*. Program for crystal structure determination. Univ. of Göttingen, Federal Republic of Germany.

Acta Cryst. (1989). C**45**, 1944–1948

Structure of *cyclo*(-L-Prolylglycyl-)$_2$ Trihydrate

BY G. SHOHAM

Department of Inorganic and Analytical Chemistry, The Hebrew University of Jerusalem, Jerusalem, 94013 Israel

S. K. BURLEY

Gibbs Chemical Laboratory, Department of Chemistry, Harvard University, Cambridge, MA 02138, *USA and Department of Medicine, Brigham and Women's Hospital, 75 Francis Street, Boston, MA* 02115, *USA*

AND W. N. LIPSCOMB*

Gibbs Chemical Laboratory, Department of Chemistry, Harvard University, Cambridge, MA 02138, *USA*

(*Received* 23 *December* 1988; *accepted* 31 *March* 1989)

Abstract. $(C_{14}H_{20}N_4O_4)_2.3H_2O$, $M_r = 670{\cdot}721$, monoclinic, $P2_1$, $a = 7{\cdot}353$ (2), $b = 21{\cdot}921$ (7), $c = 9{\cdot}878$ (2) Å, $\beta = 96{\cdot}77$ (2)°, $V = 1581{\cdot}1$ (1) Å^3, $Z = 2$, $D_x = 1{\cdot}409$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 8{\cdot}22$ cm^{-1}, $F(000) = 716$, $T = 293$ K, $R = 0{\cdot}034$ for 2456 unique observed reflections. The two independent copies of the tetrapeptide found in the asymmetric unit have similar structures, which are both consistent with the results of NMR studies of *cyclo*-(-L-Pro-Gly-)$_2$ in solution. The structures are asymmetric and have a *trans–cis–trans–cis* peptide backbone, in which the two L-Pro-Gly peptide bonds are *trans* and the two Gly-L-Pro peptide bonds are *cis*. A detailed comparison with other cyclic tetrapeptides is given, and a brief comparison with the results of single-crystal X-ray structures of other cyclic oligopeptides containing L-proline alternating with glycine is presented.

Introduction. The amino acids L-proline and glycine are known to play central roles in determining protein secondary structure, and there has been considerable interest in oligopeptides bearing these two residues. Of particular note are cyclic peptides composed of L-proline alternating with glycine, and single-crystal structures of *c*(*cyclo*)(-L-Pro-Gly-) (Von Dreele, 1975). *c*(-L-Pro-Gly-)$_3$ (Kartha, Varughese & Aimoto, 1982) and *c*(-L-Pro-Gly-)$_4$ (Chiu, Brown & Lipscomb, 1977) have been described. We report here a crystal structure containing the cyclic tetrapeptide *c*(-L-Pro-Gly-)$_2$ in two crystallographically independent environments. Both molecules resemble the conformation detected in solution by NMR (Deber, Fossel & Blout, 1974). The structural parameters are compared with those obtained from studies of other cyclic tetrapeptides, and of cyclic hexa- and octapeptides that are composed of L-proline alternating with glycine.

Experimental. Asymmetric crystal from slow evaporation from an equivolume solution of H_2O and dioxane, 0·5 × 0·5 × 1·0 mm, Nicolet $P2_1$ diffractometer, graphite monochromator, Cu $K\alpha$ radiation, $\theta/2\theta$ method, $\sin\theta/\lambda < 0{\cdot}56169$ Å^{-1}, lattice parameters determined from 2θ values of 50 reflections (25 Friedel pairs) with $30 < 2\theta < 50°$, empirical absorption correction (range 1·00 to 0·78) (North, Phillips & Mathews, 1968), h −8 to 8, k 0 to 24, l 0 to 11,

* Address correspondence to this author.

0108-2701/89/121944-05$03.00

reflections 311, 06$\bar{1}$ and 004 as intensity standards, intensity variation < 8%, linear decay correction 6%. 3326 independent reflections measured, 870 excluded during refinement [$|F_o| < 2\sigma(|F_o|)$]. Structure solved by direct methods using *SHELXS*86 (Sheldrick, 1985), first *E* map revealed the positions of all of the non-H atoms comprising the two oligopeptides and of two water molecules of crystallization, and a third water of crystallization was detected during refinement; least-squares refinement, $|F|$ magnitudes, isotropic then anisotropic temperature factors with unit weights using *SHELX*76 (Sheldrick, 1976), gave $R = 0{\cdot}034$, $wR = 0{\cdot}034$ and $S = 0{\cdot}62$ with H atoms at positions calculated or located by difference synthesis. 498 parameters varied: x,y,z, and U_{ij} for all non-H atoms, and a U for each of the H atoms, which were allowed to 'ride' on the corresponding non-H atom at calculated positions with ideal X—H bond lengths (C—H = 1·08, N—H = 0·98, O—H = 0·965 Å). In the final refinement cycle $(\Delta/\sigma)_{max} = 0{\cdot}37$, $(\Delta/\sigma)_{mean} = 0{\cdot}01$. Final difference synthesis gave $\Delta\rho_{max} = 0{\cdot}14$ and $\Delta\rho_{min} = -0{\cdot}15$ e Å^{-3}. Scattering factors from *International Tables for X-ray Crystallography* (1974). R.m.s. calculations were made using the algorithm of Kabsch (1976, 1978), and all non-H atoms were included in the calculations.

Table 1. *Final positional parameters* ($\times 10^4$) *and equivalent isoptropic temperature factors* (Å^2) *of the non-*H *atoms with e.s.d.'s in parentheses*

$$B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}
Molecule (1)				
N_1	2780 (4)	−4667 (1)	2349 (3)	2·82
C_1^α	1386 (5)	−4182 (2)	2161 (3)	2·68
C_1^β	−156 (5)	−4478 (2)	1192 (4)	3·65
C_1^γ	23 (6)	−5156 (2)	1520 (5)	4·50
C_1^δ	2074 (6)	−5255 (2)	1763 (4)	3·94
C_1	627 (5)	−3953 (2)	3425 (4)	2·68
O_1	−73 (4)	−3440 (1)	3415 (3)	3·36
N_2	629 (4)	−4331 (2)	4494 (3)	2·77
C_2^α	−201 (5)	−4168 (2)	5701 (3)	3·25
C_2	948 (5)	−4343 (2)	7029 (4)	3·15
O_2	274 (4)	−4651 (2)	7884 (3)	4·15
N_3	2668 (4)	−4132 (2)	7270 (3)	3·05
C_3^α	3592 (5)	−3708 (2)	6428 (4)	2·94
C_3^β	5085 (6)	−3424 (2)	7469 (4)	3·93
C_3^γ	5570 (6)	−3933 (2)	8490 (4)	3·98
C_3^δ	3753 (6)	−4262 (2)	8597 (4)	4·07
C_3	4466 (5)	−4037 (2)	5310 (4)	2·65
O_3	5101 (3)	−4561 (1)	5451 (3)	3·28
N_4	4537 (4)	−3718	4164 (3)	2·79
C_4^α	5371 (5)	−3963 (2)	3018 (4)	2·96
C_4	4623 (5)	−4573 (2)	2483 (4)	2·91
O_4	5684 (4)	−4960 (1)	2173 (3)	3·91
Molecule (2)				
N_5	941 (4)	−2354 (1)	867 (3)	2·69
C_5^α	24 (5)	−1768 (2)	1010 (3)	2·70
C_5^β	−1566 (5)	−1787 (2)	−144 (4)	3·28
C_5^γ	−2079 (5)	−2456 (2)	−240 (4)	3·70
C_5^δ	−270 (5)	−2797 (2)	46 (4)	3·30
C_5	−761 (5)	−1681 (2)	2368 (4)	2·90
O_5	−1367 (4)	−1175 (1)	2609 (3)	4·26
N_6	−760 (4)	−2161 (2)	3207 (3)	2·77
C_6^α	−1593 (5)	−2145 (2)	4473 (4)	3·40
C_6	−353 (5)	−2229 (2)	5809 (4)	3·32
O_6	−907 (4)	−2542 (2)	6689 (3)	5·51
N_7	1235 (4)	−1919 (2)	6045 (3)	3·20
C_7^α	2146 (5)	−1550 (2)	5097 (4)	3·04
C_7^β	3634 (6)	−1213 (2)	6033 (4)	4·26
C_7^γ	4154 (6)	−1672 (3)	7149 (4)	4·62
C_7^δ	2347 (6)	−1962 (2)	7393 (4)	4·42
C_7	2992 (5)	−1949 (2)	4073 (4)	2·69
O_7	3342 (4)	−2490 (1)	4286 (3)	3·57
N_8	3348 (4)	−1663 (2)	2944 (3)	2·78
C_8^α	4044 (5)	−1997 (2)	1840 (4)	3·18
C_8	2747 (5)	−2473 (2)	1116 (3)	2·80
O_8	3409 (4)	−2950 (1)	746 (3)	3·80
Water molecules of crystallization				
O(*W*1)	7196 (4)	−5374 (1)	7349 (3)	4·47
O(*W*2)	5984 (6)	−5778 (2)	9924 (4)	6·49
O(*W*3)	2333 (5)	−5500 (2)	5205 (3)	4·67

Discussion. The amino-acid residues have been numbered such that residues 1 to 4 comprise the first (1) copy of *c*(-L-Pro-Gly-)$_2$ and 5 to 8 the second (2). Positional parameters and equivalent isotropic temperature factors for all non-H atoms are given in Table 1.* The conformations of the two crystallographically independent *c*(-L-Pro-Gly-)$_2$ molecules are illustrated in Figs. 1(*a*) and 1(*b*), respectively. The standard IUPAC–IUB Commission on Biochemical Nomenclature (1970) numbering system for amino acids was used, and the α-C atoms are labeled accordingly in the *ORTEP*II (Johnson, 1976) stereodrawings. Bond lengths and angles for the non-H atoms of the two cyclic tetrapeptides are given in Tables 2 and 3. There are no significant differences from the corresponding average values for polypeptides given in Benedetti (1982) and Momany, McGuire, Burgess & Scheraga (1975). The backbone and side-chain torsion angles are in Table 4.

The conformation that molecule (1) adopts is not symmetric. There are no intramolecular hydrogen bonds, and, hence, no β turns in the structure, which are typical of larger cyclic oligopeptides (Benedetti, 1982). The peptide bond directions alternate between *cis* and *trans* to give the 'crownlike' *trans–cis–trans–cis* conformation typical of cyclic tetrapeptides (Karle, 1982). The two L-Pro-Gly peptide bonds adopt the *trans* conformation and the two Gly-L-Pro peptide bonds adopt the *cis* conformation. The L-Pro 1 ψ_1 angle is nearly *cis* and the L-Pro 3 ψ_3 angle is nearly *trans* (IUPAC–IUB Commission on Biochemical Nomenclature, 1970). These data are consistent with the structural model for the solution conformation of *c*(-L-Pro-Gly-)$_2$ determined by NMR (Deber *et al.*, 1974). Three of the four peptide bonds are very close to planar with a maximum deviation from planarity of 5·0° for ω_1, but the fourth peptide bond differs substantially from planarity ($\omega_4 = -25{\cdot}1°$) because of crystal-packing effects.

* Lists of structure-factor amplitudes, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52122 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Molecule (2) does not differ substantially from molecule (1), and their similarity is readily apparent in the stereodrawing illustrated in Fig. 2. The r.m.s. difference between the two structures is 0·40 Å, with deviations of up to 0·7 Å occurring within the proline side chains. Molecule (2) is asymmetric, and contains no intramolecular hydrogen bonds. Again, the directions of the peptide bonds alternate to give the characteristic 'crownlike' *trans–cis–trans–cis* pattern, with the ψ angles of L-Pro 5 and L-Pro 7 being nearly *cis* and *trans*, respectively. The most remarkable difference between the two crystallographically independent conformations of *c*(-L-Pro-Gly-)$_2$ concerns the degree of strain, which is imposed both by the requirement of ring closure and by the molecular environment. Unlike molecule (1), which is strained and has one peptide bond that differs by 25·1° from planarity, all of the peptide bonds of molecule (2) lie within 10·7° of planarity. Such a small range of deviations from planarity is common (Kolaskar, Lakshminarayanan, Sarathy & Sasisekharan, 1975), and is consistent with energy increases due to strain of only about 2 kJ mol^{-1} or less for each peptide bond (Benedetti, 1982).

The crystal structure of these two crystallographically independent copies of *c*(-L-Pro-Gly-)$_2$ with three water molecules of crystallization is illustrated in Fig. 3 and the hydrogen-bond data are given in Table 5. Molecules (1) and (2) lie with their rings nearly parallel to one another and to the *xz* plane, and are related by translations of about 0·64, 5·22 and 0·85 Å along the *x*, *y* and *z* axes, respectively. Two intermolecular hydrogen bonds between molecules (1) and (2) result [N_4—H···O_7 = 2·840 (7), N_6—H···O_1 = 2·851 (7) Å]. The remaining hydrogen bonds involve the three water molecules of crystallization, which occur as sheets of water molecules, lying parallel to the *xz* plane, that separate pairs of hydrogen-bonded cyclic tetrapeptides. All ten available hydrogen-bond donors participate in hydrogen bonds, but only ten of the 22 oxygen lone pairs act as acceptors in hydrogen bonds and there are no

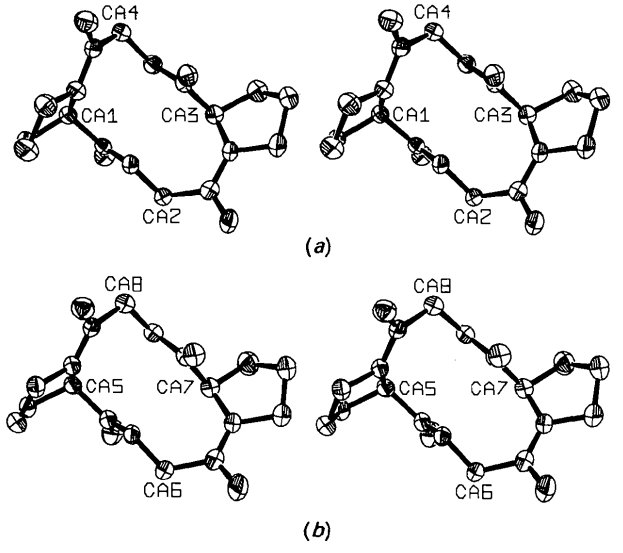

Fig. 1. Stereoscopic views of the two crystallographically independent copies of *c*(-L-Pro-Gly-)$_2$ perpendicular to their peptide rings with the thermal ellipses drawn at the 50% probability level. The α-C atoms are labelled according to the standard IUPAC–IUB numbering system. (*a*) Molecule (1). (*b*) Molecule (2).

Table 2. *Bond lengths* (Å) *of the two crystallographically independent* *c*(-L-Pro-Gly-)$_2$ *molecules with e.s.d.'s given in parentheses*

Molecule (1)	i^a = 1 (L-Pro)	2 (Gly)	3 (L-Pro)	4 (Gly)	Average	Literature
$N_iC_i^\alpha$	1·474 (5)	1·447 (5)	1·467 (5)	1·452 (5)	1·460	1·449
$C_i^\alpha C_i$	1·511 (5)	1·522 (5)	1·524 (5)	1·516 (5)	1·519	1·522
C_iO_i	1·238 (5)	1·231 (5)	1·241 (5)	1·217 (5)	1·232	1·229
N_iC_{i-1}	1·361 (5)	1·342 (5)	1·341 (5)	1·337 (5)	1·345	1·335
$C_i^\alpha C_i^\beta$	1·539 (5)		1·545 (5)		1·542	1·520
$C_i^\beta C_i^\gamma$	1·525 (7)		1·518 (6)		1·522	1·520
$C_i^\gamma C_i^\delta$	1·514 (6)		1·532 (6)		1·523	1·520
$C_i^\delta N_i$	1·484 (5)		1·482 (5)		1·483	1·460
Molecule (2)	i^b = 5 (L-Pro)	6 (Gly)	7 (L-Pro)	8 (Gly)	Average	Literature
$N_iC_i^\alpha$	1·466 (5)	1·457 (5)	1·457 (5)	1·456 (5)	1·459	1·449
$C_i^\alpha C_i$	1·532 (5)	1·522 (5)	1·523 (5)	1·532 (5)	1·527	1·522
C_iO_i	1·229 (5)	1·213 (5)	1·227 (5)	1·227 (5)	1·224	1·229
N_iC_{i-1}	1·347 (5)	1·340 (5)	1·349 (5)	1·332 (5)	1·342	1·335
$C_i^\alpha C_i^\beta$	1·535 (5)		1·536 (6)		1·536	1·520
$C_i^\beta C_i^\gamma$	1·513 (6)		1·508 (6)		1·511	1·520
$C_i^\gamma C_i^\delta$	1·523 (6)		1·519 (6)		1·521	1·520
$C_i^\delta N_i$	1·490 (5)		1·480 (5)		1·485	1·460

Notes: (*a*) When $i = 1$, $i-1 = 4$. (*b*) When $i = 5$, $i-1 = 8$.

Table 3. *Bond angles* (°) *of the two crystallographically independent* *c*(L-Pro-Gly-)$_2$ *molecules with e.s.d.'s given in parentheses*

Molecule (1)	i^a = 1 (L-Pro)	2 (Gly)	3 (L-Pro)	4 (Gly)	Average	Literature
$C_{i-1}N_iC_i^\alpha$	124·9 (3)	122·3 (3)	127·4 (3)	121·9 (3)	124·1	121·9
$N_iC_i^\alpha C_i$	116·9 (3)	113·7 (3)	111·9 (3)	115·3 (3)	114·4	111·1
$C_i^\alpha C_iO_i$	119·2 (3)	120·1 (3)	122·8 (3)	119·0 (3)	120·3	120·4
$C_i^\alpha C_iN_{i+1}$	118·7 (3)	118·8 (3)	115·3 (3)	118·9 (3)	117·9	116·6
$O_iC_iN_{i+1}$	121·9 (3)	120·9 (3)	121·8 (3)	122·0 (3)	121·7	122·9
$N_iC_i^\alpha C_i^\beta$	103·0 (3)		102·6 (3)		102·8	105·0
$C_i^\alpha C_i^\beta C_i^\gamma$	103·9 (3)		103·8 (3)		103·9	106·6
$C_i^\beta C_i^\gamma C_i^\delta$	103·5 (3)		104·7 (3)		104·1	106·3
$C_i^\gamma C_i^\delta N_i$	103·5 (3)		103·3 (5)		103·4	103·2
$C_i^\delta N_iC_{i-1}$	117·9 (3)		119·4 (3)		118·7	126·0
$C_i^\beta C_i^\alpha C_i$	109·6 (3)		110·2 (3)		109·9	113·0
Molecule (2)	i^b = 5 (L-Pro)	6 (Gly)	7 (L-Pro)	8 (Gly)	Average	Literature
$C_{i-1}N_iC_i^\alpha$	127·3 (3)	122·9 (3)	128·5 (3)	120·7 (3)	124·9	121·9
$N_iC_i^\alpha C_i$	114·8 (3)	118·2 (3)	111·3 (3)	116·0 (3)	115·1	111·1
$C_i^\alpha C_iO_i$	117·8 (3)	118.2 (3)	122·3 (3)	118·2 (3)	119·1	120·4
$C_i^\alpha C_iN_{i+1}$	118·1 (3)	120·5 (3)	115·0 (3)	120·0 (3)	118·4	116·6
$O_iC_iN_{i+1}$	124·1 (3)	121·1 (3)	122·7 (3)	121·8 (3)	122·5	122·9
$N_iC_i^\alpha C_i^\beta$	102·9 (3)		103·2 (3)		103·1	105·0
$C_i^\alpha C_i^\beta C_i^\gamma$	103·6 (3)		102·8 (3)		103·2	106·6
$C_i^\beta C_i^\gamma C_i^\delta$	104·9 (3)		104·1 (3)		104·5	106·3
$C_i^\gamma C_i^\delta N_i$	103·6 (3)		103·4 (5)		103·5	103·2
$C_i^\delta N_iC_{i-1}$	119·2 (3)		119·9 (3)		119·6	126·0
$C_i^\beta C_i^\alpha C_i$	108·7 (3)		111·0 (3)		109·9	113·0

Notes: (*a*) When $i = 1$, $i-1 = 4$, and when $i = 4$, $i+1 = 1$. (*b*) When $i = 5$, $i-1 = 8$, and when $i = 8$, $i+1 = 5$.

Table 4. *Torsion angles (°) of the two crystallographically independent c(-L-Pro-Gly-)$_2$ molecules*

$\varphi_i = C_{i-1}N_iC_i^{\alpha}C_i$, $\psi = N_iC_i^{\alpha}C_iN_{i+1}$, $\omega_i = C_i^{\alpha}C_iN_{i+1}C_{i+1}^{\alpha}$, $\chi^0{}_i = C_i^{\delta}N_iC_i^{\alpha}C_i^{\beta}$, $\chi^1{}_i = N_iC_i^{\alpha}C_i^{\beta}C_i^{\gamma}$, $\chi^2{}_i = C_i^{\alpha}C_i^{\beta}C_i^{\gamma}C_i^{\delta}$, $\chi^3{}_i = C_i^{\beta}C_i^{\gamma}C_i^{\delta}N_i$, $\chi^4{}_i = C_i^{\gamma}C_i^{\delta}N_iC_i^{\alpha}$.

Molecule (1)

	i^a = 1 (L-Pro)	2 (Gly)	3 (L-Pro)	4 (Gly)
φ_i	−95·6	−137·1	−86·2	55·0
ψ_i	−26·7	56·5	149·0	42·6
ω_i	−175·0	4·2	178·4	25·1
$\chi^0{}_i$	−9·4		−16·2	
$\chi^1{}_i$	29·0		31·6	
$\chi^2{}_i$	−38·2		−35·9	
$\chi^3{}_i$	31·8		25·6	
$\chi^4{}_i$	−14·1		−5·6	

Molecule (2)

	i^b = 5 (L-Pro)	6 (Gly)	7 (L-Pro)	8 (Gly)
φ_i	−96·0	−116·5	−72·7	65·0
ψ_i	−8·5	46·7	160·4	38·9
ω_i	−175·3	−9·6	−175·9	−10·7
$\chi^0{}_i$	−18·4		−15·6	
$\chi^1{}_i$	33·2		33·3	
$\chi^2{}_i$	−36·3		−39·0	
$\chi^3{}_i$	24·8		29·4	
$\chi^4{}_i$	−3·6		−8·3	

c(-L-Ala-L-Pro-D-Phe-L-Pro-)[c]

	i^a = 1 (L-Pro)	2 (L-Ala)	3 (L-Pro)	4 (D-Phe)
φ_i	−99	−131	−86	60
ψ_i	3	38	159	46
ω_i	−177	7	−176	7
$\chi^0{}_i$	−24		−15	
$\chi^1{}_i$	36		33	
$\chi^2{}_i$	−37		−35	
$\chi^3{}_i$	23		29	
$\chi^4{}_i$	1		−9	

Notes: (*a*) When $i = 1$, $i - 1 = 4$, and when $i = 4$, $i + 1 = 1$. (*b*) When $i = 5$, $i - 1 = 8$, and when $i = 8$, $i + 1 = 5$. (*c*) Adapted from Chiang & Karle (1982). The side-chain torsion angles for the residues 2 and 4 were omitted for the sake of clarity.

bifurcated hydrogen bonds. Both Fig. 3 and Table 5 demonstrate that the environments of molecules (1) and (2) differ substantially from one another, and these differences are probably responsible for the degree of strain observed in molecule (1). All four carbonyl O atoms of molecule (1) act as hydrogen-bond acceptors, but only the carbonyl O atoms of the two L-Pro residues in molecule (2) participate in hydrogen bonds. Failure to make all possible hydrogen bonds is not uncommon in single-crystal structures of peptides (Karle, 1978).

The two conformations of c(-L-Pro-Gly-)$_2$ we report are very similar to one another despite their different crystal environments. In addition, they both resemble the NMR structure of the compound in solution (Deber *et al.*, 1974). Studies of c(-L-Pro-Gly-)$_3$ (Kartha *et al.*, 1982) demonstrated that this structure is not symmetric and, like c(-L-Pro-Gly-)$_2$, has no β turns or internal hydrogen bonds, which are characteristic of cyclic hexapeptides (Karle, 1981). In this case, ring closure is effected with minimal strain using only one peptide bond in the *cis* conformation. The cyclic octapeptide c(-L-Pro-Gly-)$_4$ has been examined in chloroform solution (Madison, Deber & Blout, 1977) and in the crystalline state complexed with rubidium (Chiu *et al.*, 1977). Unlike the homologous cyclic tetra- and hexapeptides, the 24-membered ring is made up solely of *trans* peptide units.

Finally, it is also useful to compare c(-L-pro-Gly-)$_2$ with other cyclic tetrapeptides. This class of molecules has been extensively reviewed by Karle (1982), who developed a geometric classification scheme for the cyclic tetrapeptides. c(-L-Pro-Gly-)$_2$ is of type III$_3$, which is defined to be an asymmetric ring with the peptide bonds alternating from *cis* to *trans* and the carbonyl O atoms directed ↓↓↓↑. Chiang & Karle (1982) reported the structure of a similar compound c(-L-Ala-L-Pro-D-Phe-L-Pro-) that was the first example of a type III$_3$ cyclic tetrapeptide detected crystallographically. The backbone torsion angles for c(-L-Ala-L-Pro-D-Phe-L-Pro-) are similar to those of molecule (1) and very similar to those of molecule (2)

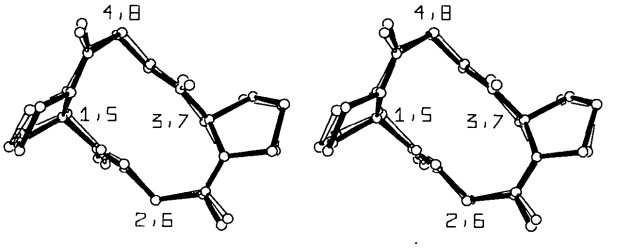

Fig. 2. A stereoscopic view of molecule (1) (shaded bonds) superimposed on molecule 2 (open bonds).

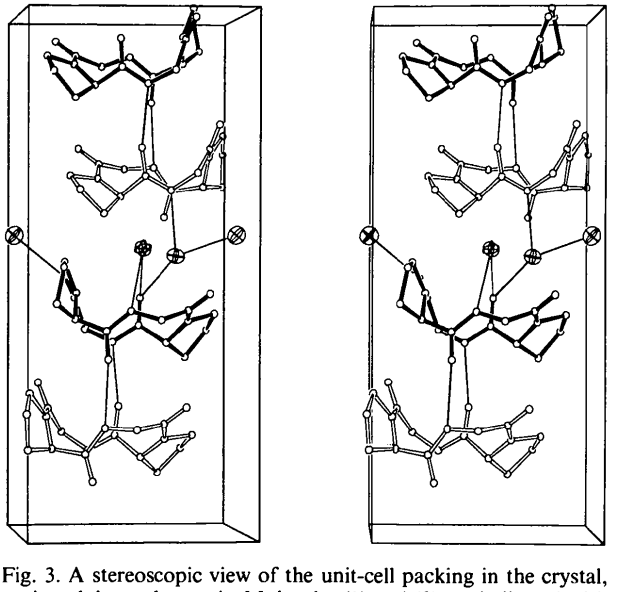

Fig. 3. A stereoscopic view of the unit-cell packing in the crystal, viewed down the *a* axis. Molecules (1) and (2) are indicated with shaded bonds and open bonds, respectively. Water molecules of crystallization are represented by thermal ellipses drawn at the 50% probability level. Hydrogen bonds are indicated by a thin solid line connecting the two non-H atoms.

Table 5. *Hydrogen-bond data with e.s.d.'s given in parentheses*

Donor	Acceptor		Donor	Acceptor	
N_2···H	O(*W*3)	2·902 (7) Å	O(*W*1)···H	O_2	2·762 (7) Å
N_4···H	O_7	2·840 (7)	O(*W*1)···H	O_3	2·895 (7)
N_6···H	O_1	2·851 (7)	O(*W*2)···H	O_4	2·873 (7)
N_8···H	O(*W*1)	2·863 (7)	O(*W*2)···H	O(*W*1)	2·935 (7)
			O(*W*3)···H	O_3	2·885 (7)
			O(*W*3)···H	O_5	2·778 (7)

(see Table 4). These similarities are borne out by the calculated r.m.s. differences between *c*(-L-Ala-L-Pro-D-Phe-L-Pro-) and molecules (1) and (2), which are 0·34 and 0·16 Å, respectively.

We thank Drs C. M. Deber, V. Olsher and E. R. Blout for supplying the sample. This work was supported by the National Science Foundation (grants CHE-8210536 and PCM-77-11398 awarded to WNL) and the National Institutes of Health (grant GM-06920 awarded to WNL). In addition, SKB thanks the Medical Foundation Inc. for research support, and GS thanks the Bat-Sheva Foundation of Israel for general financial support. Finally, we thank Referee IV, who noted the similarity between the title compound and *c*(-L-Pro-L-Ala-L-Pro-D-Phe-).

References

BENEDETTI, E. (1982). *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins* 6, edited by B. WEINSTEIN, pp. 105–184. New York: Marcel Dekker.

CHIANG, C. C. & KARLE, I. L. (1982). *Int. J. Pept. Protein Res.* **20**, 133–138.

CHIU, Y. H., BROWN, L. D. & LIPSCOMB, W. N. (1977). *J. Am. Chem. Soc.* **99**, 4799–4803.

DEBER, C. M., FOSSEL, E. T. & BLOUT, E. R. (1974). *J. Am. Chem. Soc.* **96**, 4015–4017.

International Tables for X-ray Crystallography (1974) Vol. IV, pp. 72–72. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

IUPAC–IUB COMMISSION ON BIOCHEMICAL NOMENCLATURE (1970). *J. Mol. Biol.* **52**, 1–17.

JOHNSON, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

KABSCH, W. (1976). *Acta Cryst.* A**32**, 922–923.

KABSCH, W. (1978). *Acta Cryst.* A**34**, 827–828.

KARLE, I. L. (1978). *Int. J. Quantum Chem. Quantum Biol. Symp.* **5**, 91–101.

KARLE, I. L. (1981). *Peptides*, **4**, 1–53.

KARLE, I. L. (1982). *Molecular Structure and Biological Activity*, edited by J. F. GRIFFIN & W. L. DUAX, pp. 215–227. New York: Elsevier North-Holland.

KARTHA, G., VARUGHESE, K. I. & AIMOTO, S. (1982). *Proc. Natl Acad. Sci. USA*, **79**, 4519–4522.

KOLASKAR, A. S., LAKSHMINARAYANAN, A. V., SARATHY, K. P. & SASISEKHARAN, V. (1975). *Biopolymers*, **14**, 1081–1094.

MADISON, V., DEBER, C. M. & BLOUT, E. R. (1977). *J. Am. Chem. Soc.* **99**, 4788–4798.

MOMANY, F. A., MCGUIRE, R. F., BURGESS, A. W. & SCHERAGA, H. A. (1975). *J. Phys. Chem.* **79**, 2361–2374.

NORTH, A. C. T., PHILLIPS, D. C. & MATHEWS, F. S. (1968). *Acta Cryst.* A**24**, 351–359.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

SHELDRICK, G. M. (1985). *SHELXS*86. In *Crystallographic Computing* 3, edited by G. M. SHELDRICK, C. KRÜGER & R. GODDARD, pp. 175–189. Oxford Univ. Press.

VON DREELE, R. B. (1975). *Acta Cryst.* B**31**, 966–970.

Acta Cryst. (1989). C**45**, 1948–1951

Structure Cristalline de (*p*-Chlorophényl)-3 [(Diméthyl-4,6 pyridyl-2) méthyl]-4 Diphényl-4,6 Oxo-2 Tétrahydro-1,2,3,4 Triazine-1,3,5

PAR BERNARD VIOSSAT

Laboratoire de Chimie Générale, UFR de Médecine et de Pharmacie, 34, Rue du Jardin des Plantes, F-86034 Poitiers CEDEX, France

NGUYEN-HUY DUNG

Laboratoire de Physique (Laboratoire de Chimie Minérale Structurale associé au CNRS UA 200), Faculté des Sciences Pharmaceutiques et Biologiques de Paris V, 4, Avenue de l'Observatoire, F-75270 Paris CEDEX 06, France

ET PAUL-LOUIS COMPAGNON ET TAN KIMNY

Laboratoire de Chimie Organique et Pharmacie Chimique, Université de Bourgogne, Faculté de Pharmacie, 7, Boulevard Jeanne d'Arc, F-21100 Dijon, France

(*Reçu le* 13 *juillet* 1988, *accepté le* 20 *mars* 1989)

Abstract. $C_{29}H_{25}ClN_4O$, $M_r = 481·0$, monoclinic, $P2_1/n$, $a = 21·63$ (1), $b = 8·072$ (7), $c = 15·46$ (1) Å, $\beta = 108·57$ (6)°, $V = 2558·7$ (3) Å^3, $Z = 4$, $D_m = 1·27$ (2), $D_x = 1·25$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 0·183$ mm^{-1}, $F(000) = 1008$, room temperature, $R = 0·072$ for 1008 independent reflections [$I >$

0108-2701/89/121948-04$03.00