

Further refinement of the structure of L-leucyl-L-prolylglycine.* By RICHARD E. MARSH, *Arthur Amos Noyes Laboratory of Chemical Physics, California Institute of Technology, Pasadena, California 91125, USA*

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Abstract

Further least-squares refinement of the structure of L-leucyl-L-prolylglycine, based on the original visually estimated set of intensities [Leung & Marsh (1958). *Acta Cryst.* 11, 17–31], has led to a reduction in R from 0.129 to 0.055 and to small changes (up to 0.04 Å) in the atomic coordinates. Disorder in the pyrrolidine ring and partial occupancy of the site of the water molecule of crystallization have been confirmed.

Introduction

L-Leucyl-L-prolylglycine was the first tripeptide to be studied by three-dimensional X-ray diffraction analysis (Leung & Marsh, 1958) (LM). Intensities were estimated visually from Weissenberg photographs and the structure was solved by Patterson methods; atomic coordinates were refined through three cycles of diagonal least squares, and the anisotropic B 's were adjusted from difference maps (Leung, Marsh & Schomaker, 1957). (This was in the early days of digital computing: a structure-factor least-squares cycle took about 8 h of computing time, and a three-dimensional Fourier summation about 30 h.) The final R was 0.129 for 1697 observed reflections, and standard deviations in the bond lengths were estimated at about 0.015 Å. Perhaps for no reason other than nostalgia I thought it worthwhile to find out how much the structure would be improved by using today's refinement techniques based on the original, visual data. While the improvement in R – from 0.129 to 0.055 – was large and the e.s.d.'s were reduced by a factor of about 3, the description of the structure has changed in only minor ways.

Experimental

Crystals of L-leucyl-L-prolylglycine 'mono'-hydrate, $C_{13}H_{23}N_3O_4 \cdot \sim 1H_2O$, are monoclinic space group $P2_1$, with $a = 9.442$ (2), $b = 6.724$ (1), $c = 12.105$ (1) Å, $\beta = 100^\circ 11' (2)$ (LM). Starting parameters and observed F 's were taken from Tables 1, 3, 4, and 5 of LM, and an initial set of F_c 's closely matched the earlier values ($R = 0.126$ compared to 0.129). At this time, and once later on during the refinement, a few dozen reflections showing relatively poor agreement were checked against the original photographs and notebooks. Fourteen errors were found: eight

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mistakes in indexing, three numerical blunders, one error in transcription, and in two cases the intensity was underestimated because of α_1 – α_2 splitting. As a result, ten intensities were changed and four were assigned weights of zero. Refinement was by least-squares minimization of $\sum w(F_o^2 - F_c^2)^2$ with $w^{-1} = F_o^4$ if $F_o \geq 6.0$ and $w^{-1} = 36F_o^2$ if $F_o \leq 6.0$. [This is analogous to Hughes's (1941) weighting scheme for refinement on F rather than F^2 , as used by LM.] Included in the parameter list were a scale factor, an extinction parameter (Larson, 1967), and population factors for the partially occupied water site O(5) and for the disordered atom C(6) of the pyrrolidine ring. All parameters of the C, N, and O atoms, plus the scale, extinction, and population factors, were included in one matrix; later in the refinement, the coordinates and isotropic B 's for 19 H atoms were adjusted in a second matrix, difference maps having confirmed the approximate positions given by LM. The H atoms attached to C(5), C(6), and C(7) were placed in two sets of calculated positions as indicated by the disorder, and were not adjusted. At a late refinement stage, when C(5) showed relatively large anisotropy and unreasonable geometry, it was presumed to accompany C(6) in disorder and it, too, was split into two sites; since the sites were quite close together (about 0.5 Å), the B 's were taken as isotropic. This

Table 1. Coordinates ($\times 10^4$) and B_{eq} values (Hamilton, 1959) of the C, N, and O atoms

	x	y	z	B_{eq} (Å ²)
C(1)	875 (3)	4933 (6)	8371 (2)	2.9 (1)
C(2)	1700 (3)	5129 (6)	7413 (2)	3.0 (1)
C(3)	2023 (3)	3486 (6)	5694 (2)	3.0 (1)
C(4)	1582 (4)	1717 (6)	4918 (2)	3.1 (1)
C(5) ^(a)	2208 (9)	–271 (10)	5300 (5)	2.8 (1)
C(5) ^(b)	2735 (14)	–19 (14)	5404 (7)	2.9 (2)
C(6) ^(a)	3560 (9)	–316 (16)	4784 (8)	4.1 (2)
C(6) ^(b)	2983 (15)	–1118 (16)	4358 (8)	3.4 (2)
C(7)	3153 (4)	684 (6)	3623 (3)	3.6 (1)
C(8)	1372 (3)	3471 (6)	3142 (2)	2.7 (1)
C(9)	1946 (3)	3810 (6)	2053 (2)	2.7 (1)
C(10)	3221 (4)	5259 (6)	2256 (2)	3.3 (1)
C(11)	4226 (4)	5202 (7)	1392 (2)	3.8 (1)
C(12)	5055 (5)	3251 (10)	1478 (4)	5.3 (1)
C(13)	5267 (5)	6947 (9)	1592 (4)	5.4 (1)
N(1)	1324 (3)	3599 (6)	6563 (2)	3.0 (1)
N(2)	1994 (3)	2047 (5)	3821 (2)	2.9 (1)
N(3)	737 (3)	4622 (6)	1224 (2)	2.9 (1)
O(1)	–50 (3)	3601 (6)	8337 (2)	4.7 (1)
O(2)	1156 (2)	6206 (–)*	9138 (2)	3.4 (1)
O(3)	2977 (3)	4630 (6)	5558 (2)	4.2 (1)
O(4)	396 (2)	4528 (5)	3368 (2)	3.4 (1)
O(5) ^(c)	2158 (4)	9799 (8)	424 (3)	4.6 (1)

Notes: (a) Site population factor = 0.59 (2). (b) Site population factor = 0.41. (c) Site population factor = 0.72 (1).

* Not refined.

model led to small but obviously significant improvements in R and the goodness-of-fit (GOF).

The final R was 0.055 and the GOF 0.115 for 1717 reflections and 276 parameters, compared with 0.129 and 0.310 for the LM model. (Since the weights are on an arbitrary scale, the absolute values of the GOF are without significance.) Included in the total number of reflections are 23 unobserved ones whose calculated F values exceeded the reported threshold, by a maximum of 30%. A final difference map showed features ranging up to $0.3 \text{ e } \text{Å}^{-3}$, mostly in the regions expected for valence electrons. Values of the residual $\sqrt{w(F_o^2 - F_c^2)}$ seemed to be distributed quite evenly through the data. Final parameters are given in Table 1;* atom labelling is shown in Fig. 1.

Discussion

The largest changes from the parameters of LM were in the anisotropic B 's, the scale factor [final value, 0.958 (5)], and the extinction parameter [$28.3 (5.2) \times 10^{-6}$], which was not included by LM. These parameters are, of course, correlated. The extinction parameter probably reflects, as much as anything, systematic errors in estimating strong intensities and in scaling multiple-film photographs together. Except for the disordered atoms C(5) and C(6), no coordinate changed by more than 0.04 Å , which is less than three times the standard deviation estimated by LM.

Bond lengths and angles are listed in Table 2, together with the LM values. In light of the new values, a few conclusions drawn by LM should be altered:

- (1) There is no discernible alternation in the lengths of the C—C bonds in the leucine side chain;
- (2) The C(9)—C(10)—C(11) bond angle, at 116° , is not as 'surprising' as the 118° reported by LM;

* Lists of structure factors, thermal parameters and coordinates of the H atoms have been deposited with the British Library Lending Division as Supplementary Publications No. SUP 35029 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

(3) The difference in the two C(1)—O bond lengths, although too small to be of much significance, is now in the appropriate direction to be compatible with the hydrogen bonding: O(2), which forms the longer covalent bond, accepts three hydrogen bonds while O(1) accepts only two (LM, Table 9).

The occupancy factor for the water molecule O(5) ended at 0.716 (11) rather than the 0.80 proposed by LM; the distribution of C(6) [and, in this study, C(5)] between its two sites was 0.59 (2) for C(6'), C(5'), and 0.41 for C(6''), C(5'') rather than the 50/50 distribution assumed by LM. The minor (41%) contributor corresponds to an 'envelope' conformation of the pyrrolidine ring with C(6''), the flap, displaced by 0.70 Å from the plane of C(4), C(5''), C(7), and N(2); this is a common conformation for proline residues in linear peptides (Marsh & Donohue, 1967). The major contributor shows a conformation similar to that found in a number of cyclic dipeptides (Ramani, Venkatesan, Marsh & Kung, 1976), with the flap atom C(5') displaced by 0.55 Å from the plane of C(4), C(6'), C(7), and N(2); however, these latter four atoms show deviations of about

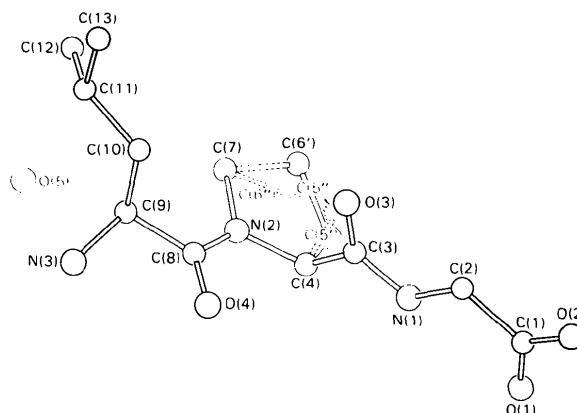


Fig. 1. The L-leucyl-L-prolylglycine molecule, with the numbering scheme used here and by LM.

Table 2. Bond distances (Å) and angles ($^\circ$)

	This work	LM (1958)		This work	LM (1958)		This work	LM (1958)
C(1)—C(2)	1.513 (5)	1.512	C(8)—C(9)	1.528 (5)	1.499	C(2)—N(1)	1.453 (5)	1.454
C(3)—C(4)	1.527 (5)	1.519	C(9)—C(10)	1.534 (5)	1.542	C(7)—N(2)	1.479 (5)	1.458
C(4)—C(5')	1.501 (8)	1.497	C(10)—C(11)	1.532 (5)	1.515	C(4)—N(2)	1.465 (4)	1.452
C(4)—C(5'')	1.634 (11)		C(11)—C(12)	1.522 (6)	1.510	C(9)—N(3)	1.485 (4)	1.492
C(5')—C(6')	1.518 (12)	1.517	C(11)—C(13)	1.523 (6)	1.511	C(1)—O(1)	1.246 (5)	1.262
C(5'')—C(6'')	1.519 (15)	1.507				C(1)—O(2)	1.257 (4)	1.247
C(6')—C(7)	1.545 (10)	1.527	C(3)—N(1)	1.340 (5)	1.314	C(3)—O(3)	1.217 (5)	1.236
C(6'')—C(7)	1.529 (12)	1.480	C(8)—N(2)	1.329 (4)	1.339	C(8)—O(4)	1.232 (4)	1.272
O(1)—C(1)—O(2)	124.7 (3)	125.4	C(4)—C(5'')—C(6'')	103.8 (8)	107.8	N(2)—C(8)—O(4)	123.0 (3)	122.4
O(1)—C(1)—C(2)	119.3 (3)	118.2	C(5')—C(6')—C(7)	105.9 (7)	104.2	N(2)—C(8)—C(9)	117.1 (3)	118.6
O(2)—C(1)—C(2)	115.9 (3)	116.4	C(5'')—C(6'')—C(7)	98.5 (8)	107.1	O(4)—C(8)—C(9)	119.9 (3)	118.9
C(1)—C(2)—N(1)	112.8 (3)	114.5	C(6')—C(7)—N(2)	101.2 (4)	103.6	C(8)—C(9)—N(3)	106.9 (3)	107.9
C(2)—N(1)—C(3)	120.2 (3)	122.2	C(6'')—C(7)—N(2)	103.9 (5)	103.2	C(8)—C(9)—C(10)	110.1 (3)	111.6
N(1)—C(3)—O(3)	123.3 (3)	123.2	C(4)—N(2)—C(7)	112.1 (3)	113.3	N(3)—C(9)—C(10)	111.3 (3)	111.6
N(1)—C(3)—C(4)	114.1 (3)	115.3	C(4)—N(2)—C(8)	120.6 (3)	120.6	C(9)—C(10)—C(11)	116.0 (3)	117.9
O(3)—C(3)—C(4)	122.5 (3)	121.4	C(7)—N(2)—C(8)	127.2 (3)	126.1	C(10)—C(11)—C(12)	110.4 (3)	110.6
C(3)—C(4)—C(5')	117.0 (4)	113.3	N(2)—C(4)—C(5')	105.1 (4)	103.7	C(10)—C(11)—C(13)	109.4 (3)	109.4
C(3)—C(4)—C(5'')	104.0 (4)		N(2)—C(4)—C(5'')	99.6 (4)		C(12)—C(11)—C(13)	110.1 (4)	109.9
C(4)—C(5')—C(6')	101.8 (6)	105.9	C(3)—C(4)—N(2)	110.6 (3)	111.2			

Table 3. *Torsion angles for the two conformations of the pyrrolidine ring*

	Major (59%) conformation	Minor (41%) conformation
$N-C_{\alpha}-C_{\beta}-C_{\gamma}^*$	32.0 (6) ^o	-30.3 (7) ^o
$C_{\alpha}-C_{\beta}-C_{\gamma}-C_{\delta}$	-37.6 (7)	45.0 (8)
$C_{\beta}-C_{\gamma}-C_{\delta}-N$	28.0 (6)	-43.2 (7)
$C_{\gamma}-C_{\delta}-N-C_{\alpha}$	-7.8 (5)	25.8 (6)
$C_{\delta}-N-C_{\alpha}-C_{\beta}$	-15.8 (4)	2.6 (5)

* N = N(2); C_α = C(4); C_β = C(5'), C(5''); C_γ = C(6'), C(6''); C_δ = C(7).

0.04 Å from their mean plane, so the envelope is somewhat crumpled. Torsion angles for the two conformations are given in Table 3. These descriptions of the ring conformations should be taken with a bit of skepticism, for some of the distances and angles (Table 2) are unusual enough to suggest that the model of twofold static disorder may not be entirely appropriate.

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Liaisons hydrogène dans les complexes de métal(III) tris(éthylènediamine). Par ANNICK WHULER, CATHERINE BROUTY et PIERRE SPINAT, *Laboratoire de Minéralogie-Cristallographie, Associé au CNRS, Université Pierre et Marie Curie, Tour 16, 4 place Jussieu, 75230 Paris CEDEX 05, France*

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Abstract

The characteristics of the hydrogen bonds observed in crystals of tris(ethylenediamine)metal(III) complexes $[M(en)_3]X_3 \cdot nH_2O$ ($M = Co^{3+}, Cr^{3+}, Rh^{3+}; X = Cl^-, Br^-, I^-, SCN^-$) have been established from the compilation of structural results of 14 compounds. Histograms have been drawn for the types of bonds which present sufficient data.

Introduction

En général, les données cristallographiques concernant les liaisons hydrogène portent sur des liaisons du type O—H...O. Or l'étude structurale systématique entreprise sur les complexes tris(éthylènediamine) $[M(en)_3]X_3 \cdot nH_2O$ a permis de compiler un nombre important d'informations sur des liaisons hydrogène de types N—H...B ($B = Cl, N, S, Br,$

Tableau 1. *Nature des liaisons hydrogène dans les cristaux de complexes de métal(III) tris(éthylènediamine)*

Complexes de type	Liaisons hydrogène observées	Références
$[M(en)_3]Cl_3 \cdot nH_2O$	N—H...Cl	Iwata, Nakatsu & Saito (1969) Whuler, Brouty, Spinat & Herpin (1975, 1976a,b,c, 1977) Whuler, Brouty & Spinat (1978) Whuler, Spinat & Brouty (1978)
	N—H...O	
	O—H...O	
	O—H...Cl	
$[M(en)_3](SCN)_3 \cdot nH_2O$	N—H...N	Brouty, Spinat, Whuler & Herpin (1976, 1977a,b) Brouty, Whuler, Spinat & Herpin (1977) Brouty, Spinat & Whuler (1977, 1978)
	N—H...S	
	N—H...O	
	O—H...S	
$[M(en)_3]Br_3 \cdot nH_2O$	N—H...Br	Spinat, Whuler & Brouty (1979)
	N—H...O	
$[M(en)_3]I_3 \cdot nH_2O$	N—H...I	Alcock, de Meester & Kemp (1978) Whuler, Spinat & Brouty (1980)
	N—H...O	
	O—H...I	