Acta Cryst. (1978). B34, 3447–3449

N-Benzyloxycarbonyl-glycyl-L-prolyl-L-leucyl-glycyl-L-proline Dihydrate

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(*Received* 11 *April* 1978; *accepted* 4 *July* 1978)

Abstract. $C_{28}H_{39}N_5O_8.2H_2O$, monoclinic, $P2_1$, a = 15·999 (1), b = 7·557 (1), c = 13·792 (1) Å, β = 100·86 (1)°, Z = 2, D_x = 1·232, D_m = 1·230 g cm^{-3}. This synthetic peptide, which has a substrate specificity for an enzyme collagenase, is folded into a typical 3_{10} conformation with proline and leucine at the corners.

Introduction. The intensity data of the title compound (Z-GPLGP) were obtained on a Rigaku automatic diffractometer. The $2\theta_{max}$ was 130° (Cu $K\alpha$), and 2906 reflections were collected. The crystal size was 0·1 × 0·1 × 0·3 mm.

The structure was solved by the vector space search method with the program *RICS* written by I. Tanaka, followed by the tangent formula method to refine the phase angles. The 3_{10} conformation of the peptide backbone was utilized as a rigid group, because this conformation was found in both *p*-bromobenzyloxycarbonyl-glycyl-L-prolyl-L-leucyl-glycine [Z(*p*-Br)-GPLG] (Ueki, Ashida, Kakudo, Sasada & Katsube, 1969) and *o*-bromobenzyloxycarbonyl-glycyl-L-prolyl-L-leucyl-glycyl-L-proline [Z(*o*-Br)-GPLGP] (Ueki, Bando, Ashida & Kakudo, 1971). Thus, 30 of the 43 non-hydrogen atoms were located in the E map. Successive structure factor–Fourier calculations showed clearly all the non-hydrogen atoms. The positions of the H atoms except two bonded to C^{γ} of Pro(1) were found in a difference Fourier synthesis. The structure was refined by a block-diagonal least-squares method and the final R index was 0·064. The weighting scheme was: for $|F_o| \neq 0$, $w = [\sigma(F_o)^2 + 0{\cdot}25|F_o| + 0{\cdot}004(F_o)^2]^{-1}$, and for $|F_o| = 0$, $w = 0{\cdot}34$. The final parameters are listed in Tables 1 and 2.†

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† Lists of structure factors and anisotropic temperature factors have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33745 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *The positional parameters of the non-hydrogen atoms* (×10⁴) *with their e.s.d.'s in parentheses*

	x	*y*	*z*		*x*	*y*	*z*
O(1)	3509 (2)	2841 (5)	3866 (2)	C(8)	3827 (3)	4016 (7)	4588 (3)
O(2)	4558 (2)	4498 (7)	4774 (3)	C(9)	3415 (3)	5707 (7)	5893 (3)
O(3)	3675 (2)	3014 (5)	6856 (2)	C(10)	3647 (3)	4649 (7)	6850 (3)
O(4)	3632 (2)	2195 (6)	9513 (3)	C(11)	4070 (3)	4655 (7)	8651 (3)
O(5)	899 (3)	465 (9)	7781 (3)	C(12)	4225 (6)	6181 (9)	9388 (4)
O(6)	1649 (2)	2811 (5)	5303 (2)	C(13)	4146 (9)	7805 (12)	8838 (6)
O(7)	500 (2)	3646 (6)	2731 (3)	C(14)	3753 (3)	7492 (7)	7813 (4)
O(8)	−84 (2)	2024 (7)	3771 (3)	C(15)	3417 (3)	3354 (7)	8908 (3)
O(9)	3843 (3)	−42 (6)	5791 (3)	C(16)	1905 (3)	2493 (8)	8653 (3)
O(10)	1695 (2)	5450 (6)	6719 (3)	C(17)	1182 (3)	3617 (9)	8917 (4)
N(1)	3203 (2)	4605 (7)	5034 (3)	C(18)	1422 (4)	4718 (11)	9839 (4)
N(2)	3795 (2)	5553 (6)	7697 (2)	C(19)	1620 (6)	3524 (18)	10760 (5)
N(3)	2593 (2)	3608 (6)	8467 (2)	C(20)	701 (6)	5933 (17)	9966 (8)
N(4)	2023 (2)	1138 (6)	7080 (3)	C(21)	1565 (3)	1280 (8)	7788 (3)
N(5)	1464 (2)	313 (6)	4417 (3)	C(22)	1780 (3)	68 (7)	6199 (3)
C(1)	3562 (4)	635 (10)	1774 (4)	C(23)	1624 (2)	1174 (7)	5272 (3)
C(2)	3270 (5)	−823 (13)	1229 (4)	C(24)	1323 (3)	1270 (7)	3488 (3)
C(3)	3195 (5)	−2396 (11)	1665 (5)	C(25)	1244 (4)	−175 (9)	2706 (4)
C(4)	3430 (7)	−2581 (11)	2662 (6)	C(26)	974 (6)	−1790 (10)	3200 (4)
C(5)	3719 (6)	−1118 (12)	3216 (4)	C(27)	1398 (4)	−1623 (8)	4284 (4)
C(6)	3796 (3)	507 (9)	2784 (3)	C(28)	496 (3)	2325 (7)	3356 (3)
C(7)	4174 (4)	2048 (11)	3404 (5)				

Discussion. The bond distances and angles are shown in Fig. 1, and the arrangement of the molecules in the crystal viewed down the *b* axis is shown in Fig. 2.

The present pentapeptide and its bromine derivative are hydrolyzed to Z-GPL-OH and H-GP-OH by collagenase, while the tetrapeptide, for instance Z(*p*-Br)-GPLG, is not. The sequence -Pro-*X*-Gly-Pro- (*X*; an arbitrary amino acid residue) is an intrinsic requirement for the specificity to collagenase. Although these oligopeptides have differences in their biochemical behavior, they have a common partial structure at the Pro(1) and Leu residues, namely the 3_{10} conformation. It is difficult to confirm the differences in their reactivity, attributed to their molecular structures, as Ueki *et al.* (1971) mentioned for Z(*o*-Br)-GPLGP, but the presence of a water molecule in the crystal is noteworthy. The 3_{10} conformation of the present peptide seems to be further stabilized by the three hydrogen bonds, one between NH of Gly(1) and CO of Gly(2) and two *via* a water molecule. Such a hydrogen-bonding system in the molecule is similar to that found in Z(*o*-Br)-GPLGP (Fig. 3), in spite of the difference in crystal packing. On the other hand, there is no water molecule in Z(*p*-Br)-GPLG (Fig. 3), so the peptide has only one hydrogen bond. The water molecule may play a certain role in allowing the peptide bond between Leu and Gly(2) to be susceptible to collagenase. However, the necessity that the fifth residue be proline cannot yet be substantiated.

The authors wish to express their sincere thanks to Dr Shumpei Sakakibara for kindly supplying this peptide.

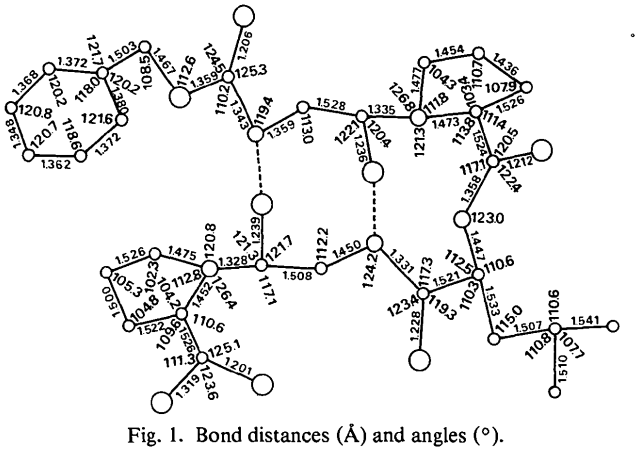

Fig. 1. Bond distances (Å) and angles (°).

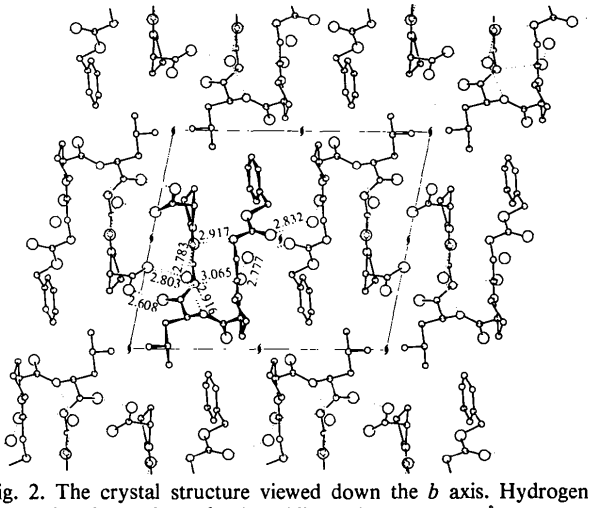

Fig. 2. The crystal structure viewed down the *b* axis. Hydrogen bonds are shown by dotted lines with distances (Å).

Table 2. *The positional parameters of the hydrogen atoms* ($\times 10^3$)

	x	*y*	*z*	Bonded to		*x*	*y*	*z*	Bonded to
H(1)	363	170	144	C(1)	H(22)	182	437	1124	C(19)
H(2)	298	−59	48	C(2)	H(23)	236	337	1051	C(19)
H(3)	290	−339	127	C(3)	H(24)	−16	498	−6	C(20)
H(4)	322	−395	312	C(4)	H(25)	84	688	974	C(20)
H(5)	399	−112	401	C(5)	H(26)	93	691	1054	C(20)
H(6)	430	302	291	C(7)	H(27)	243	169	709	N(4)
H(7)	473	193	389	C(7)	H(28)	143	−52	629	C(22)
H(8)	275	410	491	N(1)	H(29)	221	−78	620	C(22)
H(9)	289	647	595	C(9)	H(30)	183	210	350	C(24)
H(10)	387	652	591	C(9)	H(31)	77	16	202	C(25)
H(11)	455	400	859	C(11)	H(32)	184	−56	264	C(25)
H(12)	363	617	964	C(12)	H(33)	17	−177	332	C(26)
H(13)	472	604	999	C(12)	H(34)	112	−308	299	C(26)
H(14)	315	808	780	C(14)	H(35)	93	−215	475	C(27)
H(15)	403	818	737	C(14)	H(36)	214	−216	427	C(27)
H(16)	252	437	813	N(3)	H(37)	22	341	263	O(7)
H(17)	215	171	923	C(16)	H(38)	378	95	602	O(9)
H(18)	65	295	893	C(17)	H(39)	444	−4	599	O(9)
H(19)	91	443	835	C(17)	H(40)	117	587	671	O(10)
H(20)	200	531	977	C(18)	H(41)	160	55	626	O(10)
H(21)	109	279	1096	C(19)					

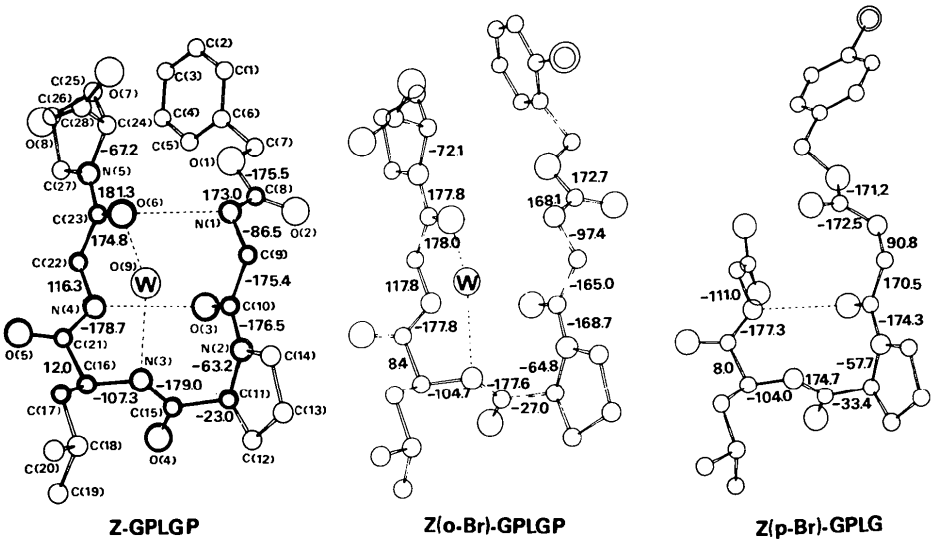

Fig. 3. Twisting angles (°) of the peptide chains. The convention is that defined by the IUPAC–IUB Commission on Biochemical Nomenclature (1970). The atoms linked by heavy bonds in Z-GPLGP are regarded as 'rigid' in the rigid-group search in the vector space. *W* represents an oxygen atom of the water molecule.

References

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Acta Cryst. (1978). B**34**, 3449–3452

1,2,3-Tris(2,4-dinitrophenoxy)benzene*

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(*Received* 15 *March* 1978; *accepted* 5 *July* 1978)

Abstract. $C_{24}H_{12}N_6O_{15}$, m.p. 206 °C, triclinic, $P\bar{1}$, a = 10·453 (1), b = 16·524 (6), c = 8·146 (3) Å, α = 104·48 (3), β = 101·11 (2), γ = 71·28 (3)°, Z = 2, M_r = 624·38, D_c = 1·62 g cm^{-3}, for observed data R = 6·7%. The molecular conformation is *anti,anti* with the central dinitrophenoxy ring on the opposite side of the benzene ring from the outer two dinitrophenoxy rings, in agreement with PMR studies. In each phenoxy ring, the 2-nitro group is distal to the benzene ring. The 4-nitro groups are nearly coplanar with their rings while the 2-nitro groups deviate from coplanarity by about 40°. The diphenyl ether linkage of the central phenoxy ring is skewed (φ,φ': −68,−3°) while the outer phenoxy-ring conformations are twist-skewed (φ,φ': 65,33; −54,−32°).

Introduction. The crystal structure of the title compound (Fig. 1) was undertaken in order to study further the conformational preferences of highly hindered diaryl ethers (Lehmann, 1974), particularly those with

* Conformations of Highly Hindered Aryl Ethers. XXVIII. Part XXVII: Lehmann (1973).

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