Crystal Structure and Conformation of *cyclo*-(Glycyl-D-leucyl-L-leucyl)$_2$

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Abstract: The synthetic cyclic hexapeptide *cyclo*-(Gly-D-Leu-L-Leu)$_2$ crystallized from an ethanol–water mixture with two molecules in the asymmetric unit. Both molecules have backbones in the form of two type II′ β-turns linked by extended glycyl residues. This is different from the conformation most readily identified in solution. In the crystal each molecule has only one 4→1 intramolecular hydrogen bond. The two molecules in the unit cell form a dimer through two intermolecular NH···O hydrogen bonds. Five water molecules and one ethanol are also present in the cell, and the crystal packing is such that the hydrophobic leucine side chains are segregated from the solvent molecules and the solvated peptide CONH groups. The space group of the crystal is $P1$ with a = 12.07 (1), b = 16.78 (2), c = 9.85 (1) Å; α = 95.27 (3), β = 92.78 (3), γ = 102.17 (3)°; and Z = 2. The structure was solved by vector search and direct phase-determination methods and refined by least squares to a discrepancy index of 0.084 for 5026 observed reflections.

Introduction

The crystallographic investigation of *cyclo*-(Gly-D-Leu-L-Leu)$_2$ (hereinafter referred to as GDL) was undertaken as part of our study on the structure and conformation of cyclic peptides. Cyclic hexapeptides have been extensively studied in solution by spectroscopic techniques and many are found to take up a conformation for the backbone having a twofold or inversion symmetry with two β-turns[1] and having two intramolecular 4→1 type of hydrogen bonds. Backbones containing both D and L amino acid residues are of special interest with regard to the type of backbone symmetry and bends that occur for the ring and their relationship to the amino acid sequence and chirality. For GDL, assuming a backbone conformation with two β-turns, there arises the possibility of turns linked by extended glycyl, L-leucyl, or D-leucyl residues resulting in three possible types of conformation for the turn region of the backbone. A nuclear magnetic resonance investigation by Kopple et al.[2] of GDL in a water–methanol mixture suggested that the predominant conformation is the one where the D residues occur in the extended part of the ring with the L-Leu and Gly taking part in the turn region. It was our aim to establish the details of the backbone conformation and nature of the bend regions of the molecule in the crystal by X-ray diffraction methods.

Experimental Section

The GDL crystals were obtained from an ethanol–water mixture and were enclosed in a capillary tube in equilibrium with the mother liquor to prevent the crystals from losing solvent of crystallization and drying up during X-ray diffraction studies. Intensity data of 5760 reflections were measured on an automated Rigaku diffractometer to a Bragg angle of 60° (Cu Kα) using $\omega/2\theta$ scan. Out of these, 5026 reflections had intensities greater than $3\sigma(I)$ and were considered observed.

The crystals are triclinic with the following cell parameters: a = 12.07 (1), b = 16.78 (2), c = 9.85 (1); α = 95.27 (3), β = 92.78 (3), γ = 102.17 (3)°.

Structure Solution and Refinement. From the unit cell parameters, it is seen that the cell contains two molecules of the hexapeptide, resulting in more than 80 nonhydrogen atoms in the asymmetric unit. Repeated attempts at the structure solution using the multisolution tangent refinement method with the program MULTAN[3] were unsuccessful. Hence, vector search methods, which use knowledge of the stereochemistry of the molecule, were attempted. A model with the backbone parameters proposed on the basis of NMR studies[2] was used as a search model. The search model neglected atoms beyond C$^\beta$ in the side chain and contained 28 atoms. The backbone conformational parameters that gave the cyclization geometry of the search model are given in Figure 2a.

A rotation search[4] (Crowther's fast rotation program modified by Craven) yielded two main peaks, and the orientation represented by the first peak was used in computing coordinates and phases for tangent refinement recycling with 477 reflections having large E values. The electron density map computed using this set of phases contained the initial model with slight deviations and also two half-rings of 16 atoms each. Two separate recycling calculations were next made. In the first calculation, in addition to the input model, one partial ring was included, whereas in the second, the input model and the other partial ring were used. In the first case not only did the partial ring not develop, but even the connectivity of the input model was lost. However, in the second run, in addition to the input model remaining intact, the partial ring developed into a molecular fragment of 27 atoms having connectivity very similar to that of the input model. Continuation of the recycling procedure with these two fragments did not reveal the leucyl side chain atoms presumably because these had larger thermal motions, and these atoms were obtained by cycles of structure factor and difference electron density calculations. In addition to the 80 atoms in the two GDL molecules, the unit cell also contained five molecules of water and a molecule of ethanol located from the maps.

All of the 88 nonhydrogen atoms were refined using block diagonal least-squares technique with the thermal motions denoted by anisotropic thermal parameters. A total of 52 hydrogen atoms attached to N, C$^\alpha$, C$^\beta$, and C$^\gamma$ were also fixed from sterochemical consideration. These hydrogens, though included in the structure factor calculations, however, were not refined. The final R index $[(\sum||F_o| - |F_c||)/(\sum|F_o|)]$ for the 5026 reflections used in the refinement is 0.084. The quantity minimized was $w(|kF_o| - |F_c|)^2$ where $w = 1/(\sigma(F))^2$. The coordinates of the nonhydrogen atoms are given in Table I. A list of structure factors, anisotropic thermal parameters, and hydrogen positions are provided in the Supplementary Material. For nonhydrogen atoms, atomic scattering factors from the "International Tables"[5] were used, and for hydrogens, the scattering factors given by Stewart, Davidson, and Simpson[6] were used. Bond lengths and angles are listed in Figure 1. It is interesting to note that the molecular conformation is appreciably different from that of the starting model. The starting model (Figure 2a) had glycines at the corners of the β-turns, whereas in the crystal structure, glycines occur in the extended region (Figure 2b) making the type of β-bends in the two cases different. Even the main chain conformations show significant deviations. However, it was close enough for the vector search to succeed. A comparison of the atomic parameters used as starting models for the vector search procedure with the final atomic coordinates shows that 14 of the main chain input atoms deviated less than 0.5 Å from the final atomic positions, and, hence, the phases computed from this model are

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(1) Venkatachalam, C. M. *Biopolymers* **1968**, *6*, 1425–1436.
(2) Kopple, K. D.; Go, A.; Schamper, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 4289–4295.
(3) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sect. A* **1971**, *27*, 368–376.
(4) Craven, B. M. Technical Report TR-75-2, 1975 University of Pittsburgh.
(5) "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, U. K., 1968; Vol. III, p 202.
(6) Stewart, R. F.; Davidson, E. R.; Simpson, W. T., *J Chem. Phys.* **1965**, *42*, 3175–3187.

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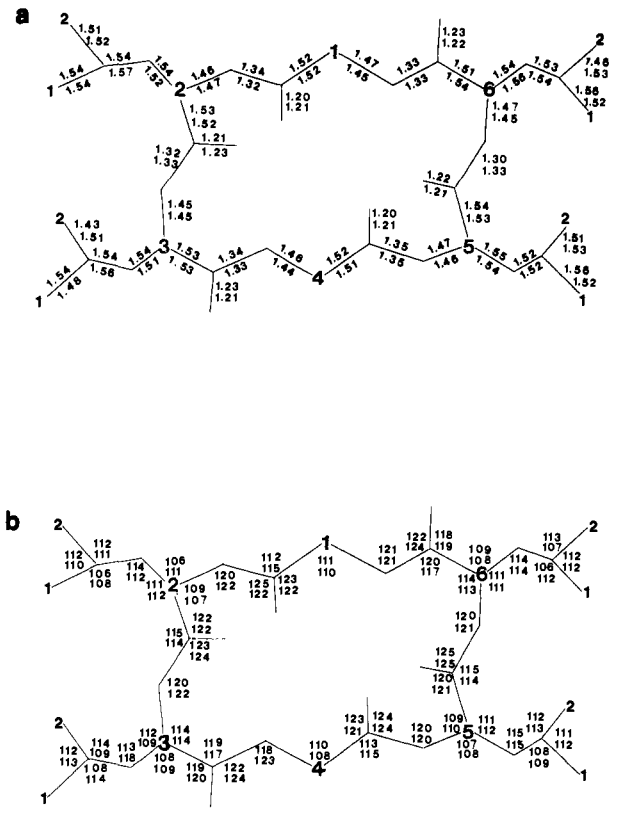

Figure 1. (a) Bond lengths (Å) and bond angles (°) in GDL. The α-carbon atoms are numbered 1 to 6. The upper and lower values are for molecules A and B, respectively. The average standard deviations in bond lengths and angles are 0.005 Å and 0.6°, respectively. For bond lengths and angles involving C^δ atoms, the standard deviations are 0.008 Å and 0.8°. C^δ_1 and C^δ_2 atoms are numbered 1 and 2, respectively.

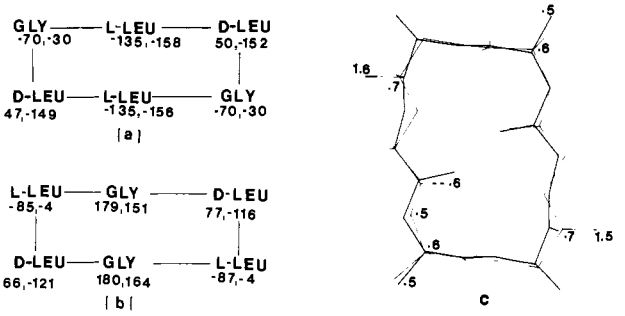

Figure 2. (a) The (ϕ,ψ) values for the input model. The absolute configuration has been changed for easy comparison with the values in Figure 2b. (b) (ϕ,ψ) values of molecule A in the crystal structure. (c) Superposition of the main chain (thick line) and C^β atoms of molecule A with the initial model (thin line). The height differences more than 0.5 Å between identical atoms are marked.

good enough for the recycling procedure to succeed. Superposition (Figure 2c) of the main chain and C^β atoms in molecule A with those in the initial model shows that the overall agreement for the main chain is good.

Results and Discussion

Molecular Conformation. The conformation of the two molecules A and B of *cyclo*-(Gly-D-Leu-L-Leu)$_2$ (Figure 3) are nearly the same, and have only approximate C_2 symmetry. All of the peptide units are in the trans configuration, and deviations from planarity are small. The backbones consist of two type II′ β-turns[1] linked by extended Gly residues; this form is roughly enantiomeric to the backbones found for *cyclo*-(Gly-L-Pro-D-Ala)$_2$[7] and *cyclo*-(Gly-L-Pro-D-Phe)$_2$.[8] The relevant torsion angles for the main chain and the side chains are given in Table II.

In the molecule A of the present crystal which has a near-C_2 symmetry, there is a weak 4→1 hydrogen bond between N1 and O4 with a hydrogen–oxygen distance of 2.25 Å and nitrogen–oxygen distance of 3.17 Å. We consider the N4···O1 interaction too weak to be called a hydrogen bond as the nitrogen–oxygen and hydrogen–oxygen distances are 3.42 and 2.48 Å, respectively. Neither are N4 and O1 involved in any other hydrogen bond. The O1···O4 distance of 2.99 Å is rather short as it is also in *cyclo*-

Table I. Final Positional and Thermal Parameters with Estimated Standard Deviations in Parentheses[a]

N	CODE	X/A	Y/B	Z/C	BIEQ1
1.	C1	2661 71	47651 71	53271301	21.1
2.	C2	10151 91	48781 71	47591221	20.7
3.	O	97691 31	35691 21	47051 81	13.9
4.	OW1	53641 31	62521 21	97941 31	7.8
5.	OW2	49491 31	37761 21	2211 31	11.1
6.	OW3	14911 61	59371 41	94471 81	16.4
7.	OW4	11121 51	38431 41	100431 61	20.1
8.	OWE	3081 21	68201 21	62761 51	17.9
9.	N 1A	33901 21	40881 11	68691 31	6.1
10.	CA1A	33391 41	48181 21	77921 41	7.6
11.	C 1A	37871 31	55961 21	71291 31	5.6
12.	O 1A	45161 21	56471 11	62431 31	10.3
13.	N 2A	33001 21	62091 11	75701 31	6.6
14.	CA2A	37691 31	70421 21	72511 41	5.4
15.	CB2A	32731 31	76171 21	82421 41	7.5
16.	CG2A	37251 31	85371 21	81261 51	8.9
17.	CD12A	30941 61	89991 31	91401 81	15.1
18.	CD22A	49931 41	87871 31	84151 71	6.8
19.	C 2A	34121 21	71131 21	57661 41	5.5
20.	O 2A	24271 21	70381 21	53611 31	9.5
21.	N 3A	42551 21	72571 11	49531 31	5.6
22.	CA3A	40211 31	77931 21	35411 31	6.2
23.	CB3A	50291 31	79601 21	29711 41	7.4
24.	CG3A	53211 41	88301 21	37391 51	7.7
25.	CD13A	63681 61	93191 31	31281111	14.8
26.	CD23A	44011 81	92401 31	37241131	15.3
27.	C 3A	36931 31	66041 21	25711 41	7.1
28.	O 3A	33931 41	66431 21	13751 31	9.6
29.	N 4A	37221 31	58881 11	30471 31	7.0
30.	CA4A	33061 41	51421 21	21181 51	7.0
31.	C 4A	34081 31	43951 21	29441 41	6.9
32.	O 4A	40201 31	44331 11	38551 31	6.1
33.	N 5A	27791 31	36901 11	21961 31	6.2
34.	CA5A	29061 31	28991 21	26251 41	5.3
35.	CB5A	21541 31	27211 21	15991 51	5.7
36.	CG5A	21581 41	13531 21	19051 61	6.8
37.	CD15A	12721 61	7581 31	8791 91	7.1
38.	CD25A	33201 51	11641 21	18101 81	10.2
39.	C 5A	25121 21	28311 21	40791 41	5.7
40.	O 5A	15281 21	28341 21	47041 31	9.6
41.	N 6A	32801 21	27291 11	49791 31	5.6
42.	CA6A	29891 31	25871 21	63821 41	7.2
43.	CB6A	37541 31	20831 21	70391 41	7.9
44.	CG6A	36461 41	17221 21	63181 51	11.0
45.	CD16A	44891 61	8271 31	71351 81	17.5
46.	CD26A	24911 61	7291 31	62221101	9.9
47.	C 6A	30271 31	33621 21	73171 41	7.7
48.	O 6A	27111 31	37971 11	84781 31	12.3
49.	N 1B	70401 21	41411 11	69661 31	8.1
50.	CA1B	67011 31	48311 21	77001 51	8.8
51.	C 1B	75481 31	56151 21	75371 41	6.7
52.	O 1B	85051 31	56191 21	72321 71	13.4
53.	N 2B	71841 21	62961 11	78091 41	7.6
54.	CA2B	78821 21	71091 21	76431 41	5.4
55.	CB2B	77011 31	77381 21	87701 41	6.5
56.	CG2B	84411 41	86101 21	86321 51	6.0
57.	CD12B	81621 51	92141 31	97651 91	8.9
58.	CD22B	96951 51	86081 41	87571 91	8.3
59.	C 2B	75541 21	73261 11	62331 41	3.5
60.	O 2B	66331 21	74951 11	59661 31	6.3
61.	N 3B	83311 21	72981 11	53321 31	5.7
62.	CA3B	81471 31	74751 21	39341 41	5.8
63.	CB3B	92741 31	77211 21	33281 41	7.2
64.	CG3B	100731 41	85191 31	40321 61	7.3
65.	CD13B	95391 71	92351 41	41531121	8.7
66.	CD23B	11701 61	86751 51	33301121	12.2
67.	C 3B	74091 31	67551 21	30081 41	5.8
68.	O 3B	70401 31	68661 11	18911 31	6.6
69.	N 4B	72251 31	60281 21	34911 21	5.8
70.	CA4B	65941 41	52911 21	27121 51	5.8
71.	C 4B	69921 31	45761 21	32351 41	5.3
72.	O 4B	76361 21	46701 11	42461 31	5.9
73.	N 5B	65951 21	38471 11	24951 31	5.6
74.	CA5B	70201 31	31311 21	28371 41	7.0
75.	CB5B	65761 41	24361 21	16791 41	8.5
76.	CG5B	69821 41	16491 21	18371 51	12.5
77.	CD15B	64091 71	10001 31	6971 71	12.2
78.	CD25B	82741 61	17741 41	18861101	15.6
79.	C 5B	66171 21	28911 11	42181 31	6.1
80.	O 5B	56161 21	26751 11	43811 31	8.1
81.	N 6B	74491 21	29101 11	51631 31	7.2
82.	CA6B	71981 31	27091 21	65311 41	9.0
83.	CB6B	82481 41	24971 21	72881 51	11.3
84.	CG6B	86351 51	17531 31	65961 71	18.3
85.	CD16B	76821 81	9921 41	64061151	16.2
86.	CD26B	96501 71	16301 51	74691151	21.2
87.	C 6B	68471 31	34051 21	74241 41	7.1
88.	O 6B	64221 21	32561 11	84961 31	10.6

[a] CA4B is the α-carbon atom of the fourth residue in molecule B. B(eq) is the isotropic equivalent of anisotropic thermal parameters.

(7) Kostansek, E. C.; Lipscomb, W. N.; Thiessen, W. E. *J. Am. Chem. Soc.* **1979**, *101*, 834–837.

(8) Brown, J. N.; Yang, C. H. *J. Am. Chem. Soc.* **1979**, *101*, 445–449.

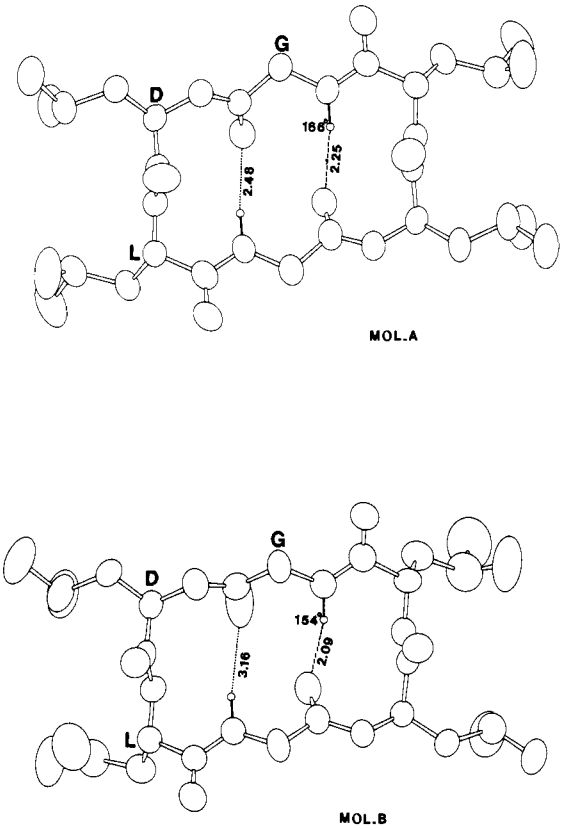

Figure 3. Conformation of the two molecules A and B. Both of the molecules are made up of two type II′ B-bends. There is only one 4→1 type hydrogen bond per molecule. The N—H···O hydrogen bond angles are 166 and 154° in molecules A and B. The deviation from the C_2 symmetry is larger for molecule B. The α-carbon atoms designated as G, D, and L belong to the first, second, and third residues. G stands for glycine, D for D-leucine, and L for L-leucine.

Table II. Torsion Angles[a]

residue	residue no.	Φ	Ψ	ω	χ_1	χ_{21}	χ_{22}
Gly	1	179	151	168			
		147	162	−177			
D-Leu	2	77	−116	−175	177	178	−60
		94	−108	179	180	178	−62
L-Leu	3	−87	−4	175	−63	177	−58
		−80	−13	−178	−62	179	−54
Gly	4	180	163	171			
		155	−171	174			
D-Leu	5	66	−121	−175	−178	174	−64
		68	−121	179	178	175	−62
L-Leu	6	−85	−4	176	−62	−179	−57
		−77	−14	177	−60	179	−55

[a] "IUPAC-IUB Nomenclature", *Biochemistry* 9, 3471 (1970). The upper and lower values are for molecule A and molecule B, respectively.

(Gly-L-Pro-D-Ala)$_2$ and *cyclo*-(Gly-L-Pro-D-Phe)$_2$. Molecule B has a stronger internal hydrogen bond between N1 and O4 with N···O and H···O distances of 2.97 and 2.09 Å. As in molecule A there is no hydrogen bond between N4 and O1 as the N···O and H···O distances are 4.10 and 3.16 Å, respectively. Owing to greater deviation from the twofold symmetry, the O1···O4 distance (3.23 Å) is greater in molecule B. O1B is hydrogen-bonded to OW5, but N4B is unassociated as in molecule A.

In both the molecules the leucine side chains have extended conformations, with the dihedral angles close to the classical staggered arrangement.

The crystals of cyclic hexapeptides with C_2 sequence symmetry so far examined divide into two classes, those in which the backbone has exact or approximate C_2 symmetry; e.g., two type-II

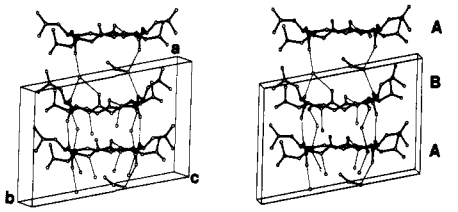

Figure 4. The packing diagram of the crystal. The hydrogen bonds between the two molecules and also involving peptides and solvent molecules are shown. The leucyl side chains extend in the *b* direction and are clustered together.

Table III. Hydrogen Bond Distances (Å) and Angles (deg)

dist	angle	data set	D···A	H···A	D–H···A
N 1A	O4A[a]	*x*, *y*, *z*	3.17	2.25	166
N 2A	OW3	*x*, *y*, *z*	2.92	1.98	170
N 3A	O2B	*x*, *y*, *z*	2.93	1.99	171
N 5A	OW4	*x*, *y*, *z* − 1	2.92	1.97	173
N 4A	O1A	*x*, *y*, *z*	3.42	2.48[b]	172
N 6A	O5B	*x*, *y*, *z*	2.93	1.99	172
N 1B	O4B[a]	*x*, *y*, *z*	2.97	2.09	154
N 2B	OW1	*x*, *y*, *z*	3.01	2.15	149
N 3B	OW5	*x* + 1, *y*, *z*	2.82	1.87	174
N 5B	OW2	*x*, *y*, *z*	2.90	1.95	175
N 4B	O1B	*x*, *y*, *z*	4.10	3.16[b]	172
N 6B	O	*x*, *y*, *z*	2.86	1.93	168
O	O 5A	*x* + 1, *y*, *z*	2.70		
OW1	O 3A	*x*, *y*, *z* + 1	3.06		
OW1	O 3B	*x*, *y*, *z* + 1	2.79		
OW2	O 6A	*x*, *y*, *z* − 1	3.05		
OW2	O 6B	*x*, *y*, *z* − 1	2.74		
OW3	O 3A	*x*, *y*, *z* + 1	2.88		
OW4	O 6A	*x*, *y*, *z* + 1	2.78		
OW5	O 2A	*x*, *y*, *z*	2.72		
OW5	O 1B	*x* − 1, *y*, *z*	2.90		

[a] Intramolecular (4 → 1) hydrogen bonds. [b] Considered too large for hydrogen bond. N–H distances are assumed to be 0.95 Å.

β-turns, and those in which the backbone is approximately centrosymmetric, e.g., one type-I and one type-II turn. Peptides with four glycine residues (*cyclo*-(Gly-L-Leu-Gly),[9] *cyclo*-(Gly-L-Tyr-Gly),[10] and *cyclo*-(Gly-L-Pro-Gly)$_2$[11]) fall into the latter category. Those with two or no glycine residues have so far shown C_2 backbones. *cyclo*-Gly-D-Leu-L-Leu)$_2$ is the first in this category which also contains no proline.

Crystal Packing. The packing of the two hexapeptide molecules A and B in the triclinic unit cell are shown in Figure 4. The molecules are stacked one over the other with the 18-membered rings approximately perpendicular to the *a* axis. The two crystallographically independent molecules form a dimer through two strong *intra*-dimer peptide–peptide hydrogen bonds O2B···N3A and O5B···N6A. The dimers also receive additional stabilization by formation of *intra*-dimer hydrogen bonds through the two molecules OW1 and OW2 with OW1 bonded to O3A and O3B and OW2 bonded to O6A and O6B. A similar role for water molecules in stabilizing the secondary structure by interchain hydrogen bonds via water bridges has been proposed[12,13] for collagen. The water OW5 accepts a hydrogen from N3B and donates a hydrogen to O1B to form a nine-membered ring. In the *a* direction, the dimers are linked through oxygens of the ethanol as well as OW5, while in the *c* direction there is extensive interdimer linkings by hydrogen bonds through water molecules OW1, OW2, OW3, and OW4. Thus, a network of hydrogen bonds exist among solvent molecules and the peptides in the *a* and

(9) Brown, J. N., personal communication.
(10) Shamala, N. *J. Indian Inst. Sci.* **1977**, *59*, 91–112.
(11) Kostansek, E. C.; Thiessen, W. E.; Schomburg, D.; Lipscomb, W. N. *J. Am. Chem. Soc.* **1979**, *101*, 5811–5815.
(12) Ramachandran, G. N.; Chandrasekaran, R. *Biopolymers* **1968**, *6*, 1649–1958.
(13) Ramachandran, G. N.; Ramakrishnan, C. In "Biochemistry of Collagen"; Ramachandran G. N.; Reddi, A. H., Eds.; Plenum: New York, 1976; pp 45–84.

c directions. The hydrogen bond parameters are given in Table III.

The main interactions between the *ac* layers are the van der Waals forces among the isobutyl groups of the leucyl side chains that stretch out in the *b* directions. This results in the side chains of dimers from adjacent cells in the *b* direction clustering together inbetween the dimers. This molecular shape with the leucyl side chains at the four corners of the bend regions, stretching out in the *b* direction and the resulting crystal packing, allows the peptide bonds to be easily accessible to the polar solvent molecules and at the same time segregates and clusters together the hydrophobic side chains. Analogous clustering of Phe and Pro side chains to allow formation of water channels is observed for [Phe[4],Val[6]]-antamanide dodecahydrate.[14] The conformation of proteins in aqueous medium is greatly influenced by the entropy factors, and, hence, the folding of the peptide chains are such that the solvent exposure of the hydrophilic groups is maximized with the concomitant minimization of exposure to hydrophobic groups. The folding and packing of the present cyclic peptide molecule are also clearly influenced by such entropy effects.

Comparison with the Conformation in Solution. Superficially, the proton NMR spectra of *cyclo*-(Gly-D-Leu-L-Leu)$_2$ and its close analogue *cyclo*-(Gly-D-Val-L-Leu)$_2$ in dimethyl sulfoxide (Me_2SO) solution are consistent in some aspect with the above conformation of the peptide backbone. However, consideration of the NMR and circular dichroism spectra of these and additional analogues in a range of solvents leads to the conclusion that the dimethyl sulfoxide spectra probably represent an average over two conformations present in comparable amounts. One of these may be the form present in the crystal. In aqueous solutions of water-soluble analogues, such as *cyclo*-(Gly-D-Orn-L-Orn-Gly-D-Val-L-Leu), a single backbone type is clearly indicated, but this is the form with type II L-Yyy-Gly β-turns and extended D-Xxx residues.[2] From the point of view of the short-range intrapeptide interactions, e.g., the calculated conformational energies of the constituent dipeptide units, conformations of this alternative type are as stable as those with type II′ D-Xxx-L-Yyy β-turns. With only small energy differences between alternative backbones, interpeptide interactions will certainly be a deciding factor in the crystal. Such a driving force in the present case is the segregation of polar (peptide bond and water) groups from nonpolar (isobutyl side chains) groups to maximize the polar interactions. It should be noted, however, that here it is still a form of the two β-turn backbone conformation that occurs as in most other cyclic hexapeptides.

Acknowledgment. The diffraction data on GDL were collected at the Protein Institute, Osaka, Japan. Thanks are due to Mr. K. Sakaguchi for technical assistance, Professor M. Kakudo for his hospitality, and the Japanese Ministry of education for the award of visiting professorship to one of us (G. K.). The work was supported by the New York State Department of Health and by the National Institutes of Health, Grant GM-22490.

Supplementary Material Available: Listing of structure factor amplitudes, coordinates of 52 hydrogen atoms included in the structure factor calculation, and the anisotropic thermal parameters (29 pages). Ordering information is given on any current masthead page.

(14) Karle, I. L.; Duesler, E. *Proc. Natl. Acad. Sci.* **1977**, *74*, 2602–2606.

The Nature of the $^1n\pi^* \leftarrow S_0$ Transition. 4.[1] The First Excited Singlet State of Acetaldehyde

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Abstract: Medium-resolution electronic-absorption spectroscopy of CH_3CHO and CH_3CDO and laser-induced fluorescence spectroscopy of CH_3CHO are used to study the first excited $^1n\pi^*$ state. A vibrational analysis of the vibronic band system in both absorption and emission gives the following Franck-Condon active $1 \leftarrow 0$ vibrational frequencies for the first excited $^1n\pi^*$ state in CH_3CHO (CH_3CDO): ν_4'[carbonyl stretch] = 1119 cm^{-1} (1173 cm^{-1}); ν_{14}'[out-of-plane bend] = 151 cm^{-1} (112 cm^{-1}); ν_{15}'[methyl torsion] = 187 cm^{-1} (189 cm^{-1}). The system origin (0–0 band) is assigned to the 28 872-cm^{-1} band in CH_3CHO and the 28 975-cm^{-1} band in CH_3CDO. The absorption spectrum of CH_3CHO is characterized by large splittings between the inversion components of ν_{14} in the excited state. The observed out-of-plane bending vibrational levels in the excited state were least-squares fit to the eigenfunctions of a quartic-quadratic potential surface. The optimized surface predicts an equilibrium out-of-plane angle in the excited state of ~26° and a barrier to inversion of ~138 cm^{-1}. We conclude that the barrier to inversion and the out-of-plane angle in the first excited $^1n\pi^*$ state of acetaldehyde are less than their corresponding values in both H_2CO and HCOF. The barrier to rotation of the methyl group in CH_3CHO increases from 400 cm^{-1} in the ground state to ~660 cm^{-1} in the $^1n\pi^*$ excited singlet state. The observed characteristics of the $^1n\pi^*$ state of acetaldehyde are rationalized in terms of significant delocalization of the π^* molecular orbital onto the methyl group.

Although the first excited $n\pi^*$ singlet state of acetaldehyde has been spectroscopically studied in considerable detail,[3-9] no conclusive assignments of the system origin, Franck-Condon active vibrational modes, or the geometry of the excited state are available. As in other aliphatic carbonyl compounds which have been shown to have pyramidal $^1n\pi^*$ states,[10-15] there is spectro-

(1) (a) Parts 1, 2, and 3 of this series are from 1b, 1c, and 1d, respectively. (b) Birge, R. R.; Pringle, W. C.; Leermakers, P. A. *J. Am. Chem. Soc.* **1971**, *93*, 6715. (c) Birge, R. R.; Leermakers, P. A. *Ibid.* **1971**, *93*, 6726. (d) Birge, R. R.; Leermakers, P. A. *Ibid.* **1972**, *94*, 8105.

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(3) Henri, V.; Schou, S. A. *Z. Phys.* **1928**, *49*, 774.

(4) Leighton, P. A.; Blacet, F. E. *J. Am. Chem. Soc.* **1933**, *55*, 1766.

(5) Eastwood, E.; Snow, C. P. *Proc. R. Soc. London, Ser. A* **1935**, *149A*, 434.

(6) Walsh, A. D. *J. Chem. Soc.* **1953**, 2318.

(7) Rao, V. R.; Rao, I. A. *Indian J. Phys.* **1954**, *28*, 491.

(8) Innes, K. K.; Giddings, L. E., Jr. *J. Mol. Spectrosc.* **1961**, *7*, 435.

(9) Longin, P. *C. Rend. Hebd. Seances Acad. Sci.* **1960**, *251*, 2499.

(10) Brand, J. C. D. *J. Chem. Soc.* **1956**, 858.

(11) Robinson, G. W.; DiGiorgio, V. E. *Can. J. Chem.* **1958**, *36*, 31.

(12) Giddings, L. E., Jr.; Innes, K. K. *J. Mol. Spectrosc.* **1961**, *6*, 528.

(13) Giddings, L. E., Jr.; Innes, K. K. *J. Mol. Spectrosc.* **1962**, *8*, 328.

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