molecules differ little in total energy. That packing forces can influence the dihedral angle has been observed in analogous compounds (Chu, 1975; Chu & Mangion, 1975; Chu & Yang, 1977; Hoffschwelle, Simonsen & Martin, 1981; Phelps & Cordes, 1974) with the observed differences in the dihedral angle between the crystallographically distinct molecules ranging from 1·3 to 9·2°. An examination of the intermolecular contacts reveals no unusually close non-H interactions. The closest non-H contacts are between atoms C(10A) and C(2)*B* ($\frac{1}{2}+x, \frac{1}{2}-y, z$) at a distance of 3·334 (4) Å and between C(3) and O(3) ($\frac{1}{2}-x, \frac{1}{2}+y, z$) at a distance of 3·182 (4) Å. There are no O···O contacts less than 3·50 Å. There are, however, some short O···H contacts. These short contacts all involve the pseudo-equatorial O atoms. Atom O(2) is 2·39 (4) Å from atom H(C1)*B* at $x, -y, \frac{1}{2}+z$ while atom O(4) is 2·31 (4) Å from atom H(C9) at $1-x, y, \frac{1}{2}-z$. Atom O(2)*B* is 2·50 (4) Å from atom H(C4) at $-x, -y, 1-z$. Because the pharmacological activity of some members of the phenothiazine ring system (obtained by replacement of one S by a N in thianthrene) has been ascribed, in part, to the dihedral angle (Martin, Korp, Turley & Bernal, 1978), it is important to understand how substituents affect the geometry of these heterocycles. Because crystal-packing forces can mask the effects of these substituents, the interpretation of results from a single structural investigation can be misleading. As a result systematic studies such as the one in which we are currently involved are necessary for a fuller understanding of these compounds.

This work was supported by the Robert A. Welch Foundation, Grant No. F-017.

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Crystal Form II of Cycloamanide A, *cyclo*(-L-Prolyl-L-valyl-L-phenylalanyl-L-phenylalanyl-L-alanyl-glycyl-)–Water–Ethanol (1/1/3), $C_{33}H_{42}N_6O_6.H_2O.3C_2H_6O$, Containing an Unusual β-Bend

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(*Received* 22 *September* 1983; *accepted* 21 *December* 1983)

Abstract. $M_r = 618·7 + 156·2$, orthorhombic, $P2_12_12_1$, $a = 16·716$ (2), $b = 24·007$ (3), $c = 10·918$ (1) Å, $Z = 4$, $V = 4381·4$ Å^3, $D_x = 1·175$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 3·34$ cm^{-1}, $F(000) = 1672$, $R_F = 7·2\%$ for 4007 data with $|F_o| > 0$. Cycloamanide A, isolated from *Amanita phalloides*, occurs in more than one crystalline pseudo polymorph. Form I [Chiang, Karle & Wieland (1982). *Int. J. Pept. Protein Res.* **20**, 414–420] has four H_2O solvent molecules while form II has one H_2O and three C_2H_5OH solvent molecules. The crystals are not isomorphous, although the peptide molecules are isostructural. The unusual intramolecular hydrogen bond in the β-bend encompassing the

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0108-2701/84/081381-06$01.50

sequence L-Phe-L-Ala occurs in both crystal forms. The β-bend has torsional angles characteristic of a type II′ bond (for a D, L sequence) rather than the expected type I (for an L,L sequence). The φ, ψ values are +60, −122 and −86, −5°, respectively. One water molecule is buried in an excessively hydrophobic region to provide hydrogen bonds to two amide and two carbonyl moieties.

Introduction. The possible influence upon the conformation of a peptide by the nature of the solvent or by crystallographic packing forces is being examined by studying the structures of particular peptides that occur in several crystal forms. As an example, *cyclo*-(-L-Leu-L-Tyr-δ-Ava-δ-Ava-),* crystallized from dimethyl sulfoxide/water, occurs in space group $P2_12_12_1$ with one molecule each of H_2O and Me_2SO per peptide, whereas the same peptide crystallized from a water/acetone mixture occurs in space group $P2_1$ with four H_2O molecules per peptide (Karle, 1976; Karle & Flippen-Anderson, 1978). The conformation of the peptide remains the same in the two crystal forms. Further, crystals of [Phe^{4}Val^6]antamanide grown from the nonpolar mixture of *n*-hexane/methyl acetate or from the polar mixture of water/acetone/CH_3CN each crystallize in space group $P2_12_12_1$ but with different dimensions for the *c* axis. From the polar solvent, crystals contain 12 water molecules per peptide, whereas from the non-polar solvent the crystals have three H_2O molecules plus an undetermined number of grossly disordered nonpolar molecules per peptide. Nevertheless, the conformation of [Phe^{4}Val^6]-antamanide is identical in the two crystal forms (Karle, 1977; Karle & Duesler, 1977).

The stability of the cyclic peptide conformation is demonstrated again in the present study. Two different crystal forms of cycloamanide, a minor component of *Amanita phalloides* (Gauhe & Wieland, 1977), grow from water/ethanol solutions, each in space group $P2_12_12_1$ but with the lengths of the *a* axes differing by 3·4 Å. The structure of the form containing four H_2O molecules per peptide (form I) has been reported (Chiang, Karle & Wieland, 1982). The present crystal (form II) contains one H_2O and three ethanol molecules per peptide. A remarkable feature of this natural peptide in both crystal forms is the very unusual occurrence of a β-bend with an L,L sequence but with conformational angles characteristic of a D,L sequence forming a type II′ hydrogen bond.

Experimental. Crystal data for the title compound (form II) are given in the *Abstract*. For comparison, for form I: $C_{33}H_{42}N_6O_6.4H_2O$, $a = 13{\cdot}307\ (2)$, $b = 24{\cdot}820\ (4)$, $c = 11{\cdot}231\ (1)$ Å and $D_x = 1{\cdot}237$ g cm^{-3}.

The title compound was dissolved in hot ethanol; cold water was added slowly. Upon standing, crystals grew in the form of clear prisms. Crystals grown at different times, from the same original sample, grew in the two different forms. The pseudopolymorphs were discovered only by measuring the cell parameters of crystals taken from different crystallizing vessels. For data collection, a crystal (colorless plate 0·5 × 0·5 × 0·2 mm) was sealed in a thin glass capillary. X-ray intensity data measured on a four-circle diffractometer with the $\theta/2\theta$ scan technique to $2\theta_{max} = 130°$, $0 \le h \le 19$, $0 \le k \le 28$, $0 \le l \le 12$; 4186 independent data. Cu $K\alpha$ radiation with a graphite monochromator. Reflections 800, 0,10,0 and 014, serving as monitors and measured at intervals of 60 measurements, did not indicate any decay. Lorentz and polarization corrections, normalized $|E|$ values obtained by means of a *K* curve. Structure solved by direct phase determination and partial structure development (Karle, 1968) using the tangent formula (Karle & Hauptman, 1956). In retrospect, since in both crystals the peptide molecule has been shown to have the same conformation and to be similarly placed with respect to a screw axis parallel to the *c* axis, other procedures for deriving the structure of form II using the known coordinates from form I could have been used equally well. The molecules in the solvent region were located and identified as three ethanol molecules by the use of difference maps interspersed with cycles of least-squares refinement. H atoms were placed in idealized positions.

Coordinates for all the atoms, including H atoms, and anisotropic thermal parameters were refined on *F* using the restrained least-squares procedure. The most recent version of the program uses six parameters for the thermal factors (Flippen-Anderson, Gilardi & Konnert, 1983). Restraints were placed upon the allowable ranges for each bond length, for each skip distance (for defining the bond angle), and for the planarity of the two phenyl rings. Near the end of the refinement, all restraints were relaxed. Weights according to Gilardi (1973). Final $R_F = 7{\cdot}2\%$ for 4007 data with $|F_o| > 0$, $R_w = 7{\cdot}4\%$, $S = 1{\cdot}21$. Maximum shift/error 1·1 for the disordered atom C_1^γ, while the mean shift/error was near 0·18. Peaks in final difference synthesis $\le |0{\cdot}17|$ e Å^{-3}. Atomic scattering factors from Stewart, Davidson & Simpson (1965). In-house computer programs were used.

Fractional coordinates and B_{eq} values for the C, N and O atoms are listed in Table 1.* Bond lengths and bond angles are listed in Table 2. The labeling of the atoms is shown in Fig. 1.

* δ-Ava = δ-aminovalerate.

* Lists of structure factors, anisotropic thermal parameters and H-atom fractional coordinates have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39115 (24 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Fractional coordinates and thermal parameters for cycloamanide A (crystal form* II)

The e.s.d.'s for x, y and z are near 0·00025, 0·00017 and 0·0004, respectively, for the backbone atoms, and increase up to 0·0004, 0·00025 and 0·0007 for atoms in the side chains.

$$B_{eq} = \tfrac{4}{3}\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	B_{eq}(Å^2)
N_1	0·3788	0·5528	0·4291	3·6
C_1^{α}	0·3874	0·5939	0·5271	3·9
C_1'	0·3114	0·6247	0·5613	3·6
O_1	0·3126	0·6551	0·6520	4·6
C_1^{β}	0·4509	0·6345	0·4776	5·9
C_1^{γ}	0·4536	0·6245	0·3458	10·1
C_1^{δ}	0·4244	0·5669	0·3178	4·9
N_2	0·2476	0·6181	0·4893	3·6
C_2^{α}	0·1711	0·6453	0·5152	3·9
C_2'	0·1044	0·6019	0·5298	3·8
O_2	0·0599	0·6032	0·6184	5·5
C_2^{β}	0·1494	0·6906	0·4225	5·3
C_{21}^{γ}	0·2195	0·7305	0·4089	9·8
C_{22}^{γ}	0·0745	0·7219	0·4620	7·8
N_3	0·0985	0·5644	0·4375	3·9
C_3^{α}	0·0346	0·5232	0·4350	4·0
C_3'	0·0713	0·4646	0·4203	3·7
O_3	0·1282	0·4563	0·3531	4·6
C_3^{β}	−0·0213	0·5330	0·3263	5·5
C_3^{γ}	−0·0624	0·5900	0·3313	5·8
C_{31}^{δ}	−0·0448	0·6292	0·2413	7·2
C_{31}^{ϵ}	−0·0835	0·6812	0·2478	8·7
C_3^{η}	−0·1357	0·6940	0·3419	8·5
C_{32}^{ϵ}	−0·1509	0·6560	0·4279	8·6
C_{32}^{δ}	−0·1155	0·6034	0·4232	7·4
N_4	0·0316	0·4247	0·4832	3·7
C_4^{α}	0·0500	0·3650	0·4648	3·6
C_4'	0·1374	0·3534	0·4969	3·7
O_4	0·1609	0·3628	0·6022	5·1
C_4^{β}	0·0223	0·3440	0·3399	4·1
C_4^{γ}	−0·0661	0·3532	0·3181	4·2
C_{41}^{δ}	−0·0927	0·3936	0·2373	5·7
C_{41}^{ϵ}	−0·1744	0·4022	0·2195	6·9
C_4^{η}	−0·2292	0·3710	0·2800	7·2
C_{42}^{ϵ}	−0·2039	0·3302	0·3573	7·6
C_{42}^{δ}	−0·1238	0·3209	0·3781	6·1
N_5	0·1845	0·3318	0·4124	3·7
C_5^{α}	0·2684	0·3194	0·4362	3·8
C_5'	0·3241	0·3684	0·4151	4·2
O_5	0·3960	0·3640	0·4385	5·7
C_5^{β}	0·2948	0·2697	0·3579	4·9
N_6	0·2922	0·4144	0·3700	4·2
C_6^{α}	0·3380	0·4640	0·3425	4·3
C_6'	0·3414	0·5038	0·4514	3·8
O_6	0·3105	0·4942	0·5499	5·4
O(*B*)	0·5971	0·5412	0·1380	7·9
C(1*B*)	0·6761	0·5545	0·1273	13·9
C(2*B*)	0·6982	0·5985	0·1927	20·2
O(*C*)	0·5666	0·4450	0·2633	10·8
C(1*C*)	0·5619	0·4357	0·4027	12·2
C(2*C*)	0·6138	0·4762	0·4729	19·0
O(*D*)	0·5025	0·2722	0·4566	9·0
C(1*D*)	0·5706	0·2824	0·3876	12·2
C(2*D*)	0·5525	0·2801	0·2679	15·2
O_w(*A*)	0·2191	0·5791	0·2342	5·5

Discussion. A comparison of the conformation of *cyclo*(-L-Pro-L-Val-L-Phe-L-Phe-L-Ala-Gly-) as it occurs in crystals of form I and form II is shown in Fig. 1. The conformations in the two forms are almost identical. Values for the torsional angles, listed in Table 3, show that for φ_i, ψ_i and χ_{i1} the largest differences are 8° while the r.m.s. differences are 5°.

Table 2. *Bond lengths* (Å) *and angles* (°)

Estimated standard deviations are of the order of 0·006 Å for bond lengths and 0·4° for bond angles in the peptide backbone and increase to a maximum of 0·01 Å for bond lengths and 0·6° for bond angles in the side groups.

i	L-Pro 1	L-Val 2	L-Phe 3	L-Phe 4	L-Ala 5	Gly 6	Av.
Bonds							
N_i–C_i^{α}	1·464	1·464	1·456	1·480	1·457	1·447	1·461
C_i^{α}–C_i'	1·517	1·535	1·544	1·528	1·518	1·526	1·528
C_i'–O_i	1·230	1·221	1·217	1·235	1·233	1·216	1·225
C_i'–N_{i+1}	1·334	1·354	1·351	1·319	1·322	1·353†	1·338
C_i^{α}–C_i^{β}	1·539	1·528	1·529	1·526	1·534		1·531
C_i^{β}–C_i^{γ}	1·460*	1·521	1·530	1·513			
		1·522					
C_i^{γ}–C_i^{δ}	1·499*		1·392	1·385			
			1·378	1·400			
C_i^{δ}–C_i'			1·409	1·395			
			1·395	1·378			
C_i'–C_i^{η}			1·383	1·356			
			1·334	1·360			
N_i–C_i^{δ}	1·475						
Angles							
$C'_{i-1}N_iC_i^{\alpha}$	120·1	122·1	121·3	121·0	122·0	123·4	121·6
$N_iC_i^{\alpha}C_i'$	115·2	110·5	109·3	110·1	114·0	111·9	111·8
$C_i^{\alpha}C_i'N_{i+1}$	117·8	115·3	113·4	118·8	117·1	114·9	116·2
$C_i^{\alpha}C_i'O_i$	118·2	120·5	121·4	119·0	120·0	123·7	120·4
$N_{i+1}C_i'O_i$	123·9	124·2	125·1	122·2	122·8	121·3	123·2
$C_i'C_i^{\alpha}C_i^{\beta}$	110·8	112·4	107·7	115·8	110·0		111·3
$N_iC_i^{\alpha}C_i^{\beta}$	103·8	113·3	111·0	112·3	109·7		
$C_i^{\alpha}C_i^{\beta}C_i^{\gamma}$	105·3	109·3	112·6	112·8			
		111·0					
$C_i^{\beta}C_i^{\gamma}C_i^{\delta}$	110·0*		118·9	121·0			
			121·5	121·2			
$C_i^{\gamma}C_i^{\delta}C_i'$			117·8	120·4			
			120·7	120·1			
$C_i^{\delta}C_i'C_i^{\eta}$			121·6	120·8			
			120·9	121·5			
$C_i^{\delta}C_i^{\gamma}C_i^{\delta}$			119·5	117·8			
$C_i'C_i^{\eta}C_i'$			119·4	119·3			
$C_i^{\gamma}C_i^{\beta}C_i^{\gamma}$		110·5					
$C_i^{\gamma}C_i^{\delta}N_i$	102·3						
$C_i^{\delta}N_iC_i^{\alpha}$	113·3						
$C_i^{\delta}N_iC'_{i-1}$	125·9						

* The C^{γ} atom in the Pro residue is disordered among at least two positions corresponding to different conformations for the pyrrolidine ring. The disorder is indicated by the elongated thermal ellipsoid. The average position, as determined by the X-ray analysis, makes the pyrrolidine ring appear flatter, makes the bond lengths appear shorter and the angle larger than the true values.

† For $i = 6$, N_{i+1} is N_1.

A most unusual feature in this peptide concerns the conformational values for L-Phe[4]. On a φ,ψ plot (Ramachandran & Sasisekharan, 1968), shown in Fig. 2, L-Phe[4] falls in a region characteristic for D residues and completely excluded for L residues. Furthermore, the β-bend containing the only 4→1 hydrogen bond, N(6)H···O(3), encompasses residues L-Phe[4] and L-Ala[5]. As a consequence, the β-bend is not type I, characteristic for L,L sequences, but type II′, characteristic for D,L sequences (Venkatachalam, 1968; Karle, 1981).

One feature distinguishing the different types of β-bends is the conformational relationship of the first two N atoms. In types I and I′ for L,L and D,D sequences, N(1) is approximately *cis* to N(2), whereas in types II and II′ for L,D and D,L sequences N(1) is *transoid* to N(2), Fig. 3. The equivalent N atoms in the present peptide in Fig. 1 are N(4) and N(5) which are

Table 3. *Conformational angles* (°)

The values in parentheses are for the alternate crystal form with four molecules of solvent water per peptide molecule (Chiang, Karle & Wieland, 1982). The present crystal contains $1H_2O.3C_2H_5OH$ per asymmetric unit.
The convention followed for labeling atoms and conformational angles is that proposed by the IUPAC–IUB Commission on Biochemical Nomenclature (1970). In the fully extended backbone, $\varphi_i = \psi_i = \omega_i = 180°$. Torsional angles in the side chains are represented by χ_{ij}.
The estimated standard deviations are near 1·0°.

	L-Pro 1	L-Val 2	L-Phe 3	L-Phe 4	L-Ala 5	Gly 6
$\varphi_i(N_i-C_i^\alpha)$	−74 (−77)	−121 (−128)	−127 (−121)	60 (54)*	−86 (−88)	−91 (−84)
$\psi_i(C_i^\alpha-C_i')$	−10 (−7)	−52 (−46)	144 (137)	−122 (−118)*	−5 (−4)	−176 (−173)
$\omega_i(C_i'-N_{i+1})$	179 (177)	−176 (−175)	170 (174)	180 (180)	−179 (177)	−179 (−178)†
$\chi_{i1}(N_iC_i^\alpha C_i^\beta C_i^\gamma)$	18 (26)	−51 (−55)	−61 (−53)	−57 (−64)		
		−173 (176)				
$\chi_{i2}(C_i^\alpha C_i^\beta C_i^\gamma C_i^\delta)$	−24 (−37)		−65 (−66)	−73 (−80)		
$\chi_{i3}(C_i^\beta C_i^\gamma C_i^\delta N_i)$	20 (33)					
$\chi_{i4}(C_i^\gamma C_i^\delta N_i C_i^\alpha)$	−8 (−18)					
$C_i^\delta N_i C_i^\alpha C_i^\beta$	−6 (−5)					

* Note that residues 4 and 5 are both L but they form a β-bend with angles characteristic for a D,L bend rather than an L,L bend.
† For $i = 6$, N_{i+1} is N_1.

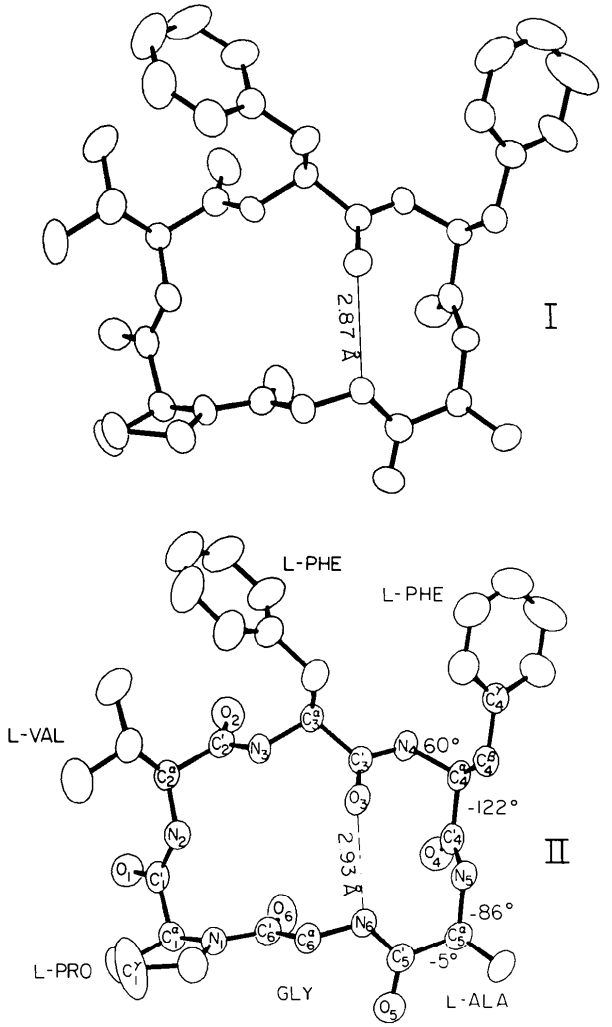

Fig. 1. Computer drawings of the conformations of *cyclo*(-L-Pro-L-Val-L-Phe-L-Phe-L-Ala-Gly-) in two different crystal forms. Top: form I; bottom: form II. The thermal ellipsoids are drawn at the 50% probability level (*ORTEP*; Johnson, 1965).

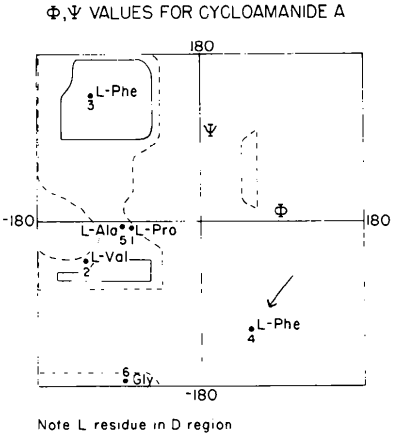

Fig. 2. The φ_i and ψ_i torsional angles for *cyclo*(-L-Pro-L-Val-L-Phe-L-Phe-L-Ala-Gly-) on a φ,ψ plot where the solid and dashed lines represent fully and partially allowed conformational regions for L residues (Ramachandran & Sasisekharan, 1968).

obviously *transoid* rather than in the expected *cis* conformation. At least two other structures have been reported in which a type II bond occurred where type I was expected, or *vice versa* (Hossain & van der Helm, 1978; Aubry, Protas, Boussard & Marraud, 1977). In the above structures the aberrant peptide residue was Ala. The present structure represents an example in which a much larger side group, *i.e.* Phe, has forbidden conformational angles and is involved in an aberrant type of hydrogen bond.

In the calculation of the allowable regions for the φ,ψ map, limiting factors were the minimum interatomic distances between pairs of atoms. The normal limits for C···N and C···C were assigned 2·9 and 3·0 Å, respectively, and the 'extreme' limits were 2·8 and 2·9 Å for C···N and C···C (Ramachandran & Sasisekharan, 1968). In the present structure, C_4^β in the aberrant Phe^4 residue is at a distance of only 2·84 Å

from N_5. To achieve a separation even as large as 2·84 Å required an increase of 2–4° in the values for the $C_4'C_4^{\alpha}C_4^{\beta}$ and $C_4^{\alpha}C_4'N_5$ angles from the average values that have been observed in other peptides and those that have been used theoretically for the calculation of the allowable regions in the φ,ψ map. Another rather short approach of 2·98 Å, although allowable, occurs between C_4^{γ} and N_4. There is no difficulty in building a space-filling model of this molecule.

Thermal parameters for the peptide atoms, represented by ellipsoids at the 50% probability level in Fig. 1, are similar in both crystal forms except for atom C_1^{γ} in the Pro[1] residue. In form I, the pyrrolidine ring has an envelope conformation with C_1^{γ} *endo* with respect to N_2. In form II, atom C_1^{γ} has a very elongated thermal ellipsoid that indicates more than one position for this atom and therefore more than one conformation for the pyrrolidine ring. The coordinates for the C_1^{γ} atom represent a weighted, averaged position for the multiple conformations. These coordinates do not represent a real conformation and consequently do not yield physically meaningful parameters such as bond lengths and bond angles (marked by asterisks in Table 2). Furthermore, the coordinates of C_1^{γ} are used to calculate the torsional angles χ_{11} to χ_{14} that yield an apparently flatter pyrrolidine ring than the envelope conformation in form I, as shown by the smaller χ_{1j} magnitudes in Table 3. There undoubtedly is considerable contribution to the averaged conformation from an envelope conformation with the C_1^{γ} atom *exo* with respect to N_2.

Crystal packing

Peptide columns. The arrangements of the peptide and solvent molecules in forms I and II are shown in the sterodiagrams in Fig. 4. Peptide molecules are arranged in the same manner in both crystal forms, *i.e.* molecules are stacked over each other in the **c** direction. A twofold screw axis that passes through the interior of the peptide backbone rings relates the adjacent molecules. The rigidity of the columns is enhanced not only by the intramolecular hydrogen bond, $N_6H\cdots O_3$, but also by hydrogen bonds between adjacent molecules in a stack. There are direct hydrogen bonds between $N_5H\cdots O_1$ atoms. Additionally there is an embedded water molecule, labeled *A* in Fig. 4, that participates in four hydrogen bonds. Water *A* is an acceptor for hydrogen bonds with N_2 and N_3 from one peptide molecule and a donor to O_4 and O_6 of an adjacent molecule in the stack. Hydrogen-bond lengths are given in Table 4. The embedded water provides a means for hydrogen bonding in a region where the amide and carbonyl groups of a peptide are surrounded by bulky hydrophobic side groups.

Solvent structure. The principal difference between the two crystal forms occurs in the spacing of the peptide columns in the **a** direction, Fig. 4. This spacing appears to be dependent upon the nature of the solvent that cocrystallizes between the peptide columns. In form I, the three water molecules *B*, *C* and *D* wind around a twofold screw axis to form a helix, parallel to the peptide columns, in which there are hydrogen bonds connecting the adjacent water molecules: $B\rightarrow C\rightarrow D\rightarrow B'\rightarrow C'$, *etc.* Additionally, each of these water molecules also forms hydrogen bonds with atoms in the peptide columns, specifically $N_4H\rightarrow O_W(B)$, $O_W(C)\rightarrow O_2$ and $O_W(D)\rightarrow O_5$.

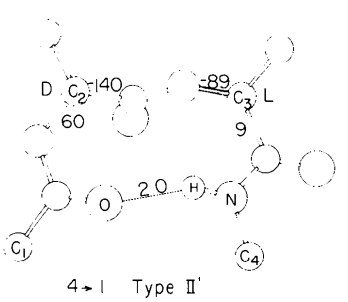

Fig. 3. An example of a typical type II′ β-bend drawn by computer from a selected structure determined by X-ray diffraction. The representative φ and ψ values (torsional angles about N—C^{α} and C^{α}—C′) are shown. Type II′ β-bends have a D,L sequence.

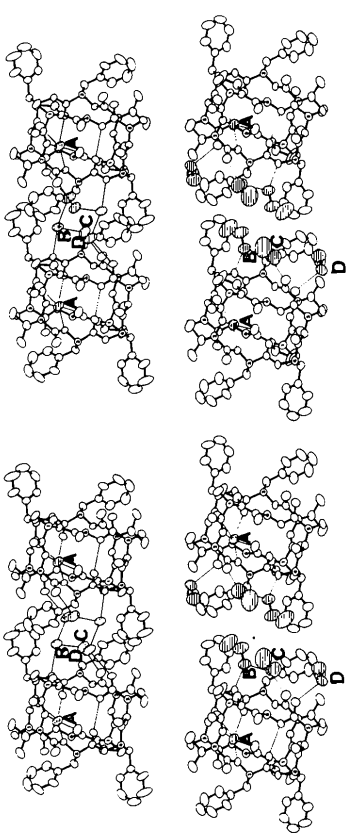

Fig. 4. A comparison of the stereodiagrams depicting the packing of form I with four H_2O solvent molecules (top) and of form II with one H_2O and three C_2H_5OH solvent molecules (bottom). The atoms in the solvent molecules are cross-hatched. On either side of the solvent structure are the columns of peptide molecules where the columns are related by one translation unit in the **a** direction. The two overlapped peptide molecules in each column are related by a twofold screw axis passing through the interior of the backbone rings. The axial directions are **a**→, **b**↑ and **c** is directed out of the page. Note that in form I the H_2O molecules have been relabeled from the previous publication: $W(1)\rightarrow O_W(4)$; $W(2)\rightarrow O_W(B)$; $W(3)\rightarrow O_W(D)$; and $W(4)\rightarrow O_W(C)$ (Chiang, Karle & Wieland, 1982).

Table 4. *Hydrogen bonds*

E.s.d.'s are 0·05, 0·05, 0·006 Å and 2°, respectively, for *D*—H, H···*A*, *D*···*A* and ∠*D*H···*A*.

Donor	Acceptor	*D*—H (Å)	H···*A* (Å)	*D*···*A* (Å)	∠*D*H···*A* (°)	Symmetry of acceptor*
N_2	$O_w(A)$	0·91	2·13	2·98	153	*a*
N_3	$O_w(A)$	0·94	2·09	3·02	167	*a*
$O_w(A)$†	O_4			2·84		*b*
$O_w(A)$	O_6‡			2·72		*b*
N_4	O(*B*)	0·96	1·93	2·86	162	*c*
O(*B*)	O(*C*)	0·96	1·87	2·73	148	*a*
O(*C*)	O_2	0·89	2·02	2·88	165	*b*
O(*D*)	O_5	0·93	1·93	2·84	165	*a*
N_5	O_1	0·87	2·04	2·86	158	*b*
N_6§	O_3	0·87	2·12	2·93	152	*a*

* Where $a = x, y, z$; $b = \frac{1}{2} - x, 1 - y, -\frac{1}{2} + z$; $c = \frac{1}{2} - x, 1 - y, \frac{1}{2} + z$.

† The H atoms were not located on $O_w(A)$.

‡ In the paper for form I (Chiang, Karle & Wieland, 1982) there is a misprint in Table 4 where O_2 should be O_6.

§ Intramolecular.

Form II contains three ethanol molecules rather than the water molecules *B*, *C* and *D* of form I. The O atoms of the ethanol molecules are labeled *B*, *C* and *D* in the lower diagram of Fig. 4. The ethanol O atoms form hydrogen bonds with the peptides, specifically $N_4H \rightarrow O(B)$, $O(C) \rightarrow O_2$ and $O(D) \rightarrow O_5$, in a fashion analogous to form I. Further, the proton on O(*B*) is donated to form a hydrogen bond with O(*C*) of ethanol *C*. The hydrophobic termini of the ethanol molecules are directed to the space between the peptide columns. The increase of 3·4 Å in the length of the *a* axis is accounted for by the space occupied by the C_2H_5 moieties.

Aside from hydrogen bonds and the immediate vicinity around them, there are only three approaches between ethanol molecules and their nearest neighbors that are less than 3·94 Å. They are $C(2B)\cdots C^{\varepsilon}_{32}$ (3·86 Å), C(1*C*)···C(1*D*) (3·69 Å) and $C(1C)\cdots C^{\alpha}_{6}$ (3·86 Å). The large thermal parameters associated with the C_2H_5 moieties are correlated with weak intermolecular attractions and consequently the large space in the cell surrounding the C_2H_5 chains.

The packing motifs in forms I and II suggest that in the crystallization process there is an initial association of peptide molecules into columns where the peptide molecules are related by a twofold screw symmetry. Subsequently solvent is attracted to the polar groups on the periphery of the columns. If the initial attraction involves an H_2O molecule, then the crystal proceeds to grow in form I; whereas if by chance the initial attraction is to the hydroxyl of an ethanol, then form II ensues. In either case, the conformation of the peptide is independent of the solvent.

This research was supported in part by NIH grant GM30902. We thank Professor Th. Wieland for the sample of cycloamanide A.

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