La Fig. 2 représente la projection de la structure sur le plan (010). Un réseau de liaisons hydrogène et de contacts de van der Waals est responsable de la cohésion cristalline (Tableau 4).

Les molécules s'étendent parallèlement à la rangée [101]. Dans cette direction, deux molécules voisines sont reliées entre elles soit par deux ponts hydrogène faisant intervenir chacun un ion chlore: N(12^{i})—Cl(25^{ii}) à laquelle participe H(121^{i}) [N(12^{i})—H(121^{i})$\cdots$Cl(25^{ii}) = 153,0 (3)°] et O(10^{i})—Cl(25^{iii}) à laquelle participe H(100^{i}) [O(10^{i})—H(100^{i})$\cdots$Cl(25^{iii}) = 174,0 (4)°], soit par un contact de van der Waals: O(17^{i})—C(15^{iv}).

Quant à la troisième liaison hydrogène, elle affecte deux molécules se déduisant par une période suivant **b**: O(21^{i})—N(19^{ii}) à laquelle participe H(190^{ii}) [O(21^{i})$\cdots$H(190^{ii})—N(19^{ii}) = 166;0 (4)°].

Il vient d'être montré récemment que les conformations cristallines des dérivés adrénolytiques β de synthèse correspondent toujours à des conformations priviligiées (c'est-à-dire à des énergies conformationnelles minimales) (Gadret *et al.*, 1978). La conformation du chlorhydrate d'acébutolol est comparable à celle des autres AOPA adrénolytiques β déjà étudiés et elle ne saurait à elle seule expliquer l'action spécifique de ce médicament sur les récepteurs β_1. Il semble donc possible d'admettre que la nature et l'encombrement stérique des substituants portés par C(2) et C(4) aient une importance primordiale dans l'explication de cette spécificité.

Les auteurs remercient les laboratoires Rhône–Poulenc qui leur ont fourni l'échantillon étudié.

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Methyl L-Alanyl-*O*,*N*-dimethyl-L-tyrosyl-L-alanate

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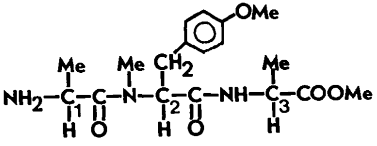
Abstract. $C_{18}H_{27}N_3O_5$, $M_r = 365{\cdot}4$, monoclinic, $P2_1$ (systematic absences $0k0$, k odd), $a = 12{\cdot}581$ (9), $b = 6{\cdot}265$ (3), $c = 13{\cdot}095$ (7) Å, $\beta = 106{\cdot}36$ (5)°, $Z = 2$, $D_c = 1{\cdot}18$ Mg m^{-3}. The structure was refined to a final R of 0·048 for 1639 reflections. This tripeptide crystallizes with a *cis* 1,2-peptide bond and has a new type of intramolecular hydrogen bond for a peptide: from the 3-NH to the 1-amino group, forming an eight-membered ring.



(I)

Introduction. In a preparation of the title compound (I) as an intermediate in the synthesis of the antitumor agents bouvardin and deoxybouvardin (Jolad *et al.*, 1977), we obtained a nicely crystalline substance which in chloroform-*d* solution showed two sets of ^{1}H NMR peaks indicating the presence of two species in approximately equal amounts. To determine whether these two species were diastereomers from an undesired epimerization during the synthesis or (more likely) *cis* and *trans* isomers about the 1,2-peptide bond (Hruby, 1974) and to learn why, unlike most tripeptides, this substance crystallizes well, we subjected it to an X-ray study.

A crystal 0·2 × 0·3 × 0·5 mm grown from benzene was used. A Syntex $P2_1$ diffractometer with a graphite

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monochromator (Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å) and pulse-height analyzer was used for preliminary pictures and intensities. Systematic absences defined space group $P2_1$, with cell constants $a = 12{\cdot}581$ (9), $b = 6{\cdot}265$ (3), $c = 13{\cdot}095$ (7) Å, and $\beta = 106{\cdot}36$ (5)° determined by least-squares treatment of 20 reflections; with $Z = 2$, $D_c = 1{\cdot}18$ Mg m^{-3}. Intensities were collected using 2° θ–2θ scans with variable scan rate 2·0 to 29·3° min^{-1} in 2θ and background to scan time ratio 1·0. 1940 independent reflections with $2\theta < 50°$ were measured, of which 1639 with $I > 3\sigma(I)$ were considered observed. There were no significant variations in the intensities of three check reflections monitored every 100 reflections. Lorentz and polarization corrections were applied, but no correction was made for absorption.

The crystal structure was solved by direct methods with *MULTAN* (Germain, Main & Woolfson, 1971). The *E* map revealed all nonhydrogen atoms. Full-matrix least-squares refinement in which positional and isotropic thermal parameters were varied reduced *R* to 0·112. Anisotropic refinement brought *R* to 0·069. The H positions were calculated, and their inclusion with the last isotropic temperature factors of the attached atom in further refinements of nonhydrogen-atom parameters reduced *R* to 0·048. Refinement was terminated at this stage since the ratios of shifts in parameters to estimated standard deviations were <0·2. The refinement was based on F_o, the quantity minimized being $\sum w(F_o - F_c)^2$. The scattering factors used were those of Hanson, Herman, Lea & Skillman (1964).*

Discussion. The final atomic coordinates and thermal parameters are given in Table 1, with standard deviations taken from the least-squares matrix. Table 2 gives bond lengths, Table 3 bond angles, and Table 4 selected torsion angles. Fig. 1 depicts a molecule with thermal ellipsoids and Fig. 2 shows the molecular packing. The absolute configuration was not determined crystallographically but is assumed as the preparation was from L-amino acids; the X-ray study shows all three amino acids to have the same configuration. The 1,2-peptide bond is *cis* in the crystals, and the two substances seen by NMR in about equal amounts on dissolution of these crystals in chloroform must be the *cis* and *trans* isomers about this bond since epimerization at a chiral center in this compound under these conditions is unreasonable.

Table 1. *Positional parameters* (×10^4; *for* H ×10^3) *with estimated standard deviations in parentheses*

	x	*y*	*z*		*x*	*y*	*z*
O(1)	5670 (2)	−2406 (5)	−1099 (2)	H(1)N(1)	536	−712	0
O(2)	9783 (2)	−5271 (6)	860 (2)	H(2)N(1)	589	−902	−55
O(3)	8540 (4)	−10373 (7)	2227 (3)	HN(3)	745	−705	80
O	9483 (3)	−8732 (7)	3697 (2)	HC(1α)	608	−692	−185
N(1)	5934 (2)	−7470 (6)	−366 (2)	H(1)C(1β)	410	−519	−150
N(2)	7358 (2)	−3832 (5)	−754 (2)	H(2)C(1β)	416	−740	−214
N(3)	8205 (2)	−6511 (7)	1146 (2)	H(3)C(1β)	442	−512	−263
C(1)	6252 (3)	−3983 (6)	−1061 (2)	H(1)C(N2)	768	−132	25
C(1α)	5731 (3)	−6200 (6)	−1348 (3)	H(2)C(N2)	865	−176	−33
C(1β)	4498 (3)	−5972 (8)	−1954 (4)	H(3)C(N2)	748	−65	−99
C(2)	8812 (3)	−5784 (6)	528 (3)	HC(2α)	772	−698	−86
C(N2)	7830 (3)	−1713 (6)	−430 (3)	H(1)C(2β)	949	−648	−119
C(2α)	8143 (3)	−5620 (6)	−641 (3)	H(2)C(2β)	920	−394	−134
C(2β)	8876 (3)	−5413 (7)	−1395 (3)	HC(2δ1)	761	−274	−285
C(2γ)	8192 (3)	−5815 (7)	−2530 (3)	HC(2δ2)	861	−899	−255
C(2δ1)	7554 (4)	−4227 (7)	−3137 (3)	HC(2ε1)	636	−348	−457
C(2δ2)	8137 (3)	−7840 (7)	−2972 (3)	HC(2ε2)	743	−973	−429
C(2ε1)	6838 (4)	−4626 (8)	−4141 (3)	H(1)C(2θ)	582	−440	−626
C(2ε2)	7455 (4)	−8266 (7)	−3980 (3)	H(2)C(2θ)	494	−631	−681
C(2ζ)	6790 (4)	−6659 (8)	−4556 (3)	H(3)C(2θ)	486	−522	−570
O(2η)	6100 (3)	−7249 (6)	−5534 (2)	HC(3α)	928	−565	254
C(2θ)	5384 (4)	−5685 (11)	−6119 (4)	H(1)C(3β)	747	−408	250
C(3)	8858 (4)	−8793 (8)	2694 (3)	H(2)C(3β)	707	−654	260
C(3α)	8594 (3)	−6554 (8)	2295 (3)	H(3)C(3β)	806	−549	356
C(3β)	7734 (4)	−5575 (9)	2767 (4)	H(1)Me	903	−1150	422
Me	9739 (6)	−10761 (12)	4239 (4)	H(2)Me	1019	−1046	502
				H(3)Me	1023	−1160	391

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33850 (9 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å) *with estimated standard deviations in parentheses*

		Averages
C(1)–O(1)	1·222 (5)	1·205
C(2)–O(2)	1·219 (4)	
C(3)–O(3)	1·173 (6)	
C(1)–C(1α)	1·536 (5)	1·522
C(2)–C(2α)	1·529 (4)	
C(3)–C(3α)	1·501 (7)	
C(1)–N(2)	1·338 (4)	1·338
C(2)–N(3)	1·339 (5)	
C(1α)–N(1)	1·472 (5)	1·463
C(2α)–N(2)	1·473 (5)	
C(3α)–N(3)	1·445 (5)	
C(1α)–C(1β)	1·538 (5)	1·531
C(2α)–C(2β)	1·535 (6)	
C(3α)–C(3β)	1·519 (7)	
C(3)–O	1·328 (5)	
Me–O	1·447 (8)	
C(N2)–N(2)	1·467 (5)	
C(2β)–C(2γ)	1·515 (5)	
C(2γ)–C(2δ1)	1·381 (6)	1·385
C(2γ)–C(2δ2)	1·388 (6)	
C(2δ1)–C(2ε1)	1·391 (6)	
C(2δ2)–C(2ε2)	1·383 (6)	
C(2ε1)–C(2ζ)	1·380 (7)	
C(2ε2)–C(2ζ)	1·388 (6)	
C(2ζ)–O(2η)	1·379 (5)	
C(2θ)–O(2η)	1·403 (7)	

Table 3. *Bond angles* (°) *with estimated deviations in parentheses*

O(1)–C(1)–C(1α)	120·8 (3)	C(2)–C(2α)–C(2β)	112·9 (4)
O(2)–C(2)–C(2α)	123·6 (4)	N(2)–C(2α)–C(2β)	112·3 (4)
O(3)–C(3)–C(3α)	126·7 (5)	C(2α)–C(2β)–C(2γ)	109·8 (4)
O(1)–C(1)–N(2)	121·0 (3)	C(2β)–C(2γ)–C(2δ1)	121·5 (4)
O(2)–C(2)–N(3)	124·0 (4)	C(2β)–C(2γ)–C(2δ2)	120·6 (4)
O(3)–C(3)–O	124·0 (5)	C(2δ1)–C(2γ)–C(2δ2)	117·8 (4)
N(2)–C(1)–C(1α)	118·2 (3)	C(2γ)–C(2δ1)–C(2ε1)	122·1 (5)
N(3)–C(2)–C(2α)	112·4 (4)	C(2γ)–C(2δ2)–C(2ε2)	121·2 (5)
O–C(3)–C(3α)	109·2 (5)	C(2ζ)–C(2ε1)–C(2δ1)	118·9 (5)
C(1α)–N(1)–H(1)N(1)	109	C(2ζ)–C(2ε2)–C(2δ2)	119·7 (5)
C(1α)–N(1)–H(2)N(1)	109	C(2ε1)–C(2ζ)–C(2ε2)	120·2 (5)
H(1)N(1)–N(1)–H(2)N(1)	109	C(2ε1)–C(2ζ)–O(2η)	124·0 (4)
C(1)–C(1α)–N(1)	108·5 (3)	C(2ε2)–C(2ζ)–O(2η)	115·8 (4)
C(1)–C(1α)–C(1β)	109·9 (3)	C(2ζ)–O(2η)–C(2θ)	117·3 (4)
N(1)–C(1α)–C(1β)	113·7 (3)	C(2)–N(3)–C(3α)	123·5 (4)
C(1)–N(2)–C(N2)	116·9 (4)	C(3)–C(3α)–N(3)	110·9 (4)
C(1)–N(2)–C(2α)	126·0 (4)	C(3)–C(3α)–C(3β)	110·4 (5)
C(N(2))–N(2)–C(2α)	117·0 (4)	N(3)–C(3α)–C(3β)	110·2 (4)
C(2)–C(2α)–N(2)	108·4 (4)	C(3)–O–Me	116·6 (5)

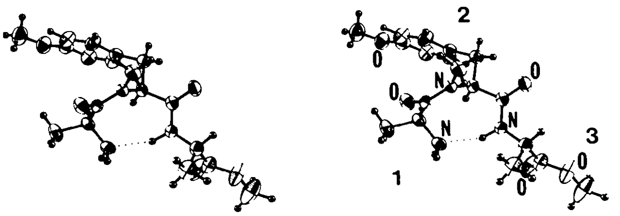

Fig. 1. Stereoscopic view of a single molecule, with 50% probability thermal ellipsoids for non-hydrogen atoms and spheres for H atoms.

Table 4. *Selected torsion angles*

	Kendrew symbol*	Angle (°)
N(1)–C(1α)–C(1)–N(2)	ψ_1	70
N(2)–C(2α)–C(2)–N(3)	ψ_2	71
N(3)–C(3α)–C(3)–O	ψ_3	163
C(1)–N(2)–C(2α)–C(2)	φ_2	−116
C(2)–N(3)–C(3α)–C(3)	φ_3	−107
C(1α)–C(1)–N(2)–C(2α)	ω_2	−1
C(2α)–C(2)–N(3)–C(3α)	ω_3	−172
N(2)–C(2α)–C(2β)–C(2γ)	χ_1	−71
C(2)–C(2α)–C(2β)–C(2γ)	χ_2	166
C(2θ)–O(2η)–C(2ζ)–C(2ε1)	–	−2

* Hruby (1974).

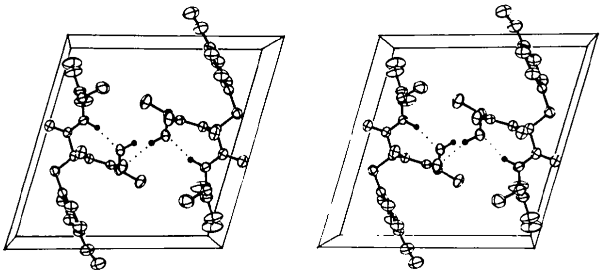

Fig. 2. Stereoscopic view of a unit cell, *b* axis projection, *a* axis horizontal; the cell depicted is shifted for clarity 0·5 in *c* from that used for the tables

The intramolecular hydrogen bond in this molecule, shown by a dotted line in Fig. 1, goes from the NH in the 3-amino acid to the N in the terminal amino group, forming an eight-membered ring [N(1)–N(3), 3·04 Å]. To our knowledge this is unprecedented, and does not occur in the peptides previously studied by X-ray crystallography, even those in which the 2-amino acid is proline and could thus reasonably have a *cis*-1,2-peptide bond (Benedetti, 1977). It is interesting to note that the peptide bond found to be *cis* in this synthetic intermediate is *trans* in crystalline bouvardin (Jolad *et al*., 1977). It will be interesting to observe the stereochemistry of this bond in further acyclic synthetic intermediates to the cyclic natural products.

Intermolecular hydrogen bonds from the amine NH protons to the carbonyl O atoms of the 1-amino acids in adjacent molecules serve to connect molecules in the crystal. One of these bonds, to the other molecule in the cell depicted, is shown as a dotted line in Fig. 2 [this N(1)–O(1) is 3·15 Å]; the other is approximately parallel to the *b* axis and joins molecules in the *y* direction [this N(1)–O(1) is 3·23 Å].

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N-(1-Phenyl-1-phospholanio)-4-nitroanilide

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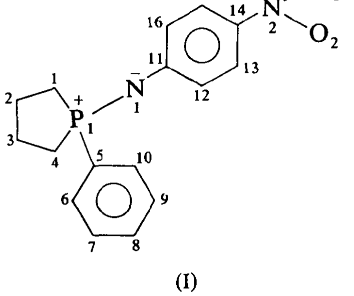
Abstract. $C_{16}H_{17}N_2O_2P$, M_r = 300·31, monoclinic, $P2_1/c$, a = 9·69 (3), b = 16·34 (4), c = 10·82 (4) Å, β = 117·90 (3)° from diffractometer measurements (Mo $K\bar{\alpha}$ radiation), V = 1513·7 Å^3, Z = 4, D_c = 1·317 Mg m^{-3}, $F(000)$ = 632, μ = 0·145 mm^{-1}. The heterocyclic ring has an irregular conformation.

Introduction. The title compound (I) was recrystallized from a benzene–ether mixture. It was hygroscopic, and a crystal 0·6 mm long, sealed in a Lindemann-glass capillary, was used for all measurements. Systematic absences (from precession photographs) $h0l$: $l = 2n + 1$, $0k0$: $k = 2n + 1$ indicated space group $P2_1/c$. Data were collected for $hk0$–10 with $\theta_{\max}$ = 25° on a Stoe STADI-2 two-circle diffractometer (graphite-monochromated Mo $K\bar{\alpha}$ radiation). This gave 2136 data of which 1357 unique reflexions with $I > 3\sigma(I)$ were used in subsequent calculations. Lorentz and polarization corrections (but none for extinction or absorption) were applied, and the data scaled by a Wilson plot. The structure was solved by direct methods with *SHELX*76 (Sheldrick, 1976), which was used for all calculations. Complex neutral-atom scattering factors were taken from *International Tables for X-ray Crystallography* (1974). Full-matrix least-squares refinement (including isotropic H atoms) converged at R = 0·047 for 1357 observed reflexions ($R = \sum||F_o| - |F_c||/\sum|F_o|$). In the final cycle all shifts in parameters were less than their e.s.d.'s. Positional parameters are given in Table 1, bond distances and angles in Table 2.*

Discussion. The structure determination (Fig. 1) was undertaken to investigate ring strain (Cadogan, Gosney



(I)

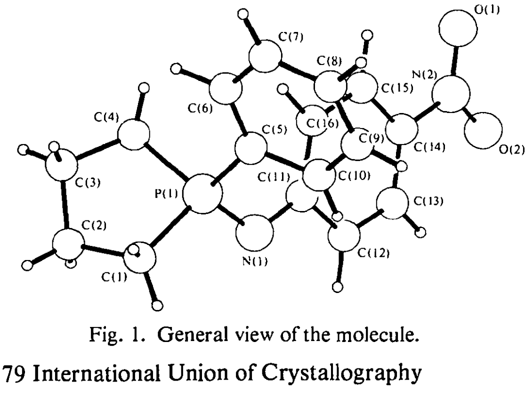


Fig. 1. General view of the molecule.

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* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33854 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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