

Fig. 2. Projection of the crystal structure of 4'-amino-2,2,3'-trichloroacetophenone down the *a* axis.

The small dihedral angle (1.091°) between the least-squares planes of the phenyl ring and the acetyl group [C(4), C(7), O(1), C(8)] also indicates a strong conjugation.

The increase in the C(7)–C(8) bond distance in the present structure compared to that in *p*-aminoacetophenone [$1.498(6) \text{ \AA}$] can be explained as the effect of substitution at C(8). This lengthening is also observed in the structure of chloramphenicol which has similar substitution (Chatterjee *et al.*, 1979; Ravindra Acharya *et al.*, 1979).

The coplanarity of the acetyl group with the phenyl ring results in a short C(5)–H(5)···O(1) contact [C(5)···O(1) = $2.790(8)$, H(5)···O(1) = 2.47 \AA , \angle C(5)–H(5)···O(1) = 94.96°].

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Cyclic Dipeptides Containing Proline. Structure and Conformation of *cyclo*-(L-Phe-L-Pro-), $C_{14}H_{16}N_2O_2$

BY F. MAZZA

Istituto di Strutturistica Chimica 'G. Giacomello' CNR, CP n. 10, 00016 Monterotondo Stazione, Roma, Italy

AND G. LUCENTE, F. PINNEN AND G. ZANOTTI

Istituto di Chimica Farmaceutica and Centro di Studio per la Chimica del Farmaco, Università di Roma, P. le A. Moro, 00185 Roma, Italy

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Abstract. $M_r = 244.3$, monoclinic, $P2_1$, $a = 10.789(2)$, $b = 10.061(2)$, $c = 5.668(3) \text{ \AA}$, $\beta = 92.70(3)^\circ$, $V = 614.6(4) \text{ \AA}^3$, $Z = 2$, $D_x = 1.32 \text{ Mg m}^{-3}$, $\lambda(\text{Mo } K\alpha) = 0.71069 \text{ \AA}$, $\mu = 0.1 \text{ mm}^{-1}$, $F(000) = 260$, room tem-

perature, final $R = 0.038$ for 1739 independent observed reflections. The diketopiperazine ring has a pronounced boat conformation with equatorial C^β atoms. The degree of folding along the line joining the two C^α

Of the two amino H atoms only one, H(N)1, takes part in an intermolecular N(amino)–H···O(carboxyl) hydrogen bond [N(1)–H(N)1 = 0.98 , N(1)–O(1) = $2.959(7)$, H(N)1···O(1) = 2.12 \AA , \angle N(1)–H(N)1···O(1) = 143°].

In packing (Fig. 2) a partial overlapping of the phenyl ring is observed. The dichloroacetyl group and the chlorine substituent at C(6) form bands extending along the *b* axis.

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atoms has the highest value so far encountered: $\beta = 50.7 (1)^\circ$ and the distance between the two H(C $^\alpha$) atoms is 2.37 (6) Å. One of the two peptide bonds deviates slightly from planarity: $\omega_1 = -4.5 (4)^\circ$. The pyrrolidine ring assumes a C $_2$ -C $_{endo}^\beta$ -C $_{exo}^\gamma$ half-chair conformation. The benzyl side chain is extended to nitrogen, in a conformation analogous to that found for the preferred rotamer in chloroform solution. The crystal packing is characterized by a hydrogen bond between the phenylalanine NH and CO groups of screw-related molecules.

Introduction. Cyclic dipeptides (2,5-diketopiperazines; DKP's), both in the solid state and in solution, are extensively used as suitable models to gain information on more complex peptides and proteins. A large amount of data has been obtained from studies on cyclic systems containing amino acids with aromatic side chains and/or cyclic imino acids; the constraint imposed by the presence of an additional ring and the possible interaction of the aromatic side chain with the peptidic bonds have focused attention on these models. As a continuation of our studies in this field (Cerrini, Fedeli, Lucente, Mazza, Pinnen & Zanotti, 1984) we report here the crystal and molecular structure of *cyclo*(-L-Phe-L-Pro-). This compound contains the residues of two of the most common and studied natural amino acids of the above-cited type; its structure and conformational parameters can then be usefully related to a very large number of peptidic systems.

Experimental. Title compound was prepared by deprotection of *tert*-butoxycarbonyl-L-phenylalanyl-L-proline methyl ester and acetic-acid-catalyzed cyclization of the dipeptide ester (Suzuki, Sasaki, Endo & Mihara, 1981). Thus, absolute configuration of the title compound is that, assigned on a chemical basis, of the ester used in the preparation.

Single crystals suitable for X-ray analysis obtained from an aqueous solution by slow evaporation. Approximate unit-cell dimensions and space group determined from oscillation and Weissenberg photographs; crystal 0.5 × 0.4 × 0.15 mm, automatic Syntex P2 $_1$ diffractometer, graphite monochromator, Mo K α radiation. Unit-cell parameters: least-squares fit of angular settings of 15 reflections in range $5 < \theta < 20^\circ$; h 0→15, k 0→14, l -7→7, ω -scan technique; three standard reflections 060, 332 and 141 measured after 97 showed only small deviations from means; 1895 independent reflections recorded, 1739 with $I > 2.0\sigma(I)$ considered observed and used for calculations. Lorentz and polarization corrections applied, no correction for extinction or absorption. Structure solved by MULTAN80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980), 222 reflections and 2112 Σ_2 relationships used in phase-determining procedure;

E map computed with phases of set with highest figures of merit revealed all non-H positions, refined isotropically then anisotropically by full-matrix least squares; $\sum w(|F_o| - |F_c|)^2$ minimized, $w = (a + |F_o| + c|F_c|^2)^{-1}$, with $a = 2F_o(\text{min.})$ and $c = 2/F_o(\text{max.})$. Difference Fourier map showed all H atoms in stereochemically feasible positions, H-atom positional parameters and isotropic thermal parameters derived from those of the carrier atoms included and held fixed in refinement. In final refinement cycle $(\Delta/\sigma)_{\text{max}} = 0.001$, $S = 0.3$, number of parameters refined 162; max. height in final difference Fourier synthesis 0.1 e Å $^{-3}$, final $R = 0.038$, $R_w = 0.054$, scattering factors from *International Tables for X-ray Crystallography* (1974).

Table 1. Final fractional coordinates and B_{eq} values of the non-H atoms with e.s.d.'s in parentheses

$$B_{\text{eq}} = \frac{1}{3} \sum_i \sum_j b_{ij} a_i \cdot a_j$$

	x	y	z	$B_{\text{eq}}(\text{\AA}^2)$
O $_1$	0.4429 (1)	0.2364 (4)	0.8061 (3)	3.6 (1)
C $_1^1$	0.4496 (2)	0.3419 (4)	0.6990 (4)	2.7 (1)
N $_1$	0.5017 (2)	0.5753 (4)	0.7586 (3)	2.9 (1)
C $_2^1$	0.5560 (2)	0.4429 (4)	0.7304 (3)	2.6 (1)
C $_1^\beta$	0.6504 (2)	0.4091 (4)	0.9286 (4)	3.2 (1)
C $_2^\beta$	0.7748 (2)	0.4716 (4)	0.8973 (3)	2.9 (1)
C $_1^{\beta 1}$	0.8426 (2)	0.4394 (4)	0.7015 (4)	3.8 (1)
C $_1^{\beta 2}$	0.8263 (2)	0.5620 (5)	1.0600 (4)	3.8 (1)
C $_1^{\beta 1}$	0.9570 (2)	0.4985 (5)	0.6695 (5)	4.8 (1)
C $_2^{\beta 2}$	0.9404 (3)	0.6201 (5)	1.0249 (5)	4.7 (1)
C $_1^1$	1.0052 (2)	0.5893*	0.8316 (6)	4.0 (1)
O $_2$	0.3567 (2)	0.7232 (4)	0.6175 (3)	3.8 (1)
C $_2^1$	0.4099 (2)	0.6165 (4)	0.6066 (3)	2.7 (1)
N $_2$	0.3660 (2)	0.3825 (4)	0.5334 (3)	2.9 (1)
C $_2^2$	0.3771 (2)	0.5131 (4)	0.4198 (3)	2.6 (1)
C $_2^\beta$	0.2526 (2)	0.5309 (4)	0.2845 (4)	3.5 (1)
C $_3^\beta$	0.2121 (2)	0.3886 (4)	0.2302 (4)	3.8 (1)
C $_3^1$	0.2549 (2)	0.3110 (4)	0.4506 (4)	3.5 (1)

* This coordinate was held fixed during the refinement.

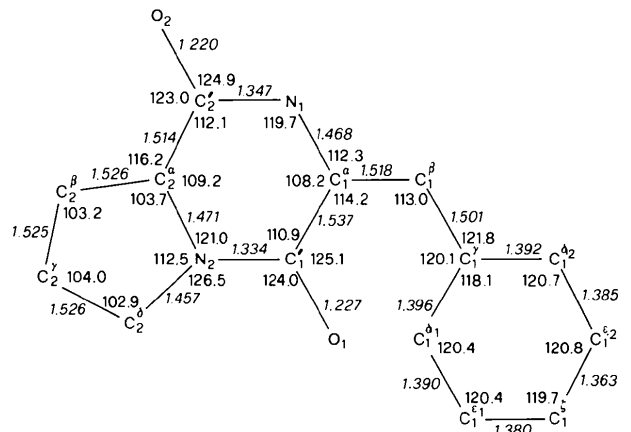


Fig. 1. Bond lengths (Å) and angles ($^\circ$) for the non-H atoms of *cyclo*(-L-Phe-L-Pro-). E.s.d.'s are in the ranges 0.003–0.006 Å for lengths and 0.2–0.3 $^\circ$ for angles.

Discussion. The final atomic parameters of *cyclo*(-L-Phe-L-Pro-) are given in Table 1;* bond lengths and valence angles involving non-H atoms are given in Fig. 1. The geometry of the molecule does not deviate significantly from that of *cyclo*(-D-Phe-L-Pro-) (Ramani, Venkatesan, Marsh & Hu Kung, 1976).

A stereochemical view of the molecule is shown in Fig. 2. The DKP ring assumes a pronounced boat conformation as shown by the unusually high values of the two pairs of ψ and ϕ torsion angles given in Table 2: these values are only a few degrees smaller than those of a cyclohexane boat form (Bucourt, 1974). Both C^β atoms are in equatorial positions and the $H(C^\alpha)$ atoms are axial. The ring is folded along the line joining the two C^α atoms and the degree of folding, expressed by β (Karle, 1981), is $50.7 (1)^\circ$: this value is the largest ever found for such ring systems with or without substituents on the amide N atoms (Radding, Donzel, Ueyama & Goodman, 1980); the highest values of β , in the range $37\text{--}41^\circ$ (Karle, 1981, and references quoted therein), have been found for DKP rings containing one proline residue or two 3,4-dehydropoline residues. The high degree of folding can be also evaluated by considering the displacements of C^α and C^β atoms from the least-squares plane of the other four ring atoms which are respectively $0.603 (4)$ and $0.551 (4) \text{ \AA}$; correspondingly the distance between the two axial $H(C^\alpha)$ atoms is reduced to $2.37 (6) \text{ \AA}$. This value approximates the sum of the van der Waals radii of H atoms (2.40 \AA) and indicates that the DKP conformation in *cyclo*(-L-Phe-L-Pro-) may represent an upper limit of the boat.

The pyrrolidine ring assumes the $C_2-C^\beta_{endo}-C^\gamma_{exo}$ (Madison, 1977) half-chair conformation, with the C^β and C^γ atoms $0.231 (4)$ and $-0.361 (4) \text{ \AA}$ respectively on opposite sides of the plane of the other three ring atoms.

* Lists of structure factors, anisotropic thermal parameters of non-H atoms and coordinates of H atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39648 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

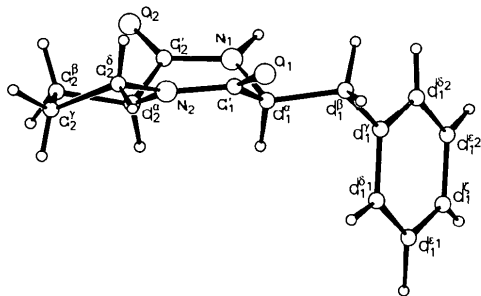


Fig. 2. A perspective view of the molecule showing the boat form of *cyclo*(-L-Phe-L-Pro-).

Table 2. Relevant torsion angles ($^\circ$) for *cyclo*(-L-Phe-L-Pro-) according to the convention of Klyne & Prelog (1960)

The e.s.d.'s are within the range $0.2\text{--}0.5^\circ$.

DKP ring		Proline ring	
$N_1-C_1-C_2-N_1$	ψ_1 49.9	$C_2^{\beta}-N_2-C_2^{\beta}-C_2^{\beta}$	θ_2 9.0
$C_1-C_1^{\alpha}-N_1-C_2^{\alpha}$	ϕ_1 -48.4	$N_2-C_2^{\alpha}-C_2^{\beta}-C_2^{\alpha}$	χ_2^1 -28.2
$C_1^{\alpha}-N_1-C_2^{\alpha}-C_2^{\beta}$	ω_2 -0.5	$C_2^{\alpha}-C_2^{\beta}-C_2^{\alpha}-C_2^{\beta}$	χ_2^2 37.3
$N_1-C_1^{\alpha}-C_2^{\alpha}-N_2$	ψ_2 46.2	$C_2^{\beta}-C_2^{\alpha}-C_2^{\beta}-N_2$	χ_2^3 -31.4
$C_1^{\alpha}-C_2^{\alpha}-N_2-C_1^{\alpha}$	ϕ_2 -44.4	$C_2^{\alpha}-C_2^{\beta}-N_2-C_2^{\alpha}$	χ_2^4 14.1
$C_2^{\alpha}-N_2-C_1^{\alpha}-C_2^{\alpha}$	ω_1 -4.5		
Phenylalanine residue		Peptide bonds	
$N_1-C_1^{\alpha}-C_1^{\beta}-C_1^{\gamma}$	χ_1^1 -79.7	$C_1^{\alpha}-N_1-C_1^{\alpha}-O_1$	178.3
$C_1^{\alpha}-C_1^{\beta}-C_1^{\gamma}-C_1^{\delta}$	θ_1^{\prime} 156.7	$C_2^{\alpha}-N_2-C_1^{\alpha}-C_2^{\alpha}$	178.0
$C_1^{\alpha}-C_1^{\beta}-C_1^{\gamma}-C_1^{\delta 1}$	$\chi_1^{1,1}$ -62.0	$C_2^{\alpha}-N_2-C_1^{\alpha}-O_1$	177.2
$C_1^{\alpha}-C_1^{\beta}-C_1^{\gamma}-C_1^{\delta 2}$	$\chi_1^{1,2}$ 118.3	$C_2^{\beta}-N_2-C_1^{\alpha}-O_1$	-0.3

The benzyl side chain is extended to nitrogen (Young, Madison & Blout, 1976) as shown by the χ_1^1 and $\chi_1^{1,2}$ torsion angles [$-79.7 (3)$ and $118.3 (3)^\circ$ respectively; see Table 2]. This conformation corresponds to that of the preferred rotamer in chloroform solution (Vicar, Budesinsky & Blaha, 1972; Young *et al.*, 1976) and is in good agreement with the second minimum of intramolecular potential energy computed for *cyclo*(-L-Phe-L-Pro-) (Madison, Young & Blout, 1976).

The crystal packing is characterized by a hydrogen bond of $2.988 (5) \text{ \AA}$ between the phenylalanine NH and CO groups of screw-related molecules, with an $H \cdots O_1(1-x, \frac{1}{2}+y, 2-z)$ contact of $2.14 (5) \text{ \AA}$ and $N-H \cdots O$ angle of $167 (2)^\circ$.

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