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Structure of *cyclo*(-L-Phenylalanyl-*N*-methyl-L-α-aminobutyryl-)*

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Abstract. 6-Ethyl-1-methyl-3-(phenylmethyl)-2,5-piperazinedione, $C_{14}H_{18}N_2O_2$, $M_r = 246{\cdot}3$, monoclinic, $P2_1$, $a = 14{\cdot}078$ (2), $b = 11{\cdot}297$ (2), $c = 8{\cdot}5080$ (8) Å, $\beta = 99{\cdot}26$ (1)°, $V = 1335{\cdot}4$ (3) Å^3, $Z = 4$, $F(000) = 528$, $D_x = 1{\cdot}22$ g cm^{-3}, λ(Cu $K\alpha$) = 1·54178 Å, $\mu = 5{\cdot}9$ cm^{-1}, room temperature, final $R = 0{\cdot}050$ for 1640 observed reflexions. Two crystallographically independent molecules adopt a conformation in which both α-amino-acid side chains are folded above the 2,5-diketopiperazine ring [$\chi_1^1 = 56{\cdot}7$ (5), $\chi_2^1 = 57{\cdot}2$ (5) for molecule *A* and $\chi_1^1 = 64{\cdot}0$ (6), $\chi_2^1 = 58{\cdot}3$ (6)° for molecule *B*]. The 2,5-diketopiperazine ring is only slightly buckled.

Introduction. It is a well known phenomenon that the aromatic part of an amino-acid residue will tend to fold over the 2,5-diketopiperazine ring (hereafter DKP) of cyclic dipeptides whenever possible. On the other hand, ^{1}H NMR studies of *cis* *N*-monosubstituted cyclic dipeptides (Liberek, Bednarek, Kitowska & Macikowska, 1977) indicated that due to Pitzer strain a side chain of an *N*-substituted amino-acid residue has a preference to fold over the DKP skeleton and that in solution the DKP ring adopts a boat conformation with the α-amino-acid side chains in quasiaxial positions. Hence in *cyclo*(-L-phenylalanyl-*N*-methyl-L-α-aminobutyryl) {*cyclo*[-L-Phe-L-*N*(Me)-Abu-]} both amino-acid side chains should compete for space over the DKP ring. It was shown by ^{1}H NMR (Liberek *et al.*, 1977) that the form predominant in solution has the aliphatic side chain in the folded conformation.

The present crystal structure analysis of *cyclo*-[-L-Phe-L-*N*(Me)-Abu-] has been performed to find out if the preference of the *N*-substituted amino-acid residue to fold over the DKP ring will be preserved in the solid state.

Experimental. Colorless crystal of dimensions 0·08 × 0·3 × 0·4 mm from methanol–water, D_m not determined, Syntex $P2_1$ diffractometer, graphite-monochromatized Cu $K\alpha$ radiation, lattice parameters for 15 reflexions with 2θ in range 15–23°, profiles measured for 1888 reflexions with $2\theta \leq 115°$ (h 0→15, k 0→12, l −9→9), ω–2θ scan technique, variable scan rate, profile analysis according to Lehmann & Larsen (1974), no significant intensity variation for two standard reflexions, absorption ignored, 1647 reflexions with $I \geq 2\sigma(I)$; structure solved by direct methods with *MULTAN*78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); anisotropic full-matrix least-squares refinement on F with *SHELX*76 (Sheldrick, 1976), unit weights, H atoms bonded to N located on a ΔF map, the remaining H atoms placed in calculated positions, methyl residues refined as rigid groups, other H atoms not refined, $R = 0{\cdot}050$ and $wR = 0{\cdot}049$, seven F_o with large $\Delta F/\sigma(F)$ omitted from last cycles; max. Δ/σ in the last cycle < 0·4, no peaks higher than 0·19 e Å^{-3} and lower than −0·22 e Å^{-3} on

Table 1. *Final fractional coordinates and equivalent isotropic thermal parameters* (Å^2)

U_{eq} is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(2*A*)	−0·2111 (4)	−0·7406	−0·1982 (6)	0·058 (2)
C(3*A*)	−0·3086 (5)	−0·7601 (7)	−0·2394 (8)	0·075 (3)
C(4*A*)	−0·3452 (5)	−0·8720 (8)	−0·2509 (8)	0·079 (3)
C(5*A*)	−0·2837 (5)	−0·9702 (7)	−0·2241 (7)	0·076 (3)
C(6*A*)	−0·1853 (4)	−0·9506 (6)	−0·1840 (7)	0·059 (2)
C(*G*1*A*)	−0·1485 (4)	−0·8366 (5)	−0·1708 (5)	0·050 (2)
C(*B*1*A*)	−0·0416 (3)	−0·8159 (6)	−0·1266 (5)	0·049 (2)
C(*A*1*A*)	−0·0049 (3)	−0·8128 (5)	0·0540 (5)	0·043 (2)
C(*P*1*A*)	−0·0367 (3)	−0·7027 (5)	0·1310 (6)	0·046 (2)
O(1*A*)	−0·0257 (3)	−0·6059 (4)	0·0680 (4)	0·063 (1)
N(2*A*)	−0·0682 (3)	−0·7101 (4)	0·2689 (5)	0·045 (2)
C(1*A*)	−0·0755 (5)	−0·5999 (6)	0·3599 (8)	0·071 (3)
C(*A*2*A*)	−0·0874 (3)	−0·8194 (5)	0·3486 (5)	0·045 (2)
C(*B*2*A*)	−0·1926 (3)	−0·8206 (6)	0·3804 (6)	0·061 (2)
C(*G*2*A*)	−0·2660 (4)	−0·8060 (6)	0·2308 (7)	0·067 (2)
C(*P*2*A*)	−0·0672 (3)	−0·9302 (5)	0·2624 (6)	0·045 (2)
O(2*A*)	−0·0851 (3)	−1·0284 (4)	0·3168 (5)	0·062 (2)
N(1*A*)	−0·0300 (3)	−0·9216 (4)	0·1284 (5)	0·044 (2)
C(2*B*)	−0·2542 (5)	−0·3126 (8)	−0·9005 (7)	0·078 (3)
C(3*B*)	−0·2620 (8)	−0·4275 (9)	−0·9573 (9)	0·107 (4)
C(4*B*)	−0·3507 (9)	−0·4794 (8)	−0·990 (1)	0·124 (5)
C(5*B*)	−0·4325 (6)	−0·4159 (9)	−0·9729 (9)	0·106 (4)
C(6*B*)	−0·4265 (4)	−0·3009 (7)	−0·9168 (7)	0·077 (3)
C(*G*1*B*)	−0·3354 (4)	−0·2475 (6)	−0·8784 (6)	0·062 (2)
C(*B*1*B*)	−0·3272 (4)	−0·1251 (5)	−0·8140 (6)	0·062 (2)
C(*A*1*B*)	−0·3168 (3)	−0·1163 (5)	−0·6330 (6)	0·054 (2)
C(*P*1*B*)	−0·4048 (4)	−0·1609 (6)	−0·5680 (7)	0·058 (2)
O(1*B*)	−0·4825 (3)	−0·1155 (5)	−0·6261 (5)	0·080 (2)
N(2*B*)	−0·3947 (3)	−0·2409 (4)	−0·4537 (5)	0·057 (2)
C(1*B*)	−0·4803 (4)	−0·2710 (7)	−0·3808 (8)	0·081 (3)
C(*A*2*B*)	−0·3054 (4)	−0·2985 (6)	−0·3825 (6)	0·058 (2)
C(*B*2*B*)	−0·3090 (5)	−0·4349 (6)	−0·3938 (8)	0·077 (3)
C(*G*2*B*)	−0·3311 (6)	−0·4793 (7)	−0·5572 (9)	0·094 (4)
C(*P*2*B*)	−0·2173 (4)	−0·2527 (6)	−0·4421 (7)	0·063 (2)
O(2*B*)	−0·1384 (3)	−0·2919 (5)	−0·3838 (5)	0·104 (2)
N(1*B*)	−0·2264 (3)	−0·1715 (4)	−0·5553 (5)	0·059 (2)

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Table 2. *Molecular dimensions*

	Molecule *A*	Molecule *B*
(*a*) Bond lengths (Å)		
C(2)–C(3)	1·378 (9)	1·383 (13)
C(2)–C(*G*1)	1·394 (7)	1·397 (9)
C(3)–C(4)	1·363 (12)	1·367 (16)
C(4)–C(5)	1·404 (11)	1·384 (15)
C(5)–C(6)	1·390 (9)	1·382 (12)
C(*G*1)–C(6)	1·386 (9)	1·407 (9)
C(*G*1)–C(*B*1)	1·509 (7)	1·485 (9)
C(*B*1)–C(*A*1)	1·540 (6)	1·527 (8)
C(*A*1)–C(*P*1)	1·507 (8)	1·521 (8)
C(*A*1)–N(1)	1·452 (7)	1·474 (7)
C(*P*1)–O(1)	1·239 (7)	1·237 (7)
C(*P*1)–N(2)	1·322 (7)	1·319 (8)
N(2)–C(*A*2)	1·454 (7)	1·458 (7)
C(1)–N(2)	1·478 (8)	1·481 (7)
C(*A*2)–C(*B*2)	1·548 (7)	1·544 (10)
C(*A*2)–C(*P*2)	1·501 (8)	1·505 (8)
C(*B*2)–C(*G*2)	1·514 (7)	1·464 (10)
C(*P*2)–N(1)	1·332 (7)	1·322 (8)
C(*P*2)–O(2)	1·243 (7)	1·226 (7)
(*b*) Bond angles (°)		
C(*G*1)–C(2)–C(3)	119·7 (5)	121·4 (7)
C(4)–C(3)–C(2)	121·1 (6)	119·5 (8)
C(5)–C(4)–C(3)	120·4 (7)	120·3 (9)
C(6)–C(5)–C(4)	118·6 (6)	121·2 (7)
C(*G*1) C(6) C(5)	120·9 (5)	119·1 (6)
C(6)–C(*G*1)–C(2)	119·4 (4)	118·5 (5)
C(*B*1)–C(*G*1)–C(2)	120·0 (4)	121·6 (5)
C(*B*1)–C(*G*1)–C(6)	120·6 (5)	119·9 (5)
C(*A*1)–C(*B*1)–C(*G*1)	114·4 (4)	115·0 (4)
C(*P*1)–C(*A*1)–C(*B*1)	112·2 (4)	113·2 (4)
N(1)–C(*A*1)–C(*B*1)	110·4 (4)	111·1 (4)
N(1)–C(*A*1)–C(*P*1)	113·5 (4)	113·1 (4)
O(1)–C(*P*1)–C(*A*1)	118·3 (4)	115·9 (4)
N(2)–C(*P*1)–C(*A*1)	120·0 (4)	119·8 (4)
N(2)–C(*P*1)–O(1)	121·5 (4)	124·2 (5)
C(1)–N(2)–C(*P*1)	118·2 (4)	117·9 (4)
C(*A*2)–N(2)–C(*P*1)	125·5 (4)	126·6 (4)
C(*A*2)–N(2)–C(1)	115·9 (4)	115·4 (4)
C(*B*2)–C(*A*2)–N(2)	110·1 (4)	113·7 (5)
C(*P*2)–C(*A*2)–N(2)	114·6 (4)	114·1 (4)
C(*P*2)–C(*A*2)–C(*B*2)	109·9 (4)	110·0 (5)
C(*G*2)–C(B2)–C(*A*2)	113·3 (4)	113·7 (5)
O(2)–C(*P*2)–C(*A*2)	119·7 (5)	118·5 (5)
N(1)–C(*P*2)–C(*A*2)	119·3 (4)	119·7 (4)
N(1)–C(*P*2)–O(2)	121·0 (4)	121·7 (5)
C(*P*2)–N(1)–C(*A*1)	126·2 (4)	126·6 (4)
(*c*) Important torsion angles (°)		
C(2)–C(*G*1)–C(*B*1)–C(*A*1)	93·2 (5)	−90·1 (6)
C(6)–C(*G*1)–C(*B*1)–C(*A*1)	−86·6 (5)	89·1 (6)
C(*G*1)–C(*B*1)–C(*A*1)–N(1)	56·7 (5)	64·0 (6)
N(1)–C(*A*1)–C(*P*1)–N(2)	11·1 (5)	0·0 (6)
C(*P*1)–C(*A*1)–N(1)–C(*P*2)	−7·6 (6)	0·9 (7)
C(*A*1)–C(*P*1)–N(2)–C(*A*2)	−8·3 (5)	−2·7 (7)
C(*P*1)–N(2)–C(*A*2)–C(*P*2)	0·9 (5)	4·3 (6)
N(2)–C(*A*2)–C(*B*2)–C(*G*2)	57·2 (5)	58·3 (6)
N(2)–C(*A*2)–C(*P*2)–N(1)	3·2 (5)	−3·2 (6)
C(*A*2)–C(*P*2)–N(1)–C(*A*1)	0·7 (5)	0·9 (7)

Table 3. *The Cremer & Pople* (1975) *puckering parameters of the DKP rings*

The sequence C(*P*1),C(*A*1),N(1),C(*P*2),C(*A*2),N(2) is used.

	Molecule *A*	Molecule *B*
q_1 (Å)	0·084 (5)	0·030 (6)
q_3 (Å)	−0·037 (5)	−0·015 (6)
Q (Å)	0·092 (5)	0·033 (7)
φ_2 (°)	211 (3)	76 (12)
θ_2 (°)	114 (3)	117 (12)

final ΔF map. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Computer programs used: *SHELX*76 (Sheldrick, 1976), *MULTAN*78 (Main *et al.*, 1978), *PLUTO* (Motherwell & Clegg, 1978) and local programs (Jaskólski, 1982).

Discussion. Final positional parameters are given in Table 1, molecular dimensions in Table 2.* Fig. 1 shows the conformation of the two crystallographically independent molecules, *A* and *B*, and the atom-numbering scheme. The overall conformation of both molecules is very similar and different from the predominant conformation observed in solution (Liberek *et al.*, 1977). The side chains of the two α-amino-acid residues of *cyclo*[-L-Phe-L-*N*(Me)-Abu-] have $\chi^1 \simeq 60°$ and are in a folded conformation. The DKP ring in molecule *B* is nearly planar while in molecule *A* it is slightly distorted from planarity towards screw boat ${}^{C_1^{\alpha}}S_{C_1'}$ (notation proposed by Boyens, 1978). Puckering parameters (Cremer & Pople, 1975) characterizing the six-membered DKP rings are given in Table 3.

The molecular packing is shown in Fig. 2. Molecules *A* are bonded *via* N(1*A*)–H(18)···O(1*A*) hydrogen bonds to form chains parallel to **b**, and molecules *B* join to those chains *via* N(1*B*)–H(36)···O(2*A*) hydrogen

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44707 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

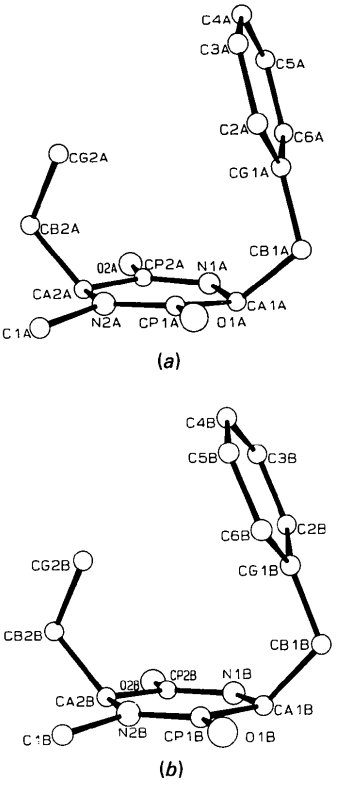

Fig. 1. The conformation of the *cyclo*[-L-Phe-L-*N*(Me)-Abu-] molecules. (*a*) Molecule *A*; (*b*) molecule *B*.

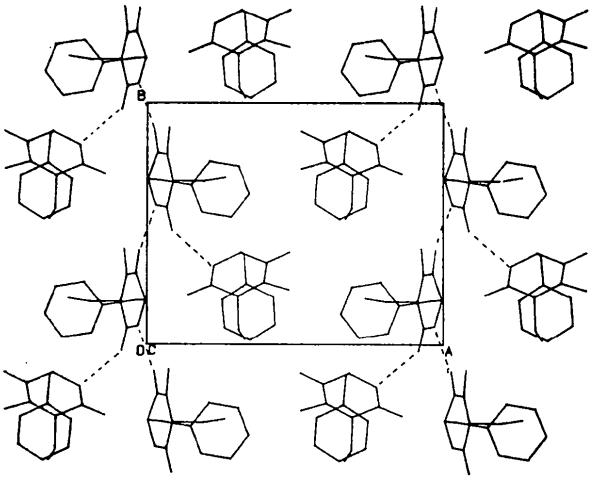

Fig. 2. The crystal structure of *cyclo*[-L-Phe-L-*N*(Me)-Abu-] viewed down **c**; dashed lines show the N–H···O hydrogen bonds [O(1*A*)···N(1*A*^{i}) 2·856 (6) Å, O(1*A*)–H(18)···N(1*A*^{i}) 158 (3)°, (i): $-x$, $0{\cdot}5+y$, $-z$; N(1*B*)···O(2*A*^{ii}) 2·907 (6) Å, O(1*A*)–H(36)···N(1*A*^{i}) 170 (3)°, (ii): x, $1+y$, $-1+z$].

bonds. In effect, molecule *B* is only a hydrogen-bond donor while molecule *A* is a donor in one H bond and an acceptor in two bonds. The packing scheme is quite different from that observed in the other mono-*N*-methylated cyclic dipeptide, *cyclo*[-L-*N*(Me)-Phe-L-Phe-] (Gdaniec & Liberek, 1987) where two crystallographically independent molecules are joined by a pair of N–H···O hydrogen bonds to form dimers as distinct units in the crystal lattice.

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Structure of 1,4-Diaminoanthraquinone Dihydrate

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Abstract. $C_{14}H_{10}N_2O_2.2H_2O$, $M_r = 274{\cdot}28$, orthorhombic, *Pnma*, $a = 15{\cdot}686$ (2), $b = 16{\cdot}200$ (2), $c = 4{\cdot}8507$ (3) Å, $V = 1232{\cdot}6$ (2) Å^3, $Z = 4$, $D_m = 1{\cdot}47$, $D_x = 1{\cdot}478$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}87$ mm^{-1}, m.p. 541 K, $F(000) = 576$, $T = 293$ K, final $R = 0{\cdot}039$ for 1024 unique reflections. The anthraquinone molecule has C_s symmetry in the crystal. The molecules are stacked along **c** with an interplanar spacing of 3·367 (2) Å. The dihedral angle between the molecules related by an *a* glide is 88·0 (1)°. The molecules related by a $\bar{1}$ and a 2_1 along **c** are linked together by three kinds of hydrogen bonds through the water molecules.

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Introduction. The molecule of 1,4-diaminoanthraquinone has rather high molecular symmetry, C_{2v}. The present work has been undertaken as part of a study to obtain experimental data on the most probable space group for symmetrical molecules. In addition, tricyclic anthraquinones have recently drawn attention because of their anticancer activity (Neidle, 1984). Thus, it is also of value to determine the molecular structure and mode of molecular overlapping in the crystal for one of the fundamental compounds of the anthraquinones.

Experimental. Crystals grown by slow evaporation from pyridine, dark purple prisms elongated along **c**. D_m by