

Table 3. Geometrical details (Å and °) of possible hydrogen bonds

The e.s.d.'s of the bonds are ~0.1 Å for N—H, O—H and Br...H; ~0.007 Å for Br...N; ~0.01 Å for N...O; ~0.04 Å for Br...OM and OM...OW. The e.s.d.'s of the angles are ~7°.

Reference atom					
Donor (D)	Acceptor	D—H	D...A	H...A	D—H...A
N(1)—HN(1)	Br(2)	1.00	3.335	2.38	160
N(2)—HN(21)	Br(1 ⁱⁱ)	0.81	3.475	2.81	141
N(2)—HN(22)	Br(1 ⁱⁱⁱ)	0.90	3.516	2.83	134
N(3)—HN(31)	Br(1 ⁱⁱ)	1.08	3.445	2.47	149
N(3)—HN(32)	O(2 ^{iv})	1.08	2.91	1.89	156
N(4)—HN(4)	Br(2 ⁱⁱ)	1.28	3.347	2.18	150
N(5)—HN(52)	Br(1 ⁱⁱⁱ)	1.08	3.453	2.50	146
OM*	Br(2)		3.38		
OW*	OM*		3.02		

Symmetry code: (i) x, y, z ; (ii) $x, y, -1 + z$; (iii) $\frac{2}{3} - y, \frac{1}{3} + x - y, \frac{1}{3} + z - 1$; (iv) $\frac{1}{3} - y, \frac{2}{3} + x - y, \frac{2}{3} + z - 1$.

* The H atoms of the disordered methanol and water molecules could not be identified.

The proposed hydrogen bonding is such that each cation forms eight hydrogen bonds in seven of which the N—H groups act as donors (to the Br anions and to the carbonyl group of an adjacent cation). The scheme is completed by an eighth hydrogen bond involving the carbonyl oxygen as acceptor. This leads to an arrangement in which each cation is linked to four adjacent cations, two *via* hydrogen bonding to Br(1) and two involving hydrogen bonds of the N—H carbonyl type.

The packing of the linked cations is such that it leaves cavities around the threefold axes which

accommodate the disordered methanol and water molecules together with the Br(2) anion.

Each of the Br(2) anions in the cavity is hydrogen bonded to two N—H groups belonging to cations related by translation along *c* and to methanol which in turn is presumably hydrogen bonded to the water molecule situated on the threefold axis.

We assume that the water molecule, when present, acts as a donor only, with the requirements of threefold symmetry attained in a disordered fashion.

The two Br anions are involved in different numbers of hydrogen bonds. Thus, Br(1) forms four such bonds to two adjacent cations, whereas Br(2) is involved in three such bonds; two to the N—H groups and one to the methanol.

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Structure of *cyclo*(-N-Hydroxyglycyl-L-phenylalanyl-)

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Abstract. 3-Benzyl-1-hydroxy-2,5-piperazinedione, C₁₁H₁₂N₂O₃, *M*_r = 220.2, orthorhombic, *P*2₁2₁2₁, *a* = 14.523 (7), *b* = 11.622 (4), *c* = 6.293 (1) Å, *V* = 1062 (1) Å³, *Z* = 4, *D*_m = 1.368 (4), *D*_x =

1.377 Mg m⁻³, λ(Cu Kα) = 1.5418 Å, μ = 0.808 mm⁻¹, *F*(000) = 464.0, *T* = 296 K, *R* = 0.055, *wR* = 0.074, for 768 observations. The diketopiperazine (DKP) ring is almost planar, the C(3) atom deviating most from the plane. The benzene ring is folded over the DKP ring, with dihedral angle of 49°

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between the ring planes. The molecules are stacked along the *a* axis.

Introduction. Some peptides contain one or more *N*-hydroxyamino acid residues in the chain and these compounds show unique biological activity as tumour inhibitors (hadacidin), antibiotics (aspergillidic acid and mycelianamide), or growth factors (rhodotorulic acid and ferrichromes) (Neilands, 1966, 1967, 1981; Maehr, 1971; Emery, 1974; Mikes & Turkova, 1964; Bapat, Black & Brown, 1969).

2,5-Diketopiperazines (DKP's), owing to their restricted conformational flexibility, represent valuable models for studying non bonding interactions between side chains and amide bonds in more complex peptides (Madison, Young & Blout, 1976; Ajo, Granozzi & Di Bell, 1977; Radding, Donzel, Ueyama & Goodman, 1980). So far there has been only one structural study on *N*-hydroxy DKP's (Yokomori, Katoh & Akiyama, 1989). We describe here the structural determination of *cyclo*-(-*N*-hydroxyglycyl-L-phenylalanyl-) (Akiyama, Katoh & Tsuchiya, 1989) by the X-ray crystallographic method.

Experimental. Colorless cubic crystals by slow evaporation of an aqueous methanol solution at room temperature. Crystal 0.3 × 0.3 × 0.1 mm. Rigaku-Denki RASA 5R-II automated diffractometer. D_m by flotation in benzene/carbon tetrachloride. Systematic absences $h00$ for h odd, $0k0$ for k odd, $00l$ for l odd. Cell constants by least squares using 15 reflections with $40 < 2\theta$ (Cu $K\alpha$) $< 80^\circ$ measured on the diffractometer. Intensity data collected in an ω - 2θ scan mode. 830 independent reflections, $2\theta < 120.0^\circ$, $0 \leq h \leq 16$, $0 \leq k \leq 13$, $0 \leq l \leq 7$. No systematic fluctuations in 233, 311, 216, monitored every 100 reflections.

Structure determined using *MULTAN78* (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Block-diagonal least-squares (*HBLISIV*: Ashida, 1981) refinement [on $\sum w(|F_o| - k|F_c|)^2$]. Weighting scheme: $w = [\sigma^2(F_o) + 0.0714|F_o| + 0.0006|F_o|^2]^{-1}$. Subsequent difference Fourier maps revealed positions for all 12 H atoms; however, all H atoms except that of the hydroxy group were fixed at calculated positions (with C—H = 1.08 Å) with fixed isotropic temperature factors ($B = 5.0 \text{ \AA}^2$). The H atom of the hydroxy group is disordered; two possible positions were found on a difference Fourier map. Final cycle of block-diagonal least squares gave $R = 0.055$, $wR = 0.074$, $S = 0.81$, using 768 observations with $|F_o| > 3\sigma(F_o)$ and 146 variables. $(\Delta/\sigma)_{\max} = 0.004$. Final difference map contained no peak higher than $0.2 e \text{ \AA}^{-3}$. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974).

Table 1. Final atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($\text{\AA}^2 \times 10^2$), with e.s.d.'s in parentheses

$$B_{eq} = (1/3)\sum_i B_{ij} a_i^* a_j^* a_i a_j$$

	<i>x</i>	<i>y</i>	<i>z</i>	B_{eq}
O(1)	-9444 (2)	-852 (2)	-8054 (5)	502 (13)
O(2)	-9853 (2)	-3873 (3)	-1705 (5)	565 (14)
O(3)	-9177 (2)	-4607 (2)	-5437 (6)	528 (14)
N(1)	-9486 (2)	-3491 (2)	-5126 (5)	401 (13)
N(2)	-9843 (2)	-1207 (2)	-4650 (5)	364 (12)
C(1)	-9344 (4)	-2766 (3)	-6908 (7)	477 (19)
C(2)	-9567 (2)	-1525 (3)	-6568 (6)	381 (15)
C(3)	-10097 (3)	-1977 (3)	-2935 (6)	394 (16)
C(4)	-9788 (3)	-3202 (3)	-3204 (7)	407 (16)
C(5)	-11155 (3)	-1929 (4)	-2567 (8)	523 (21)
C(6)	-11686 (3)	-2333 (4)	-4485 (8)	459 (18)
C(7)	-12041 (3)	-1565 (4)	-5934 (10)	561 (22)
C(8)	-12517 (4)	-1928 (6)	-7741 (10)	645 (26)
C(9)	-12646 (3)	-3082 (6)	-8062 (10)	625 (25)
C(10)	-12303 (3)	-3854 (5)	-6662 (12)	679 (28)
C(11)	-11820 (3)	-3502 (4)	-4846 (9)	570 (23)

Table 2. Bond lengths (Å) and angles ($^\circ$) with e.s.d.'s in parentheses

O(1)—C(2)	1.232 (5)	C3—C4	1.503 (5)
O2—C4	1.227 (5)	C3—C5	1.555 (6)
O3—N1	1.386 (4)	C5—C6	1.507 (7)
N1—C1	1.418 (6)	C6—C7	1.376 (7)
N1—C4	1.330 (5)	C6—C11	1.391 (7)
N2—C2	1.325 (5)	C7—C8	1.396 (8)
N2—C3	1.449 (5)	C8—C9	1.369 (9)
C1—C2	1.494 (6)	C9—C10	1.353 (9)
		C10—C11	1.402 (9)
O(3)—N(1)—C(1)	113.4 (3)	O2—C4—N1	124.3 (3)
O3—N1—C4	118.1 (3)	O2—C4—C3	119.5 (3)
C1—N1—C4	128.1 (3)	N1—C4—C3	116.1 (3)
C2—N2—C3	125.7 (3)	C3—C5—C6	112.0 (4)
N1—C1—C2	115.4 (4)	C5—C6—C7	121.4 (4)
O1—C2—N2	124.0 (3)	C5—C6—C11	120.4 (4)
O1—C2—C1	118.2 (3)	C7—C6—C11	118.2 (4)
N2—C2—C1	117.7 (3)	C6—C7—C8	122.0 (5)
N2—C3—C4	115.2 (3)	C7—C8—C9	119.0 (5)
N2—C3—C5	109.9 (3)	C8—C9—C10	120.2 (6)
C4—C3—C5	110.2 (3)	C9—C10—C11	121.4 (6)
		C6—C11—C10	119.2 (5)

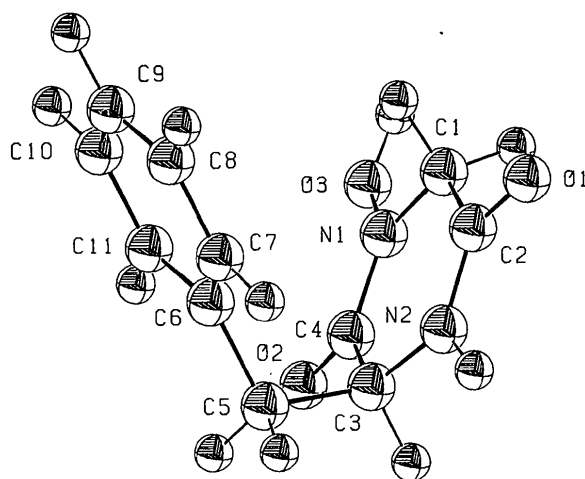


Fig. 1. View of the molecule. Thermal ellipsoids are at 50% probability (ORTEP; Johnson, 1976).

Discussion. The final atomic coordinates with their e.s.d.'s are given in Table 1.* The numbering scheme is presented in Fig. 1. The bond distances and angles are shown in Table 2.

The bond lengths and angles compare well with those of DKP compounds (Yokomori *et al.*, 1989; Suguna, Ramakumar, Nagaraj & Balaram, 1985; Gdaniec & Liberek, 1986; Lin & Webb, 1973).

The torsion angles, $\omega_1 = 10.9^\circ$, $\omega_2 = -6.1^\circ$, are a little larger than those of DKP compounds having aromatic side chains [*cyclo(-Aib-Phe-)* ($\omega_1 = -1.5^\circ$, $\omega_2 = -4.2^\circ$) (Suguna *et al.*, 1985); *cyclo(-Gly-L-Trp-)* ($3, -3^\circ$) (Morris, Geddes & Sheldrick, 1974); *cyclo(-Gly-Tyr-)* ($-4, -7^\circ$) (Lin & Webb, 1973)]. However, the DKP ring is almost planar except for the C(3) atom [deviation 0.18 Å from the least-squares plane formed by the four atoms, N(1), C(2), N(2) and C(4)]. The phenylalanyl C(5) atom occupies an axial position with $\chi^1 = \text{N}(2)-\text{C}(3)-\text{C}(5)-\text{C}(6) = 62^\circ$ and $\chi^{2,1} = \text{C}(3)-\text{C}(5)-\text{C}(6)-\text{C}(7) = 97^\circ$. These values are in good agreement with those corresponding to the theoretically calculated minimum-energy conformation for the Phe residue ($\chi^1 = 60^\circ$, $\chi^2 = 90^\circ$) (Chandrasekaran, Lakshminarayanan, Mohanakrishnan & Ramachandran, 1973) but are different from those obtained by a molecular-orbital calculation ($\chi^1 = \chi^2 = 60^\circ$) (Cailliet, Pullman & Maigret, 1971). The benzene ring is folded over the

DKP ring, $\text{N}(2)\cdots\text{C}(7) = 2.90$ and $\text{C}(4)\cdots\text{C}(11) = 2.76$ Å. The dihedral angle between the benzene ring and the DKP ring is 49° and the dihedral angles between $\text{C}(3)-\text{C}(5)-\text{C}(6)$ and the DKP ring and benzene ring are respectively 89 and 83° .

The molecular packing is shown in Fig. 2. The crystal structure is stabilized by two hydrogen bonds. One is $\text{N}(2)-\text{H}\cdots\text{O}(2)(-2-x, \frac{1}{2}+y, -\frac{1}{2}-z)$, 2.87 Å, 167.4° . Another hydrogen bond is a little complicated because the hydroxy H atom is disordered: $\text{O}(3)-\text{H}\cdots\text{O}(1)(-2-x, -\frac{1}{2}+y, -\frac{3}{2}-z)$, 2.63 Å, 111.1° ; $\text{O}(3)\cdots\text{H}'-\text{O}(1)$, 2.63 Å, 97.9° . Occupancy factors are 0.6 and 0.4 respectively. The close intermolecular distances between the DKP ring and the benzene ring are $\text{N}(1)\cdots\text{C}(7^i) = 3.14$, $\text{N}(2)\cdots\text{C}(10^i) = 3.29$, $\text{C}(1)\cdots\text{C}(6^i) = 3.45$, $\text{C}(2)\cdots\text{C}(11^i) = 3.56$, $\text{C}(3)\cdots\text{C}(9^i) = 3.14$, $\text{C}(4)\cdots\text{C}(8^i) = 2.91$ Å [(i): $\frac{1}{2}+x, -1/2-y, -1-z$]. These values show that the molecules are stacked along the *a* axis.

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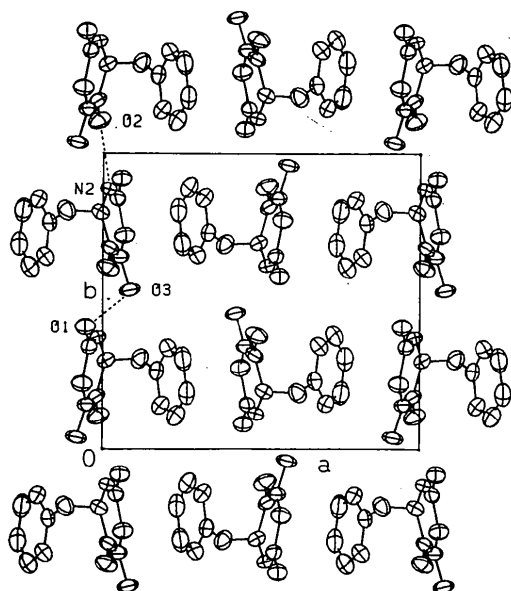


Fig. 2. The packing in the cell.

* Lists of structure amplitudes, H-atom positional parameters and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 52424 (4 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.