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Structure of 7,8,17,18-Tetrahydro-10,20-diphenyl-5,9,15,19-tetraazadibenzo[*a*,*i*]cyclohexadecene-6,16(5*H*,15*H*)-dione, $C_{32}H_{28}N_4O_2$

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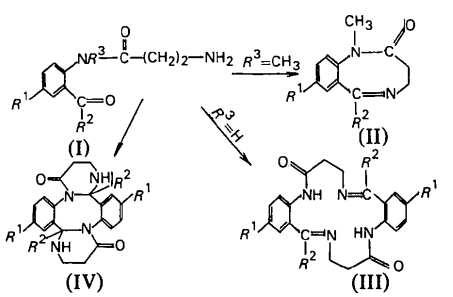
Abstract. $M_r = 500{\cdot}60$, orthorhombic, *Pcan*, $a = 7{\cdot}331\ (3)$, $b = 18{\cdot}945\ (14)$, $c = 18{\cdot}420\ (15)$ Å, $V = 2558\ (2)$ Å^3, $Z = 4$, $D_x = 1{\cdot}299$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 0{\cdot}46$ cm^{-1}, $F(000) = 1056$, $T = 298$ K. Final $R = 0{\cdot}046$ for 1044 independent observed reflections. The structure consists of a molecular packing of 16-membered heteromacrocycles with a C_2 crystallographic symmetry. The macrocycle has a deep-boat conformation, stabilized by strong NH···N = 2·650 Å intramolecular hydrogen bonds. The amide groups are in a *trans* form.

Introduction. Sulkowski (1966) described the synthesis of 1,2,3,4-tetrahydro-1,5-benzodiazocin-2-ones (II) by cyclization of 2-(β-alanylamino)benzophenones (I). These compounds produced a sedative effect upon the central nervous system. Later it was shown (Dierig, Schweininger & Fryer, 1969) that the derivatives of (I) undergo different cyclization reactions according to the nature of the R^3 substituent; when $R^3 \neq H$ cyclization gives 1,5-benzodiazocine derivatives (II) while when $R^3 = H$ a product of tentative formula 7,8,17,18-tetrahydro-5,9,15,19-tetraazadibenzo[*a*,*i*]cyclohexadecene-6,16(5*H*,15*H*)-dione (III) was obtained. The alternative formula (IV) has been suggested as well, though studies on the complexing ability (Yatsimirsky, Bogatsky, Lampeka & Komogortseva, 1979) of the reaction product gave a strong indication in favour of (III).

The present study was undertaken in order to determine the structure of the cyclization products of the compound (I) ($R^3 = H$), as well as to compare the molecular and crystal structure of (III) ($R^1 = H$, $R^2 = C_6H_5$) with (II).

The synthesis and some properties of the title compound have been previously described (Bogatsky, Benko & Andronati, 1977).

Experimental. Colourless prismatic crystals, 0·5 × 0·3 × 0·2 mm, three-circle single-crystal diffractometer DAR-UMB, graphite-monochromated Mo $K\alpha$ radiation, combined ω and $\omega/2\theta$ scan at 8° min^{-1}, 3 reflections used for measuring lattice parameters; 2938 independent reflections with $2 \leq \theta \leq 45°$ (h 0→9, k 0→23, l 0→19, 1044 with $I > 3\sigma(I)$. 17 standard reflections, ≤5% intensity variation. Corrections made for Lorentz and polarization effects. Absorption and extinction corrections neglected. Structure determined by direct methods; H atoms located from difference Fourier map. Full-matrix refinement (on F) with anisotropic non-H and isotropic H atoms gave $R = 0{\cdot}046$ ($wR = 0{\cdot}046$); weighting scheme $w = [\sigma^2(F) + F^2E_{ap}^2]^{-1}$, where E_{ap} was an apparatus error, $S = 1{\cdot}57$, $(\Delta/\sigma)_{max} = 0{\cdot}40$, min./max. $\Delta\rho$ deviations in final difference Fourier map −0·21 and 0·18 e Å^{-3}.



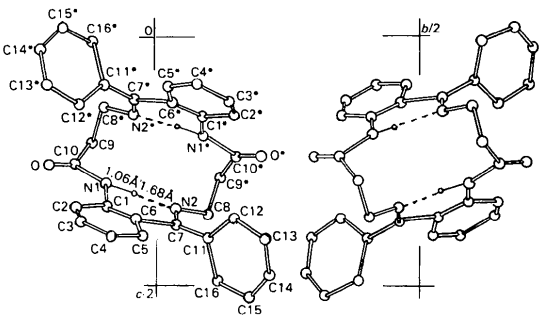


Fig. 1. Projection of the crystal structure onto the *yz* plane.

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Atomic scattering factors with f' and f'' used (Cromer & Waber, 1974). Calculations carried out using the ES-series computers and the program *YANX* (Institute of Elemento-Organic Compounds, The Academy of Sciences of the USSR).

Table 1. *Fractional atomic coordinates* ($\times 10^4$) *and thermal parameters* (Å^2 $\times 10^3$) *with e.s.d.'s in parentheses*

Thermal parameters are U_{iso} for the H atom and U_{eq} for the N, O and C atoms.

$$U_{eq} = (U_{11} + U_{22} + U_{33})/3.$$

	x	y	z	U_{eq}/U_{iso}
N(1)	4407 (4)	−923 (2)	3030 (2)	44 (1)
N(2)	3778 (4)	364 (1)	3534 (2)	42 (1)
O	4264 (4)	−2048 (1)	2578 (2)	73 (1)
C(1)	6100 (5)	−901 (2)	3388 (2)	39 (1)
C(2)	7284 (6)	−1474 (2)	3387 (2)	48 (1)
C(3)	8944 (6)	−1431 (2)	3728 (2)	56 (2)
C(4)	9466 (6)	−821 (2)	4094 (2)	59 (2)
C(5)	8289 (6)	−247 (2)	4088 (2)	49 (1)
C(6)	6586 (5)	−268 (2)	3743 (2)	36 (1)
C(7)	5406 (5)	373 (2)	3788 (2)	38 (1)
C(8)	2618 (6)	993 (2)	3568 (2)	47 (1)
C(9)	2008 (5)	−1213 (2)	2193 (2)	48 (1)
C(10)	3659 (5)	−1451 (2)	2626 (2)	48 (1)
C(11)	6228 (5)	1012 (2)	4135 (2)	36 (1)
C(12)	7369 (5)	1460 (2)	3744 (2)	47 (1)
C(13)	8122 (6)	2050 (2)	4059 (3)	58 (2)
C(14)	7734 (6)	2193 (2)	4777 (3)	58 (2)
C(15)	6614 (6)	1760 (2)	5178 (2)	50 (1)
C(16)	5878 (6)	1165 (2)	4852 (2)	44 (1)
H(N1)	3731 (69)	−439 (23)	3146 (25)	99 (16)

Table 2. *Molecular dimensions*

Bond lengths (Å)

C(1)–N(1)	1·406 (4)	C(1)–C(2)	1·390 (5)
C(2)–C(3)	1·372 (6)	C(3)–C(4)	1·392 (5)
C(4)–C(5)	1·388 (5)	C(5)–C(6)	1·401 (5)
C(6)–C(1)	1·412 (4)	C(6)–C(7)	1·493 (4)
C(7)–N(2)	1·282 (4)	N(2)–C(8)	1·465 (4)
C(8)–C(9^{i})	1·529 (5)	C(9)–C(10)	1·518 (5)
C(10)–N(1)	1·362 (4)	C(10–O	1·218 (4)
C(7)–C(11)	1·496 (4)	C(11)–C(12)	1·392 (5)
C(12)–C(13)	1·375 (5)	C(13)–C(14)	1·380 (6)
C(14)–C(15)	1·376 (5)	C(15)–C(16)	1·386 (5)
C(16)–C(11)	1·376 (5)	N(1)–H(N1)	1·06 (4)

Valence angles (°)

N(1)–C(1)–C(2)	121·8 (3)	N(1)–C(1)–C(6)	117·7 (3)
C(2)–C(1)–C(6)	120·4 (3)	C(1)–C(2)–C(3)	120·5 (4)
C(2)–C(3)–C(4)	121·0 (4)	C(3)–C(4)–C(5)	118·4 (4)
C(4)–C(5)–C(6)	122·4 (4)	C(5)–C(6)–C(1)	117·3 (3)
C(5)–C(6)–C(7)	117·9 (3)	C(1)–C(6)–C(7)	124·8 (3)
C(6)–C(7)–N(2)	120·5 (3)	C(6)–C(7)–C(11)	116·6 (3)
C(11)–C(7)–N(2)	122·8 (3)	C(7)–N(2)–C(8)	120·9 (3)
N(2)–C(8)–C(9^{i})	110·6 (3)	C(10)–C(9)–C(8^{i})	109·2 (4)
C(9)–C(10)–N(1)	112·9 (3)	C(9)–C(10)–O	121·8 (4)
N(1)–C(10)–O	125·1 (4)	C(10)–N(1)–C(1)	129·3 (3)
C(11)–C(12)–C(13)	121·2 (4)	C(12)–C(13)–C(14)	118·8 (4)
C(13)–C(14)–C(15)	121·4 (4)	C(14)–C(15)–C(16)	119·0 (4)
C(15)–C(16)–C(11)	120·9 (4)	C(16)–C(11)–C(12)	118·7 (3)

Selected torsion angles (°) (e.s.d.'s *ca* 0·6°)

C(6)–C(1)–N(1)–C(10)	176·9	C(7)–C(6)–C(1)–N(1)	2·2
N(2)–C(7)–C(6)–C(1)	4·5	C(8)–N(2)–C(7)–C(6)	−179·2
C(9^{i})–C(8)–N(2)–C(7)	121·7	C(10^{i})–C(9^{i})–C(8)–N(2)	−66·0
C(8^{i})–C(9)–C(10)–N(1)	93·6	C(9)–C(10)–N(1)–C(1)	−167·0

Symmetry code: (i) $x, -y, 0{\cdot}5 - z$.

Discussion. The final positional parameters of all the non-H atoms and the H atom of the amide group with their equivalent thermal parameters (Hamilton, 1959) are listed in Table 1.* Molecular structure and atom numbering are shown in Fig. 1. The interatomic distances, the bond angles and torsion angles are given in Table 2. The X-ray analysis confirms formula (III). The molecule is a 16-membered macroheterocycle with C_2 crystallographic symmetry and overall deep-boat conformation. The mean planes of the molecule are given in Table 3.* The table shows that a fragment consisting of atoms C(10),N(1),C(1),C(6),C(7),N(2),-C(8) is practically planar [a maximum deviation of 0·047 (4) Å, the C(9) atom is displaced by 0·375 Å] unlike the boat conformation which this fragment possesses in (II)-type compounds (Dvorkin, Simonov, Malinowsky, Andronati, Bagatsky & Danilin, 1982). The two planar fragments of the heterocycle are related by a C_2 axis making an angle of 133° to each other. The conformation of the phenyl substituents is defined by the torsion angle C(6)–C(7)–C(11)–C(12) = 81·6°. An interesting feature of this compound is the *trans* conformation of the amide fragment within the molecule. In 1,4-benzodiazepines studied earlier (Gilli, Bertolasi, Sacerdoti & Borea, 1978; Chananont, Hamor & Martin, 1981; Andronati, Dvorkin, Korotenko, Voronina, Simonov & Shibanova, 1982), the amide fragment has a *cis* conformation which results in the dimerization of the molecules by NH···O bonds. The inversion of the amide group from the *cis* to the *trans* configuration prevents the formation of intermolecular hydrogen bonds and results in the formation of two strong intramolecular hydrogen bonds N(1)H···N(2) [N(1)–H = 1·06, N(2)···H = 1·68 Å, angle N(1)–H–N(2) = 150°] which apparently contributes to the flattening of the fragment C(10),N(1),-C(6),C(7),N(2),C(8) and to the stabilization of the observed molecular conformation.

The bond distances and the bond angles within the molecule do not substantially differ from similar ones in 1,4-benzodiazepines and 1,5-benzodiazocines (Camerman & Camerman, 1972; Dvorkin *et al.*, 1982). The small shortening of the bond N(1)–C(1) = 1·406 Å is typical of amide resonance. Distances N(2)–C(7) and N(2)–C(8) = 1·282 and 1·465 Å correspond to accepted values for double and single C–N bonds respectively. The angles at N(1) and N(2) are 120·9 and 129·3°, while in 1,4-benzodiazepines and 1,5-benzodiazocines these angles are not larger than 118 and 127°.

* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and Table 3 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39972 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

There is a shortened intramolecular distance C(2)H···O = 2·883 Å [C(2)–H = 0·92, O···H = 2·29 Å, angle C(2)–H–O = 122°] which corresponds, according to the geometrical characteristics, to a weak CH···O hydrogen bond (Taylor & Kennard, 1982).

The projection of the crystal structure on the *yz* plane is given in Fig. 1. There are no contacts between separate molecules shorter than 3·5 Å within the crystal.

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Structure of Gentiopicrin Hemihydrate: (–)-(5*R*,6*S*)-5-Ethenyl-6-(β-D-glucopyranosyloxy)-5,6-dihydro-1*H*,3*H*-pyrano[3,4-*c*]pyran-1-one Hemihydrate, $C_{16}H_{20}O_9 \cdot \frac{1}{2}H_2O$

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Abstract. $M_r = 365{\cdot}34$, orthorhombic, $P2_12_12_1$, $a = 8{\cdot}175\ (2)$, $b = 12{\cdot}810\ (2)$, $c = 31{\cdot}99\ (2)$ Å, $U = 3350\ (1)$ Å^3, $Z = 8$, $D_x = 1{\cdot}449$ g cm^{-3}, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}77$ cm^{-1}, $F(000) = 1544$, $T = 294$ K, $R = 0{\cdot}042$ for 1789 reflexions [$I > 2{\cdot}5\sigma(I)$]. There are two independent molecules (*A*,*B*) in the structure with different conformations of the δ-lactone ring of the secoiridoid moiety: half-chair (*A*) and nearly planar (*B*) [with mean torsion angle 4 (1)°]. Both molecules show a skew-boat conformation of the pyran ring. The β-glucose moieties are in the chair, $^4C_1$, conformation. Molecular packing is dominated by intermolecular hydrogen bonds between the water molecule and both sugar residues [O(31)–H···O(3′)(*A*), 3·017 (7); O(31)–H···O(4′)(*B*), 2·904 (7); O(4′)(*A*)–H···O(31), 2·684 (7) Å], sugar–sugar [O(2′)(*A*)–H···O(4′)(*A*), 2·719 (6); O(6′)(*A*)–H···O(2′)(*A*), 2·731 (6); O(2′)(*B*)–H···O(6′)(*B*), 2·821 (7); O(4′)(*B*)–H···O(3′)*B*, 2·796 (7) Å], and sugar–secoiridoid moiety [O(3′)(*A*)–H···O(11)(*A*), 2·745 (6); O(3′)(*B*)–H···O(11)*A*, 2·716 (7) Å]. Molecules connected by hydrogen bonds form layers (in the *ab* plane), which are separated by ethenyl residues.

Introduction. Gentiopicrin (gentiopicroside) is one of the major secoiridoid glucoside constituents of plant drugs originating from the Gentianaceae and the principal glucoside in the roots of *Gentiana lutea* and the aerial parts of *Blackstonia perfoliata.* Although the

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