

Structures of Polycyclic Polyamines: 1,4,8,11-Tetraazatricyclo[9.3.1.1^{4,8}]hexadecane*

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Abstract. C₁₂H₂₄N₄, $M_r = 224.3$, monoclinic, space group $P2_1/c$, $a = 9.173$ (2), $b = 10.375$ (1), $c = 6.4530$ (6) Å, $\beta = 98.68$ (1)° at 115K, $V = 607.0$ Å³, $Z = 2$, $D_c = 1.227$ Mg m⁻³. R_F is 0.039 for 972 observed reflections measured with Mo $K\alpha$ radiation ($\lambda = 0.71069$ Å). The molecule consists of two asymmetric units related by a center of symmetry. The crystals are colorless needles. The molecule adopts the expected distorted 'diamond lattice' geometry.

Introduction. As part of a general program of investigation into the stereochemistry of polycyclic polyamines (Weisman, Ho & Johnson, 1980; Weisman, Johnson & Fiala, 1980; Weisman, Johnson & Coolidge, 1981) a series of structure determinations has been undertaken. The structure of the title compound, the adduct of formaldehyde and 1,4,8,11-tetraazacyclotetradecane (cyclam), is reported here. Solution conformational analysis and empirical force-field calculations will be reported elsewhere (Weisman, Coolidge & Johnson, 1982).

Diffraction intensities were collected from a crystal of poor quality and the structure was solved from this data. Subsequently, much better crystals were obtained by slow evaporation of a CH₂Cl₂/hexane solution. The crystals were too large for intensity measurements and were cut with a solvent saw, using a fine polypropylene fibre and ethanol as the solvent. All attempts to cut the crystals with a scalpel resulted in delamination. The crystal for which results are reported was approximately 0.5 × 0.3 × 0.3 mm and the intensity data were collected at 115K. 2374 reflections were measured using monochromatized Mo $K\alpha$ radiation to $2\theta_{\max} = 55^\circ$ with the $\theta/2\theta$ scan technique on a modified Picker diffractometer with a scan speed of 4° min⁻¹ in 2θ . The data were subjected to profile analysis (Grant & Gabe, 1978). The resulting data set consists of 1392 independent reflections of which 972 are considered significant

at the $3\sigma(I)$ level. Measurements of 83 systematic absences were all below this significance level. Agreement between symmetry-related reflections, $\sum |I_i - I_j| / \sum I_i = 0.011$. Lorentz and polarization factors (Le Page, Gabe & Calvert, 1979) were applied but no absorption corrections were made ($\mu = 0.072$ mm⁻¹).

The structure was solved in a routine way with *MULTAN* (Germain, Main & Woolfson, 1971) and refined first by full-matrix and later by block-diagonal least squares. The H atoms were included at calculated positions and their positional and isotropic thermal parameters were refined. The final agreement factors are $R_F = 0.039$ and $R_w = 0.020$ with counting-statistics weights, and the final difference map showed no significant features. Final positional parameters and equivalent isotropic temperature factors are shown in

Table 1. Atomic coordinates and isotropic thermal parameters

E.s.d.'s refer to the last digit printed.

	x	y	z	$B_{eq}^*/B_{iso}(\text{Å}^2)$
N(1)	0.34193 (15)	0.43603 (12)	0.52235 (20)	1.23 (5)
C(2)	0.40548 (18)	0.36426 (16)	0.71113 (24)	1.46 (6)
C(3)	0.56711 (18)	0.39551 (15)	0.79480 (24)	1.42 (7)
N(4)	0.67525 (15)	0.35982 (13)	0.65753 (20)	1.32 (5)
C(5)	0.82645 (18)	0.39115 (16)	0.7590 (3)	1.70 (7)
C(6)	0.86048 (18)	0.53596 (16)	0.7652 (3)	1.68 (7)
C(7)	0.81118 (18)	0.60057 (15)	0.5528 (3)	1.56 (7)
C(16)	0.65105 (18)	0.42360 (15)	0.45321 (25)	1.29 (6)
H(21)	0.3926 (15)	0.2708 (13)	0.6752 (19)	1.0 (3)
H(22)	0.3467 (15)	0.3802 (14)	0.8336 (20)	1.5 (3)
H(31)	0.5726 (16)	0.4883 (14)	0.8342 (21)	1.5 (3)
H(32)	0.5914 (16)	0.3444 (14)	0.9343 (21)	1.7 (3)
H(51)	0.8985 (15)	0.3496 (13)	0.6669 (19)	1.2 (3)
H(52)	0.8417 (16)	0.3550 (14)	0.9027 (20)	1.9 (4)
H(61)	0.9726 (17)	0.5484 (14)	0.8072 (22)	2.2 (4)
H(62)	0.8130 (14)	0.5774 (12)	0.8710 (19)	0.4 (3)
H(71)	0.8173 (17)	0.6978 (14)	0.5699 (21)	2.1 (4)
H(72)	0.8784 (15)	0.5709 (13)	0.4475 (20)	1.0 (3)
H(161)	0.7324 (14)	0.3927 (12)	0.3701 (18)	0.7 (3)
H(162)	0.5498 (15)	0.3980 (13)	0.3840 (19)	1.3 (3)

* B_{eq} is the arithmetic mean of the principal axes of the thermal ellipsoid.

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Table 1.* All calculations were carried out using the NRC system of programs for the PDP-8e computer (Larson & Gabe, 1978), and scattering factors were taken from *International Tables for X-ray Crystallography* (1974).

Discussion. The atomic-numbering scheme, which has been chosen to correspond with the chemical numbering of the complete molecule, is shown in Fig. 1 together with the bond distances and angles for the heavier atoms. A stereoview of the molecule is shown in Fig. 2 and torsion angles are listed in Table 2.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36894 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Torsion angles ($^{\circ}$) (e.s.d.'s are $\sim 0.2^{\circ}$)

(a) Ten-membered ring	(b) Six-membered ring		
N(1)–C(2)–C(3)–N(4)	65.4	N(4)–C(5)–C(6)–C(7)	46.9
C(2)–C(3)–N(4)–C(16)	–60.4	C(5)–C(6)–C(7)–N(8)	–50.0
C(3)–N(4)–C(16)–N(8)	–59.4	C(6)–C(7)–N(8)–C(16)	60.8
N(4)–C(16)–N(8)–C(9)	163.5	C(7)–N(8)–C(16)–N(4)	–70.1
C(16)–N(8)–C(9)–C(10)	–57.3	N(8)–C(16)–N(4)–C(5)	63.5
		C(16)–N(4)–C(5)–C(6)	–51.8

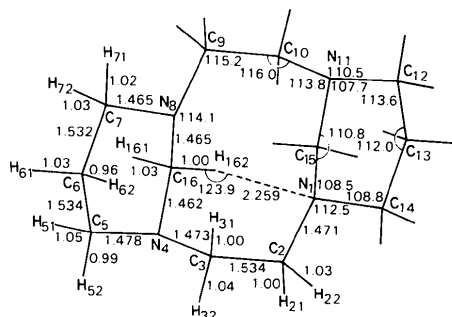


Fig. 1. Bond distances and angles in the molecule. E.s.d.'s for C–C and C–N distances are 0.002 Å and for C–H distances 0.014 Å. E.s.d.'s of bond angles not involving H atoms are 0.13°, for that involving H(162) 1.0°.

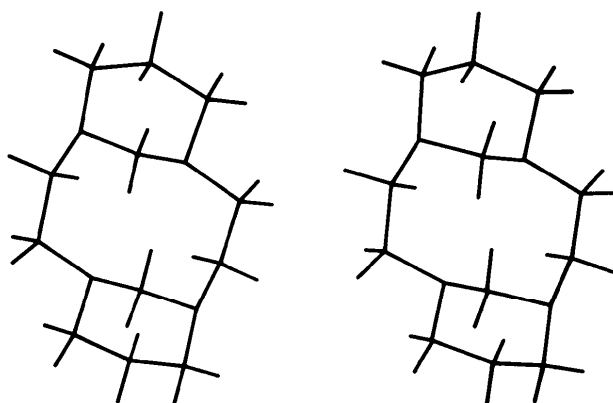


Fig. 2. A stereoview of the complete molecule.

The central ten-membered ring adopts the rectangular [2323] conformation (Dale, 1976) reported for several cyclodecane derivatives in the solid state (Dunitz, 1971). Two diagonal type (II) (Dunitz, 1971) corner positions and two type (III) side positions are occupied by atoms N(4), N(11) and N(1), N(8) respectively. This arrangement allows for minimization of transannular H–H repulsions. On each face of the ring, one intra-annular type (I) H, H(101) [H(31) at $1-x, 1-y, 1-z$], and one intra-annular type (III) H, H(162), are compressed with each other [H(101)–H(162) = 2.04 Å] and with a type (III) N lone-pair [N(1)–H(162) = 2.259 Å]. In comparison, three intra-annular H atoms [one type (I) and two type (III)] are sterically compressed on each face of cyclodecane (Dunitz, 1971). The N(1)–C(16) distance of 2.939 Å is significantly less than the corresponding cyclodecane C–C distance of 3.29 Å (Dunitz, 1971). This is a clear indication of the lower transannular repulsion in the title compound due to the presence of N atoms at two of the four type (III) positions.

Each of the two hexahydropyrimidine six-membered rings is a distorted chair (Table 2) with the ethano bridges of the ten-membered ring substituted equatorial/axial (*trans*) at the bridgehead N atoms. This hexahydropyrimidine conformation is that favored by the generalized anomeric effect (Riddell, 1980). Bonds N(1)–C(14) and N(4)–C(5) are *cisoid* to one another with reference to the ten-membered ring.

The results are in good agreement with those recently reported for a hydrate of 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazatricyclo[9.3.1.1^{4,8}]hexadecane (Alcock, Moore & Mok, 1980). Bond-length comparisons show that bonds involving substituted atoms [C(3) and C(5)] in the latter compound are probably significantly longer (mean elongation 0.010 Å) than those in the title compound, as would be expected, whereas there is no significant difference for the four other bonds (mean difference 0.003 Å).

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Structure of Senecionine, a Pyrrolizidine Alkaloid

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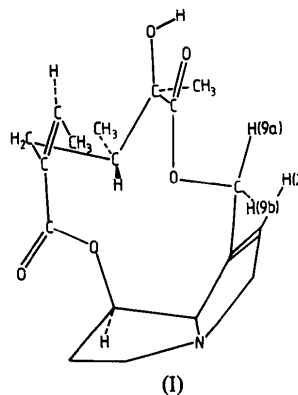
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Abstract. $C_{18}H_{25}NO_5$, $M_r = 335.4$, orthorhombic, space group $P2_12_12_1$, $a = 9.072$ (1), $b = 17.236$ (1), $c = 11.224$ (1) Å, $U = 1755.0$ (2) Å³, $Z = 4$, $D_m = 1.266$ (3), $D_c = 1.269$ Mg m⁻³, $F(000) = 720$, $\mu(Cu K\alpha) = 0.67$ mm⁻¹. The structure was solved by direct methods with diffractometer data measured with Cu $K\alpha$ radiation, and full-matrix least-squares refinement converged at $R = 0.046$ for 1694 observed reflections. With respect to the pyrrolizidine nucleus and the primary-ester system, senecionine adopts a conformation similar to the one proposed on NMR grounds, but differs at the α,β -unsaturated ester grouping; the pucker of the pyrrolizidine nucleus is *exo* and the ester carbonyl bonds are antiparallel. Inter-molecular hydrogen bonds involving the hydroxyl substituent and the N atoms, $N \cdots O$ 2.827 (4) Å, link the molecules into helices extending along the c axis.

Introduction. Senecionine (I) is a typical hepatotoxic macrocyclic pyrrolizidine alkaloid. It is one of the longest known and most commonly encountered alkaloids in the *Senecio* species, its chemical structure being established by Kropman & Warren (1949). A conformational structure (I) has been proposed for senecionine (Culvenor, 1966; Bull, Culvenor & Dick, 1968), based largely on inferences from NMR measurements. The present analysis, which is part of an investigation of stereochemical aspects of pyrrolizidine alkaloids, was performed in order to compare the proposed conformation with the crystal structure.



Experimental. Weissenberg photographs showed that the prismatic crystals grown from acetone were orthorhombic and systematic extinctions indicated the space group $P2_12_12_1$. Cell parameters were determined by least squares from 2θ values measured for 25 strong reflections with Cu $K\alpha$ radiation ($\lambda = 1.5418$ Å) on a diffractometer. The crystal density was determined by flotation.

Integrated intensities were measured with Cu $K\alpha$ radiation (graphite-crystal monochromator, $\lambda = 1.5418$ Å) from a crystal *ca* 0.20 × 0.25 × 0.45 mm aligned on a Rigaku – AFC four-circle diffractometer with the longest crystal axis c approximately parallel to the diffractometer ϕ axis. The intensities were recorded by an $\omega - 2\theta$ scan, 2θ scan rate 2° min⁻¹, scan range ($\Delta\omega$) 1.2° + 0.5° tan θ and 10s stationary background