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Structure of 2 α -Bromo-1 β ,7 β -epoxytrachelanthamidine: A New Heterocyclic Ring System

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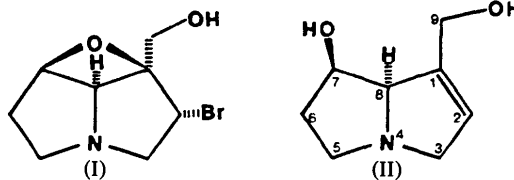
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Abstract. C₈H₁₂BrNO₂, $M_r = 234.1$, orthorhombic, $P2_12_12_1$, $a = 6.196(2)$, $b = 8.971(2)$, $c = 15.797(5)$ Å, $U = 878.1(4)$ Å³, $Z = 4$, $D_m = 1.770$, $D_x = 1.767$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.71069$ Å, $\mu = 39.71$ cm⁻¹, $F(000) = 472$, $T = 298$ K, $R = 0.037$ for 1395 observed reflections. The pyrrolizidine rings of the title compound (I) are planar within 0.277 Å, and both assume envelope conformations. The oxetane ring of (I) has all angles close to 90°. The distances O(2)⋯N' (2.826 Å) and H(O2)⋯N' (1.82 Å) suggest intermolecular H bonding between N and the O atom of the CH₂OH group. The absolute configuration of (I), which can be related to its precursor retronecine [Warren & Von Klemperer (1958). *J. Chem. Soc.* pp. 4574–4575; Warren (1970). *The Alkaloids*, Vol. XII, edited by Manske, ch. 4, pp. 246–262. London: Academic Press; and references therein], was confirmed by comparison of the refinement values of (I) with its enantiomer for which $R = 0.057$ was obtained.

Introduction. The pyrrolizidine alkaloids continue to be of great interest because of their broad range of biological activity (Roitman, 1983; Huxtable, 1979). Recently, there have been intensive studies of the antitumor activity of the *N*-oxides of the pyrrolizidine alkaloids and of their semisynthetic analogs (Zalkow, Glinski, Gelbaum, Fleischmann, McGowan & Gordon, 1985; Gelbaum, Gordon, Miles & Zalkow, 1982). Most of these alkaloids are esters of the necine base retronecine (II). Recently, we reported the X-ray structure of retronecine and its C7 epimer heliotridine (Gelbaum, Glinski, VanDerveer & Zalkow, 1985). As

part of a program to modify the retronecine skeleton, in anticipation of altering biological activity, we attempted to prepare epoxides of retronecine and heliotridine, and have recently reported X-ray structures of such epoxides (Glinski, VanDerveer & Zalkow, 1985). Surprisingly, treatment of retronecine with *N*-bromoacetamide gave the expected epoxide only as a minor product, and as a major product the new heterocyclic compound, 2 α -bromo-1 β ,7 β -epoxytrachelanthamidine (I) whose structure is reported here for the first time.



Experimental. The compound (I) is a major constituent of a reaction mixture resulting from the treatment of (II) with *N*-bromoacetamide in 30% sulfuric acid followed by basification. The reaction mixture, after chromatography, afforded crystalline (I), m.p. 444.5–446 K (uncorrected), $[\alpha]_D^{25.0^\circ\text{C}} = +0.6^\circ$ [ethanol, 1.6 g dm⁻³]. Crystal density by flotation in CBrCl₃–hexane. Axial photographs showed the crystal of (I), ca 0.60 × 0.10 × 0.15 mm (from methanol), to be orthorhombic and systematic extinctions indicated space group $P2_12_12_1$. Unit-cell parameters and orientation matrix for (I) determined on a Syntex $P2_1$ four-circle diffractometer equipped with a graphite mono-

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chromator (Bragg 2θ angle = 12.2°), take-off angle 6.74° using Mo $K\alpha$ radiation. 15 strong reflections (2θ from 14.11 to 24.22°) machine centered and used in least-squares refinement of lattice parameters and orientation matrix. Intensity data collected using θ - 2θ scans, background counts at beginning and end of each scan with X-ray source and monochromator settings identical to those used to determine unit-cell parameters. Intensities of three standard reflections: 0,0,10, 060 and 400 measured every 97 scans did not vary significantly ($\pm 5\%$). A variable scan rate from 2.02 to $29.3^\circ \text{ min}^{-1}$ used to collect a total of 1759 reflections in a complete quadrant $\pm h, +k, +l$ of data out to $2\theta = 50^\circ$ ($\sin\theta/\lambda = 0.5947 \text{ \AA}^{-1}$), 1558 unique reflections, $R_{\text{int}} = 0.023$, of these, 1395 accepted as statistically above background on the basis that $F > 3\sigma(I)$ [$\sigma(F) = (\text{total counts} + \text{sum of backgrounds})^{1/2} \times \text{scan rate}$], $\sigma(F) = \sigma(I)/(2FL_p)$.

ω scans of several low- 2θ -angle reflections gave peak width at half height of less than 0.20° indicating a satisfactory mosaic spread for the crystal. Intensity data for zero and upper levels collected at a rapid scan rate and intensities examined for systematic absences. A Lorentz-polarization correction applied. Absorption and extinction corrections not applied. Direct methods using *SHELX76* (Sheldrick, 1976) generated a series of *E* maps, one of which correctly located the Br atom. A subsequent difference Fourier map based on the Br position contained the remaining non-H atoms. All H atoms located from a difference Fourier map. Coordinates of the H atoms remained fixed and their temperature factors refined isotropically. Full-matrix least-squares refinement with all non-H atoms anisotropic gave $R = 0.037$ and $wR = 0.038$ using *F* ($S = 1.16$). Maximum least-squares shift to e.s.d. ratio 0.31; final difference Fourier map maximum $+1.27$ (0.91 \AA from Br) and minimum -0.91 e \AA^{-3} . Goodness of fit = 1.13, atomic scattering factors as in *SHELX*. A weighting scheme with $w = 1.025/[(\sigma F)^2 + 0.00091 F^2]$ (*SHELX*) was used. When the reported structure was inverted and refined, the following results were obtained: $R = 0.057$, $wR = 0.063$, maximum shift to e.s.d. 0.37, maximum residual electron density 1.39 e \AA^{-3} , 0.89 \AA from Br, goodness of fit = 2.62.

Discussion. Atomic parameters for (I) are given in Table 1.*

The *ORTEP*II (Johnson, 1976) view of (I) is shown in Fig. 1, using 50% probability ellipsoids. The thermal parameters of the H atoms have been artificially

* Lists of structure factors, H-atom coordinates and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42911 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Final atomic coordinates and equivalent isotropic thermal parameters

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

	x	y	z	$U_{\text{eq}} (\text{\AA}^2)$
Br	-0.02645 (8)	-0.01701 (6)	-0.79104 (3)	0.045
C(1)	0.2378 (6)	0.0096 (5)	-0.6422 (3)	0.033
C(2)	0.0951 (8)	-0.1019 (5)	-0.6865 (3)	0.038
C(3)	-0.0880 (8)	-0.1303 (5)	-0.6226 (3)	0.038
N	-0.1178 (5)	0.0164 (4)	-0.5793 (2)	0.032
C(5)	-0.1579 (7)	-0.0082 (6)	-0.4872 (3)	0.042
C(6)	0.0652 (9)	-0.0398 (6)	-0.4483 (3)	0.049
C(7)	0.2228 (7)	0.0353 (6)	-0.5088 (3)	0.042
C(8)	0.0872 (7)	0.0969 (5)	-0.5829 (3)	0.032
C(9)	0.4047 (8)	0.0910 (6)	-0.6933 (4)	0.048
O(1)	0.3355 (5)	-0.0647 (4)	-0.5676 (2)	0.042
O(2)	0.5360 (6)	0.1875 (4)	-0.6435 (2)	0.054

Table 2. Angles ($^\circ$) with e.s.d.'s in parentheses

C(8)-C(1)-C(2)	105.4 (3)	C(9)-C(1)-C(2)	118.5 (4)
C(9)-C(1)-C(8)	119.9 (4)	O(1)-C(1)-C(2)	108.1 (4)
O(1)-C(1)-C(8)	89.6 (3)	O(1)-C(1)-C(9)	111.4 (3)
C(1)-C(2)-Br	110.9 (3)	C(3)-C(2)-Br	109.4 (3)
C(3)-C(2)-C(1)	103.7 (4)	N-C(3)-C(2)	104.2 (3)
C(5)-N-C(3)	109.7 (4)	C(8)-N-C(3)	108.0 (3)
C(8)-N-C(5)	104.8 (3)	C(6)-C(5)-N	105.5 (3)
C(7)-C(6)-C(5)	104.1 (4)	C(8)-C(7)-C(6)	106.6 (4)
O(1)-C(7)-C(6)	115.6 (4)	O(1)-C(7)-C(8)	89.8 (3)
N-C(8)-C(1)	107.4 (3)	C(7)-C(8)-C(1)	87.1 (3)
C(7)-C(8)-N	105.4 (3)	O(2)-C(9)-C(1)	113.1 (4)
C(7)-O(1)-C(1)	92.0 (3)		

reduced to clarify the picture. Bond distances (\AA) are indicated in Fig. 1, and bond angles are listed in Table 2.

The three rings of (I) constitute the previously unreported heterocyclic system 1 α H-oxeto[2,3,4-*g,h*]-pyrrolizine. The loline group of alkaloids (Yunusov & Akramov, 1955; Bates & Morehead, 1972, and references therein) similarly possess an oxygen bridge joining C(7) and C(2). The presence of an oxygen bridge between C(1) and C(7) in (I) introduces unusual strain into the pyrrolizidine skeleton, reflected by the dihedral angle between the planes of N, C(8), C(7), and N, C(8), C(1) of only 91.8° , while in the closely related but more flexible molecules of α -epoxyretrocine or α - and β -epoxyheliotridine (Glinski, VanDerveer & Zalkow, 1985) the same value varies from 122.2 to 124.9° . In (I), C(7) as well as C(1) are parts of a rigid structure, leaving some conformational freedom only to C(2), C(3), C(5) and C(6). Ring *A*, consisting of C(1), C(2), C(3), N and C(8) is planar within 0.200 \AA , and ring *B*, consisting of C(5), C(6), C(7), C(8) and N is planar within 0.227 \AA . Both rings assume 'envelope' conformations in which C(1), C(2), C(8) and N are planar within 0.071 \AA with C(3) *endo*-buckled 0.477 \AA off-plane, and in which C(5), C(6), C(7) and C(8) are coplanar within 0.024 \AA with N *exo*-buckled 0.527 \AA off-plane. The oxetane ring, consisting of C(1), C(8),

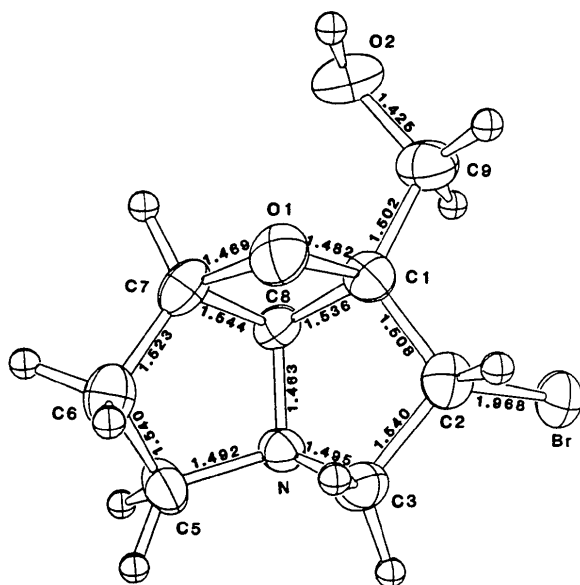


Fig. 1. 2 α -Bromo-1 β ,7 β -epoxytrachelanthamidine (the bond-length errors are within 0.007 Å).

C(7) and O(1), has all angles close to 90° ($\pm 2.9^\circ$) with O(1) 0.233 Å out of the plane of C(1), C(8) and C(7).

The intermolecular distance O(2)···N' (N' at $-1+x, y, z$) of 2.826 Å is below the combined van der Waals radii and the distance H(O2)···N' of 1.82 Å is considerably less than the combined van der Waals

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Structure of 5,5,6-Trimethyl-1,4-diphenyl-2,3,7-trioxa[2.2.1]bicycloheptane

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Abstract. C₁₉H₂₀O₃, $M_r = 296.37$, monoclinic, $P2_1/n$, $a = 19.078$ (7), $b = 7.149$ (1), $c = 24.221$ (4) Å, $\beta = 104.37$ (4)°, $V = 3199.9$ Å³, $Z = 8$, $D_x = 1.230$ g cm⁻³, $\lambda(\text{Mo K}\alpha) = 0.71069$ Å, $\mu = 0.80$ cm⁻¹, $F(000) = 1264$, $T = 298$ K, final $R = 0.038$ for 1656 unique observed reflections based on $I > 3\sigma(I)$. The two molecules of the asymmetric unit are very similar, including the torsion angles of the phenyl groups.

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radii (Hamilton & Ibers, 1968) suggesting the existence of a hydrogen bond.

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Relatively long O–O bond lengths of 1.484 (4) and 1.485 (3) Å and small C–O–C angles of 95.7 (3) and 96.7 (3)° are observed.

Introduction. We recently reported (Kirschenheuter & Griffin, 1983) that the photoinduced 9,10-dicyanoanthracene (DCA) sensitized photooxidation of 3,3,4-trimethyl-1,2-diphenylcyclobutene (1) gives a pair of epimeric ozonides: 5,5,6-trimethyl-1,4-diphenyl-2,3,7-trioxa[2.2.1]bicycloheptanes (2) and (3), respectively. These epimeric ozonides were tentatively assigned the