Discussion. Atomic coordinates and equivalent isotropic temperature factors of non-H atoms are reported in Table 1;* bond lengths and angles (*PARST*, Nardelli, 1983) are given in Table 2 and agree well with generally accepted values. Fig. 1 is a computer-generated perspective drawing of the final X-ray model of the title compound, H atoms are omitted for clarity.

The X-ray crystallographic study of (II) confirmed the oxygenation pattern of the molecule and the overall relative stereochemistry of the lanostane nucleus; assuming that the chiral centres of (II) have the same configuration as the natural (+)-lanosterol, the configuration of C(24) is *R*.

Rings *A–C* adopt the chair, half-chair and 1,2-diplanar conformations, respectively (Bucourt, 1974), though they are somewhat deformed. Ring *A* is slightly flattened, probably to relieve the severe 1,3-diaxial methyl–methyl interaction and to allow the formation of the 1,3-dioxolane ring. In ring *B* C(5) is -0.61 (2) and C(6) 0.15 (2) Å out of the mean plane through C(7)C(8)C(9)C(10), whereas in ring *C* C(12) is 0.33 (2) and C(13) 0.85 (2) Å above the mean plane through C(8)C(9)C(11)C(14). The cyclopentane ring *D* is closer to the 'half-chair' than to the 'envelope' form, C(13) is 0.36 (2) and C(14) -0.40 (2) Å out of the mean plane through the other three atoms.

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* Lists of structure factors, anisotropic thermal parameters, H-atom coordinates and least-squares-planes' data have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 42242 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

As far as the conformations of the heterocyclic rings are concerned, the 1,3-dioxolane ring is in an almost perfect half-chair conformation, whereas the five-, six- and seven-membered rings constituting the bicyclo-|3.2.1|octane system adopt the half-chair, chair and boat conformations, respectively.

The largest distortion is suffered by the seven-membered ring to relieve the otherwise intolerable repulsive interaction between the axial H(22) and one of the geminal methyls at C(25).

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Retronecine and Heliotridine, $C_8H_{13}NO_2$: Diastereoisomeric Pyrrolizidine Necine Bases

BY LESLIE T. GELBAUM, JAN A. GLINSKI, DONALD VANDERVEER AND LEON H. ZALKOW*

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332, USA

Abstract. $M_r = 155.20$, orthorhombic, $P2_12_12_1$, $Z = 4$, $\lambda(Mo\,K\bar{\alpha}) = 0.71069$ Å, $F(000) = 336$, $T = 298$ K. Retronecine: $a = 7.944$ (4), $b = 8.536$ (5), $c = 12.062$ (6) Å, $V = 817.9$ (7) Å^3, $D_m = 1.25$, $D_x = 1.26$ g cm^{-3}, $\mu = 0.54$ cm^{-1}. Heliotridine: $a = 11.904$ (2), $b = 7.620$ (1), $c = 8.800$ (1) Å, $V = 798.2$ (2) Å^3, $D_m = 1.32$, $D_x = 1.29$ g cm^{-3}, $\mu = 0.55$ cm^{-1}. Final $R = 0.040$ and 0.038 for 825 and 1328 observed reflections for retronecine and heliotridine respectively. The ring system in retronecine (I) is *exo-* and in heliotridine (II) *endo*-puckered. In both structures O(1) and O(2) are in an antiparallel conformation. There are no unusual bond distances or angles. The intermolecular distances N(4)$\cdots$O(2) for (I) (2.69) and for (II) (2.72 Å) indicate the existence of hydrogen bonding.

Introduction. The pyrrolizidine alkaloids have attracted a great deal of attention, primarily because of their causative effects in the heavy loss of livestock in many

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* To whom correspondence should be addressed.

countries of the world (Bull, Culvenor & Dick, 1968). More recently, the human-health hazards in, for example, herbal teas, honey, and grain contaminants have become of increasing concern (Huxtable, 1979; Roitman, 1983). The toxicity (hepatotoxicity) has been ascribed to the alkylation of biological nucleophiles (protein and nucleic acids) by 'metabolic pyrroles' produced in the liver from the pyrrolizidine alkaloids (McLean, 1970). On the cellular level, pyrrolizidine alkaloids also exhibit antimitotic action (McLean, 1970). Related to this is the antitumor activity of certain pyrrolizidine alkaloids (Culvenor, 1968), in particular, the pyrrolizidine alkaloid N-oxide, indicine N-oxide (Kugelman, Liu, Axelrod, McBride & Rao, 1976), and semisynthetic analogs (Gelbaum, Gordon, Miles & Zalkow, 1982). Almost all of the biologically active (toxic and antitumor) pyrrolizidine alkaloids and N-oxides contain, as their necine bases, either retronecine (I) or heliotridine (II) and are esterified at C(9) and/or C(7) (macrocyclic diester or diesters).

The absolute configurations of (I) and (II) are known from chemical interrelationships and degradations (Warren & Von Klemperer, 1958; Warren, 1970, and references therein) and the relative configurations have been confirmed numerous times by X-ray studies on alkaloids containing these necine bases, beginning with that on jacobine bromohydrin (Fridrichsons, Mathieson & Sutor, 1960). However, X-ray structures of these necines themselves have never been reported, and we provide here this information for the first time.

Experimental. (I) prepared by hydrolysis of monocrotaline (Gelbaum et al., 1982) and suitable crystals obtained from acetone. Specific rotation, $[\alpha]_D^{25 \cdot 0^{\circ}C}$ = +55·0° [ethanol, 1·0 g dm^{-3}]. (II) prepared by inversion of the C(7) hydroxyl group in (I) (Glinski & Zalkow, unpublished work) and the material so obtained was identical in physical properties and spectroscopically with synthetic (+)-heliotridine which, in turn, was identical to that derived from natural sources (Chamberlin & Chung, 1983). Suitable crystals obtained from toluene–methanol. Specific rotation, $[\alpha]_D^{25 \cdot 0^{\circ}C}$ = +31·0 [ethanol, 1·0 g dm^{-3}].

Experimental details for X-ray structures are in Table 1. Densities determined by flotation in hexane–carbon tetrachloride, Lp corrections in usual manner but no absorption or extinction corrections. Both structures solved using direct-methods program MULTAN78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Most non-H atoms located from E map, remaining non-H atoms from subsequent difference Fourier map, H coordinates for (I) calculated and H atoms refined as parts of C—H groups, hydroxyl H atoms located from difference Fourier map and refined. H atoms for (II) located from difference Fourier map and coordinates fixed. Parameters varied in full-matrix least-squares refinement on F: overall

Table 1. X-ray data collection and solution

	(I)	(II)
Crystal size (mm)	0·85 × 0·35 × 0·28	0·58 × 0·25 × 0·20
No. of reflections for lattice parameters		15
2θ range of reflections (°)	6·76–15·88	14·18–22·27
Diffractometer		Syntex P2$_1$
Radiation		Mo Kᾱ; graphite monochromator
Max. 2θ for data collection (°)		50 (sin θ/λ$_{max}$ = 0·5947 Å^{-1})
Scan type		θ–2θ
Scan speed (° min^{-1})	2·93–29·3	2·02–29·3
h,k,l range	0→9, 0→10, 0→14	±14, 0→9, 0→10
Standard reflections	006, 020, 400	006, 230, 10,0,0
Max. variations of I(%)	+2, −3	±4
No. of reflections measured	865	1643
No. of reflections >3σ(F)	825	1328
R	0·040	0·038
wR	0·040	0·047
w	2·0/[(σF)^2 + 0·0003F^2]	1·0/[(σF)^2 + 0·0035F^2]
Max. LS shift/σ	0·001	0·001
Max., min. in Δρ (e Å^{-3})	0·16, −0·27	0·27, −0·25
σ(I)		(total counts + sum of backgrounds)$^{1/2}$. scan rate
σ(F)		σ(I)/2.F.Lp
S	2·12	0·94

scale factor, coordinates and anisotropic temperature factors for non-H atoms, isotropic temperature factors for H atoms. Scattering factors as in SHELX76 (Sheldrick, 1976).

Discussion. Atomic parameters for (I) and (II) are given in Tables 2 and 3 respectively.* The ORTEPII (Johnson, 1976) drawings for (I) and (II) can be seen in Figs. 1 and 2 respectively. The bond distances (Å) are indicated on the drawings. Bond angles are listed in Tables 4 and 5 respectively.

The ring system in retronecine exists in the exo-puckered form where the angle between C(5), C(6), C(7), and C(5), N(4), C(8) is 40·7°. This agrees well with the other retronecine-based alkaloids previously reported: fulvine 46° (Sussman & Wodak, 1973), axillarine 42° (Stoeckli-Evans & Crout, 1976), mono-crotaline 37° (Stoeckli-Evans, 1979), incanine 42° (Tashkhodzhaev, Telezhenetskaya & Yunusov, 1979), trichodesmine 35° (Tashkhodzhaev, Yagudaev & Yunusov, 1979) and junceine 36·7° (Stoeckli-Evans, 1982). In contrast, heliotridine is endo-puckered with the angle between C(5), C(6), C(7) and C(5), N(4), C(8) being 42·2°. This value falls between those reported previously for the heliotridine alkaloids lasio-carpine 34·0° (Hay, Mackay & Culvenor, 1982) and heliotrine 45° (Wodak, 1975). The angle between the least-square planes defined by atoms C(1), C(2), C(3), N(4), C(8), and C(5), N(4), C(8), C(7) is 124·4° for retronecine. This compares well with the values previously reported for the retronecine-based alkaloids. This angle in heliotridine is 121·6° which is very close to the 120·6° reported for lasiocarpine but less than the

Table 2. *Final atomic coordinates for* (I) *with e.s.d.'s in parentheses and* U_{eq} *values* (Å^2)

$$U_{eq} = \tfrac{1}{3}\Sigma U_{ii}.$$

	x	y	z	U_{eq}
N(4)	−0·3130 (2)	0·1355 (2)	0·2012 (1)	0·035
O(1)	−0·0931 (2)	0·1805 (2)	0·4161 (2)	0·044
O(2)	−0·4431 (2)	0·5220 (2)	0·4317 (1)	0·054
C(1)	−0·2838 (3)	0·3806 (3)	0·2913 (2)	0·038
C(2)	−0·2262 (3)	0·3984 (3)	0·1891 (2)	0·059
C(3)	−0·2356 (4)	0·2500 (3)	0·1242 (2)	0·054
C(5)	−0·2097 (4)	−0·0038 (4)	0·2252 (2)	0·042
C(6)	−0·2498 (4)	−0·0415 (3)	0·3449 (2)	0·034
C(7)	−0·2574 (3)	0·1190 (3)	0·3986 (2)	0·043
C(8)	−0·3456 (3)	0·2159 (3)	0·3093 (2)	0·057
C(9)	−0·2834 (3)	0·5006 (3)	0·3811 (2)	0·043

130° reported for heliotrine. The ring-fusion distances N(4)—C(8) can be seen on the *ORTEP* drawings and are consistent with the values for other pyrrolizidine alkaloids.

It can be seen in the *ORTEP* drawings that in both retronecine and heliotridine O(1) and O(2) are in an antiparallel conformation. In all of the previously reported X-ray data for macrocyclic diesters of retronecine, the O atoms corresponding to O(1) and O(2) are fixed by the macrocyclic ring so that they must be on the same side. This is also observed in the recently published X-ray structures of the two C(9)-monoesters of retronecine, lycopsamine and intermedine (Mackay, Sadek & Culvenor, 1983).

Table 3. *Final atomic coordinates for* (II) *with e.s.d.'s in parentheses and* U_{eq} *values* (Å^2)

$$U_{eq} = \tfrac{1}{3}\Sigma U_{ii}.$$

	x	y	z	U_{eq}
C(1)	−0·7883 (2)	−0·5340 (2)	−0·6071 (2)	0·033
C(2)	−0·6915 (2)	−0·6157 (3)	−0·6194 (2)	0·043
C(3)	−0·5961 (2)	−0·5050 (3)	−0·5703 (3)	0·055
N(4)	−0·6479 (1)	−0·3363 (2)	−0·5207 (2)	0·039
C(5)	−0·6098 (2)	−0·1808 (4)	−0·6078 (3)	0·058
C(6)	−0·6921 (2)	−0·1633 (3)	−0·7385 (2)	0·052
C(7)	−0·8025 (2)	−0·2030 (2)	−0·6605 (2)	0·038
C(8)	−0·7720 (1)	−0·3498 (3)	−0·5483 (2)	0·033
C(9)	−0·9038 (2)	−0·6036 (2)	−0·6407 (2)	0·038
O(1)	−0·8419 (2)	−0·0589 (2)	−0·5724 (2)	0·057
O(2)	−0·9020 (1)	−0·7584 (2)	−0·7303 (1)	0·040

Table 4. *Bond angles* (°) *for* (I) *with e.s.d.'s in parentheses*

C(5)—N(4)—C(3)	115·1 (2)	C(7)—C(6)—C(5)	102·9 (2)
C(8)—N(4)—C(3)	108·4 (2)	C(6)—C(7)—O(1)	111·1 (2)
C(8)—N(4)—C(5)	107·2 (2)	C(8)—C(7)—O(1)	109·0 (2)
C(8)—C(1)—C(2)	110·8 (2)	C(8)—C(7)—C(6)	101·9 (2)
C(9)—C(1)—C(2)	126·7 (2)	C(1)—C(8)—N(4)	104·3 (2)
C(9)—C(1)—C(8)	122·0 (2)	C(7)—C(8)—N(4)	106·7 (2)
C(3)—C(2)—C(1)	112·0 (2)	C(7)—C(8)—C(1)	117·2 (2)
C(2)—C(3)—N(4)	104·6 (2)	C(1)—C(9)—O(2)	113·5 (2)
C(6)—C(5)—N(4)	104·0 (2)		

Table 5. *Bond angles* (°) *for* (II) *with e.s.d.'s in parentheses*

C(8)—C(1)—C(2)	110·9 (2)	C(9)—C(1)—C(2)	128·2 (2)
C(9)—C(1)—C(8)	120·9 (2)	C(3)—C(2)—C(1)	112·3 (2)
N(4)—C(3)—C(2)	105·0 (2)	C(5)—N(4)—C(3)	114·3 (2)
C(8)—N(4)—C(3)	107·5 (2)	C(8)—N(4)—C(5)	105·8 (2)
C(6)—C(5)—N(4)	105·4 (2)	C(7)—C(6)—C(5)	101·5 (2)
C(8)—C(7)—C(6)	103·4 (2)	O(1)—C(7)—C(6)	112·3 (2)
O(1)—C(7)—C(8)	106·8 (1)	N(4)—C(8)—C(1)	104·2 (2)
C(7)—C(8)—C(1)	115·3 (1)	C(7)—C(8)—N(4)	106·7 (2)
O(2)—C(9)—C(1)	112·9 (1)		

Fig. 1. Retronecine (the bond-length errors are within 0·003 Å).
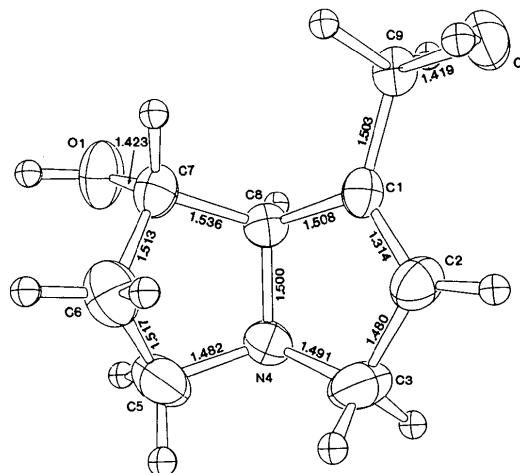

Fig. 2. Heliotridine (the bond-length errors are within 0·003 Å).

Intermolecular contacts between N(4) and O(2) indicate hydrogen bonding in both structures (Hamilton & Ibers, 1968). For (I) N(4)···O(2) is 2·69 and N(4)···H(O2) is 1·79 Å. For (II) N(4)···O(2) is 2·72 and N(4)···H(O2) is 1·74 Å. The combined van der Waals radii are N···O 2·9 and N···H(O) 2·7 Å.

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Diastereoisomeric Epoxides of Heliotridine and Retronecine, $C_8H_{13}NO_3$

BY JAN A. GLINSKI, DONALD VANDERVEER AND LEON H. ZALKOW*

School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332, USA

Abstract. $M_r = 171·1$, $\lambda(\text{Mo } K\bar{\alpha}) = 0·71069$ Å, $T = 298$ K. β-Epoxyheliotridine (I): orthorhombic, $P2_12_12_1$, $a = 6·2951$ (3), $b = 7·7019$ (5), $c = 17·722$ (1) Å, $U = 859·25$ (9) Å^3, $Z = 4$, $D_m = 1·321$, $D_x = 1·322$ g cm^{-3}, $\mu(\text{Mo } K\bar{\alpha}) = 0·63$ cm^{-1}, $F(000) = 368$. α-Epoxyheliotridine (II): monoclinic, $P2_1$, $a = 6·251$ (2), $b = 8·578$ (1), $c = 8·069$ (2) Å, $\beta = 110·68$ (2)°, $U = 404·8$ (2) Å^3, $Z = 2$, $D_m = 1·403$, $D_x = 1·405$ g cm^{-3}, $\mu(\text{Mo } K\bar{\alpha}) = 0·66$ cm^{-1}, $F(000) = 184$. α-Epoxyretronecine (III): monoclinic, $P2_1$, $a = 6·509$ (1), $b = 8·340$ (1), $c = 7·799$ (1) Å, $\beta = 105·85$ (1)°, $U = 407·29$ (1) Å^3, $Z = 2$, $D_m = 1·395$, $D_x = 1·396$ g cm^{-3}, $\mu(\text{Mo } K\bar{\alpha}) = 0·66$ cm^{-1}, $F(000) = 184$. Full-matrix least-squares refinement converged at R values of 0·037, 0·038 and 0·032 for 1389, 1299 and 1395 reflections for (I), (II) and (III), respectively. There are no unusual bond distances or angles. There is intermolecular H bonding between N and the O atom of the CH_2OH group (N···O 2·70, 2·73 and 2·77 Å, respectively). The absolute configurations of the three diastereomers are defined by reference to the absolute configurations of the parent alkaloids heliotridine and 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, New York: Academic Press; and references therein].

* To whom correspondence should be addressed.