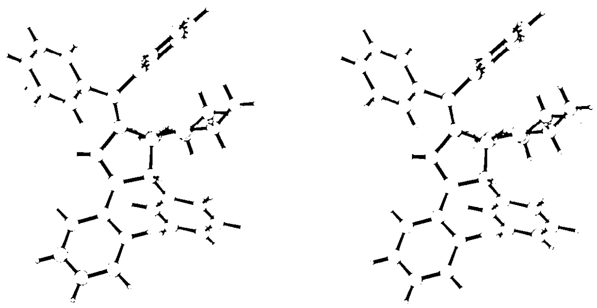

Fig. 2. A stereodrawing of the molecule viewed perpendicular to the lactam ring plane.

drawing of the molecule viewed perpendicular to the plane defined by atoms N(1), C(2) and C(3) is given in Fig. 2, and clearly shows the *cis*-axial configuration of the hydrogen atoms at C(4) and C(5). The morpholinocarbonyl group at C(4) and phenyl ring at C(5) are thus equatorial and the torsion angle C(41)—C(4)—C(5)—C(51) is 29·6 (4)°.

The conformation of the lactam ring is given by the pseudorotational phase parameters (Altona, Geise & Romers, 1968) $\Delta = -49\cdot3\ (10)°$ and $\varphi_m = 25\cdot9\ (10)°$, where the torsion angle C(3)—C(4)—C(5)—N(1) is taken as φ_0. These parameters indicate that the C(4) envelope conformation is predominant; C(4) and C(5) are displaced by −0·457 (5) and −0·058 (5) Å respectively from the plane defined by N(1), C(2) and C(3). All four aromatic rings are planar within experimental error and the morpholino ring adopts a chair conformation with an asymmetry parameter (Duax & Norton, 1975) of $\Delta C_s^{N(43)} = 2\cdot7°$. In the diphenylmethylene moiety at C(3) the two phenyl rings are orientated at a dihedral angle of 93·8 (2)° with respect to one another. The phenyl rings at N(1) and C(5) are inclined by dihedral angles of 25·9 (1) and 62·2 (1)° respectively with respect to the N(1), C(2), C(3) plane.

Our thanks are due to the Governors of Chelsea College for a research studentship (to AEB).

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Grantianine, $C_{18}H_{23}NO_7$: a Pyrrolizidine Alkaloid

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(*Received* 25 *January* 1984; *accepted* 11 *April* 1984)

Abstract. $M_r = 365\cdot1$, monoclinic, $P2_1$, $a = 12\cdot93\ (1)$, $b = 6\cdot32\ (1)$, $c = 10\cdot78\ (1)$ Å, $\beta = 102\cdot73\ (9)°$, $V = 859\cdot3$ Å^3, $Z = 2$, $D_x = 1\cdot411$, $D_m = 1\cdot40\ (2)$ Mg m^{-3}, $\lambda(\text{Mo } K\alpha) = 0\cdot71069$ Å, $\mu = 0\cdot07$ mm^{-1}, $F(000) = 388$, room temperature. Final $R = 0\cdot059$ for 1321 observed reflections. Grantianine, a retronecine-derived pyrrolizidine alkaloid, has the carbonyl bonds of the ester functions on opposite sides of the 11-membered macrocycle with an angle of 139·6 (5)° between the bonds. The γ-butyrolactone ring is *trans*-fused to the macrocycle across bond C(13)—C(14). The exocyclic methyl group at C(24) is in a quasi-axial orientation.

Introduction. The present analysis is part of a study of natural and synthetic pyrrolizidine alkaloids (PA's) which are structurally interesting. Grantianine is a rare PA and was originally isolated from *Crotalaria grantiana* (Adams, Carmack & Rogers, 1942). Recently it has been found to be the major alkaloid isolated from *Crotalaria globifera* seeds obtained from inland

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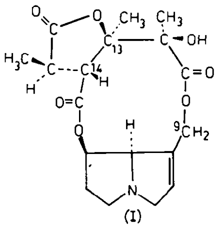
Natal at an altitude of 1050 m (Brown, Devlin & Robins, 1984). Here we report on the crystal structure of grantianine which has confirmed the chemical structure (I) proposed earlier (Adams & Gianturco, 1956) and also clarifies the relative stereochemistry of the four asymmetric centers in the acid portion of the molecule.



(I)

Experimental. Tabular crystals grown from a methanol solution. Preliminary Weissenberg and precession photographs indicated the crystals to be monoclinic, space group $P2_1$. D_m measured by flotation. Lattice parameters from axial reflections. One crystal of dimensions *ca* 0·2 × 0·4 × 0·2 mm used to collect data for layers *h*0–6*l* and *hk*0–3 with $\theta < 25°$ on a Stoe Stadi-2 two-circle diffractometer (graphite-monochromated Mo *K*α radiation) using the variable ω-scan technique [$\Delta\omega = 1 + 0{\cdot}6(\sin\mu/\tan\theta)$]; one standard reflection per layer, 2% intensity variation; 1321 unique reflections with $I > 1{\cdot}5\sigma(I)$ used in subsequent calculations. No correction for absorption. Structure solved by direct methods using *SHELX*76 (Sheldrick, 1976); 14 non-H atoms were located in an *E* map, a difference map revealed the remaining heavy atoms; all 23 H-atom positions located from difference Fourier maps. Complex neutral-atom scattering factors from *International Tables for X-ray Crystallography* (1974). Weighted anisotropic (isotropic for H atoms) blocked full-matrix least-squares refinement for 1321 reflections converged at $R = 0{\cdot}059$, $R_w = 0{\cdot}052$; function minimized $\sum w(|F_o| - |F_c|)^2$ with $w = [\sigma^2(|F_o|) + 0{\cdot}00055(|F_o|)^2]^{-1}$. In final cycle of refinement average parameter shift $< 0{\cdot}2\sigma$; residual features in final difference map between +0·24 and −0·26 e Å^{-3}.

Discussion. Final positional and equivalent isotropic thermal parameters are given in Table 1.* Bond distances and angles and their standard deviations are given in Table 2. The torsion angles in the macrocycle and in the lactone ring are given in Table 3. The torsion angles involving the C(9) H atoms are given in Table 4. The numbering scheme used is apparent from Fig. 1 (prepared using *ORTEP*; Johnson, 1976), which also shows the configuration at asymmetric centers C(12), C(13), C(14) and C(24). Grantianine is a retronecine-derived PA with an 11-membered macrocycle.

The pyrrolizidine nucleus exists in the *exo*-puckered form with a puckering angle between planes defined by atoms C(5), C(6), C(7) and C(5), N(4), C(8) of 41·2 (5)°. Values ranging from 35 to 46° have been observed previously for related structures. The angle between the mean plane through the unsaturated ring and the mean plane defined by atoms C(5), N(4), C(8), C(7) is 125·0 (2)°, equal to the average value observed previously. The ring fusion distance N(4)—C(8) is 1·490 (7) Å, close to the average value (1·50 Å) observed previously for the free alkaloids. In two PA's studied as quarternary salts values of *ca* 1·54 Å have been observed (Stoeckli-Evans & Robins, 1983; Sawhney, SenGupta, Hossain & van der Helm, 1983). Atom C(9) lies 0·19 (1) Å from the unsaturated-ring plane [planar to within 0·01 (1) Å]. A similar situation has been observed in 1,2-didehydrocrotalanine (Stoeckli-Evans & Robins, 1983) and in PA's with a 12-membered macrocycle where deviations of as much as 0·25 (1) Å have been observed (Mackay & Culvenor, 1982).

The crystal structures of eight natural and one synthetic 11-membered macrocyclic retronecine-derived PA's have now been published. The synthetic analogue 1,2-didehydrocrotalanine (Stoeckli-Evans & Robins, 1983), and trichodesmine (Tashkhodzhaev, Telezhenetskaya & Yunusov, 1979) have the ester carbonyl bonds antiparallel. In grantaline (Mackay & Culvenor, 1983), which has an oxetane ring fused to the macrocycle at bond C(13)—C(14), the carbonyl bonds lie on the same side of the macrocycle but are directed outwards from it with an angle of 94° between the bonds. Five of the remaining natural PA's have the carbonyl bonds nearly synparallel (see Stoeckli-Evans, 1982). Full details of the sixth, spectabiline (Shoudao & Benming, 1982), have not yet appeared. In grantianine the ester carbonyl bonds are on opposite sides of the macrocycle with an angle of 139·6 (5)° between the bonds, compared to 155·5° in trichodesmine and 164·5° in 1,2-didehydrocrotalanine. This latter situation resembles that observed in 12-membered (and larger) macrocyclic PA's, with an average angle of 163 (2)° between the bonds (Mackay & Culvenor, 1982).

The shortest transannular interaction in grantianine is that between atoms C(11) and O(16) of distance 2·913 (4) Å, while distance O(10)···O(16) is 3·119 (6) Å. In 1,2-didehydrocrotalanine the same distances are 2·95 (1) and 2·96 (1) Å respectively. In trichodesmine transannular distance C(15)···O(10) is the shortest (2·83 Å) and distance O(10)···O(16) is also 2·83 Å. The conformation of the 11-membered macrocycle is defined by the torsion angles (Table 3).

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* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39412 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Final positional parameters and equivalent isotropic thermal parameters* ($\times 10^4$) *with e.s.d.'s in parentheses*

$$U_{eq} = \tfrac{1}{3}\textstyle\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j.$$

	x	y	z	U_{eq}(Å^2)
C(1)	2878 (3)	5995 (9)	4793 (4)	366 (12)
C(2)	3068 (4)	8022 (11)	5035 (4)	490 (16)
C(3)	2092 (5)	9289 (11)	5060 (6)	611 (18)
N(4)	1237 (3)	7728 (7)	4752 (3)	467 (12)
C(5)	432 (4)	8213 (11)	3565 (5)	565 (17)
C(6)	77 (4)	6090 (10)	3045 (5)	539 (17)
C(7)	1081 (4)	4822 (9)	3275 (4)	407 (14)
C(8)	1693 (4)	5612 (10)	4580 (4)	446 (14)
C(9)	3693 (4)	4335 (10)	4889 (4)	452 (14)
O(10)	3706 (2)	3329 (6)	3654 (2)	430 (8)
C(11)	4160 (4)	4460 (11)	2882 (4)	459 (14)
C(12)	4212 (3)	3331 (9)	1626 (3)	467 (13)
C(13)	3112 (4)	2666 (9)	849 (4)	470 (14)
C(14)	2328 (4)	4592 (9)	511 (4)	401 (13)
C(15)	1431 (4)	4440 (9)	1193 (4)	475 (14)
O(16)	1728 (2)	5334 (6)	2355 (2)	422 (9)
O(17)	604 (2)	3591 (7)	798 (3)	702 (11)
O(18)	4547 (3)	6171 (7)	3137 (3)	641 (12)
O(19)	4580 (3)	4843 (8)	849 (3)	658 (12)
C(20)	4991 (6)	1508 (14)	1948 (6)	770 (23)
C(21)	2638 (7)	767 (12)	1378 (6)	658 (22)
O(22)	3307 (3)	1996 (6)	−392 (3)	587 (10)
C(23)	2732 (4)	3144 (10)	−1374 (4)	532 (15)
C(24)	1966 (4)	4586 (9)	−947 (4)	443 (14)
O(25)	2865 (3)	2880 (7)	−2440 (3)	698 (12)
C(26)	1882 (7)	6744 (12)	−1560 (5)	679 (22)

Table 2. *Bond distances* (Å) *and angles* (°)

C(1)–C(2)	1·320 (8)	C(12)–C(13)	1·541 (6)
C(2)–C(3)	1·500 (9)	C(12)–O(19)	1·421 (7)
C(3)–N(4)	1·465 (8)	C(12)–C(20)	1·520 (10)
N(4)–C(5)	1·492 (6)	C(13)–C(14)	1·574 (7)
N(4)–C(8)	1·490 (7)	C(13)–C(21)	1·515 (9)
C(5)–C(6)	1·487 (9)	C(13)–O(22)	1·477 (5)
C(6)–C(7)	1·499 (8)	C(14)–C(15)	1·507 (7)
C(7)–C(8)	1·538 (6)	C(14)–C(24)	1·537 (5)
C(7)–O(16)	1·467 (6)	C(15)–O(16)	1·350 (5)
C(8)–C(1)	1·518 (6)	C(15)–O(17)	1·188 (6)
C(1)–C(9)	1·474 (8)	O(22)–C(23)	1·361 (6)
C(9)–O(10)	1·479 (6)	C(23)–C(24)	1·492 (8)
O(10)–C(11)	1·328 (6)	C(23)–O(25)	1·211 (6)
C(11)–C(12)	1·544 (7)	C(24)–C(26)	1·509 (9)
C(11)–O(18)	1·198 (8)		

C(2)–C(1)–C(8)	108·8 (5)	C(11)–C(12)–C(20)	107·7 (4)
C(2)–C(1)–C(9)	125·3 (4)	C(13)–C(12)–C(20)	113·8 (5)
C(8)–C(1)–C(9)	125·4 (5)	O(19)–C(12)–C(20)	110·7 (4)
C(1)–C(2)–C(3)	113·6 (5)	C(12)–C(13)–C(14)	112·7 (4)
C(2)–C(3)–N(4)	103·5 (5)	C(12)–C(13)–C(21)	114·4 (4)
C(3)–N(4)–C(5)	113·9 (4)	C(14)–C(13)–C(21)	114·0 (5)
C(3)–N(4)–C(8)	109·4 (4)	C(12)–C(13)–O(22)	104·4 (4)
C(5)–N(4)–C(8)	107·3 (4)	C(14)–C(13)–O(22)	104·0 (3)
N(4)–C(5)–C(6)	103·7 (5)	C(21)–C(13)–O(22)	106·1 (4)
C(5)–C(6)–C(7)	103·7 (4)	C(13)–C(14)–C(15)	111·3 (4)
C(6)–C(7)–C(8)	103·3 (4)	C(13)–C(14)–C(24)	105·7 (4)
C(6)–C(7)–O(16)	111·9 (4)	C(15)–C(14)–C(24)	113·9 (4)
C(8)–C(7)–O(16)	106·9 (4)	C(14)–C(15)–O(16)	109·6 (4)
C(1)–C(8)–C(7)	119·3 (4)	C(14)–C(15)–O(17)	125·6 (4)
C(1)–C(8)–N(4)	104·6 (4)	O(16)–C(15)–O(17)	124·8 (4)
N(4)–C(8)–C(7)	105·5 (4)	C(7)–O(16)–C(15)	116·6 (4)
C(1)–C(9)–O(10)	113·1 (3)	C(13)–O(22)–C(23)	112·2 (4)
C(9)–O(10)–C(11)	115·3 (4)	O(22)–C(23)–C(24)	111·8 (4)
O(10)–C(11)–C(12)	114·3 (5)	O(22)–C(23)–O(25)	119·8 (5)
O(10)–C(11)–O(18)	124·2 (5)	C(24)–C(23)–O(25)	128·3 (5)
C(12)–C(11)–O(18)	121·5 (5)	C(14)–C(24)–C(23)	104·1 (4)
C(11)–C(12)–C(13)	112·9 (4)	C(14)–C(24)–C(26)	114·9 (5)
C(11)–C(12)–O(19)	106·9 (5)	C(23)–C(24)–C(26)	113·9 (5)
C(13)–C(12)–O(19)	104·6 (3)		

Table 3. *Torsion angles* (°) *in the macrocycle and the lactone ring* (*e.s.d. ca* 0·8° *in grantianine*)

	Grantianine	1,2-Didehydrocrotalanine	Trichodesmine
C(8)–C(1)–C(9)–O(10)	72·9	63·1	56·1
C(1)–C(9)–O(10)–C(11)	77·0	79·6	129·6
C(9)–O(10)–C(11)–C(12)	177·2	−175·8	−180·0
O(10)–C(11)–C(12)–C(13)	57·7	134·7	90·7
C(11)–C(12)–C(13)–C(14)	57·7	−52·1	−38·2
C(12)–C(13)–C(14)–C(15)	−112·5	−33·9	−57·2
C(13)–C(14)–C(15)–O(16)	86·6	106·4	142·7
C(14)–C(15)–O(16)–C(7)	−163·7	−175·6	−159·3
C(15)–O(16)–C(7)–C(8)	168·3	157·0	137·5
O(16)–C(7)–C(8)–C(1)	−20·3	−21·6	−24·8
C(7)–C(8)–C(1)–C(9)	−70·8	−75·9	−70·5

	Grantianine	Lactone *A**	Lactone *B*†
C(13)–O(22)–C(23)–C(24)	−6·9	0·1	0·0
O(22)–C(23)–C(24)–C(14)	13·6	17·9	−17·4
C(23)–C(24)–C(14)–C(13)	−14·5	−27·4	25·9
C(24)–C(14)–C(13)–O(22)	10·9	27·9	−25·8
C(14)–C(13)–O(22)–C(23)	−2·8	−18·1	16·5

* Lere-Porte, Petrissans & Brianso (1981).

† Declercq, Germain, Van Meerssche, Kok, De Clercq & Vandewalle (1980).

Table 4. *Torsion angles* (°) *involving the* C(9) H *atoms* (*e.s.d. ca* 0·8° *in grantianine*)

	Grantianine	1,2-Didehydrocrotalanine	Junceine	Senecionine
H(9*a*)–C(9)–O(10)–C(11)	−43·3	−40·7	148·2	149·8
H(9*b*)–C(9)–O(10)–C(11)	−165·3	−160·4	1·3	−27·6
H(9*a*)–C(9)–C(1)–C(2)	5·4	−7·5	20·1	136·8
H(9*b*)–C(9)–C(1)–C(2)	130·4	112·4	158·2	12·7
δ(H9) (p.p.m.)	0·82	0·62	0·13$^{\text{i}}$	1·47$^{\text{ii}}$
Angle between carbonyl bonds (°)	139·6	164·5	21·5	163·2

(i) PMR (200 MHz, $CDCl_3$). (ii) Bull, Culvenor & Dick (1968).

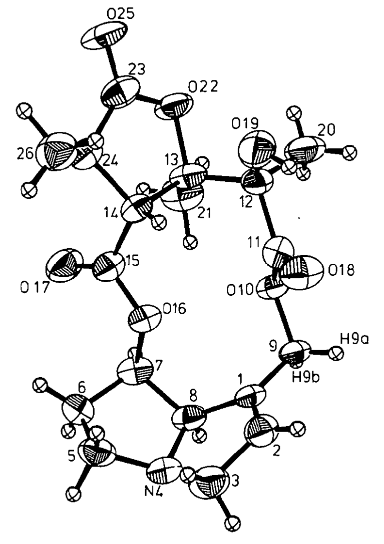

Fig. 1. A perspective view of the molecule showing the numbering scheme and vibrational ellipsoids (50% probability level).

The bond lengths and angles involving atoms C(13) and C(14) are normal. The presence of the fused lactone ring appears to perturb the torsion angles involving these atoms while the remainder are similar to those observed in 1,2-didehydrocrotalanine (*cf.* Table 3).

Atoms in the primary ester group, C(9), O(10), C(11), C(12) and O(18), are planar to within 0·01 (1) Å. The hydroxyl substituent at C(12) lies almost in this plane [torsion angle O(18)—C(11)—C(12)—O(19) −11·0 (8)°] and forms an intramolecular hydrogen bond with the carbonyl O atom, O(18). Distances O(19)···O(18), O(19)—H(19) and H(19)···O(18) are 2·611 (5), 0·85 (5) and 2·19 (8) Å, respectively, while angle O(19)—H(19)···O(18) is 111 (3)°. A similar situation has been observed in trichodesmine and the 12-membered macrocyclic PA senkirkine (Birnbaum, 1974). The C(9) methylene group has one H atom, H(9*a*), closer than the other to the plane of the ester group and the plane of the unsaturated ring [torsion angles H(9*a*)—C(9)—O(10)—C(11) −43 (3) and H(9*a*)—C(9)—C(1)—C(2) 5 (3)°]. In 1,2-didehydrocrotalanine the same torsion angles were −41 and −8° respectively. A relatively small difference in chemical shift of the H(9) atoms has been observed in the NMR spectra [δ H(9) of 0·82 p.p.m. for grantianine (Brown *et al.*, 1984), 0·71 p.p.m. for trichodesmine (Robins & Crout, 1969) and 0·62 p.p.m. for 1,2-didehydrocrotalanine (Devlin & Robins, 1982)]. The correlation between the position of the C(9) H atoms and the degree of magnetic non-equivalence as exhibited in the NMR spectra has been discussed previously (Stoeckli-Evans & Crout, 1976). It was deduced there that for PA's with the carbonyl groups antiparallel, as in 12-membered macrocyclic PA's such as senecionine (Mackay & Culvenor, 1982), as only one C(9) H atom lies closer to both the plane of the unsaturated ring and the plane of the ester group the shielding effects would be additive and δ H(9) would be large (observed values are between 1·2 and 1·5 p.p.m.). In 11-membered macrocyclic PA's for which the carbonyl groups are synparallel, as in junceine (Stoeckli-Evans, 1982), only one C(9) H atom lies close to the plane of the unsaturated ring, while the second H atom lies close to the plane of the ester group. Hence both H atoms are shielded to about the same extent and so δ H(9) will be small (observed values are between 0 and 0·7 p.p.m.). As the carbonyl groups are antiparallel in grantianine, 1,2-didehydrocrotalanine and trichodesmine, one might have expected larger values of δ H(9). However, as seen from Table 4, atom H(9*a*) lies almost in the plane of the unsaturated ring and relatively far away from the plane of the ester group.* Hence the small value of δ H(9) appears to be due mainly to the influence of the ring double bond. These assumptions depend on the fact that the conformation of the macrocycle is 'frozen' in solution. A previous report (Stoeckli-Evans & Crout, 1976) on the insensitivity of the magnetic non-equivalence to change of solvent for three macrocyclic PA's suggests that this might be so.

As observed previously (Mackay & Culvenor, 1983) the secondary ester system at C(7) is non-planar. Torsion angles C(7)—O(16)—C(15)—C(14) and C(7)—O(16)—C(15)—O(17) are −163·7 (8) and 13·7 (8)° respectively. Atom H(7) is substantially out of the plane with torsion angle H(7)—C(7)—O(16)—C(15) 47 (3)°, compared to 33° in 1,2-didehydrocrotalanine and 30° in grantaline.

The γ-butyrolactone ring is *trans*-fused to the macrocycle at bond C(13)—C(14). The exocyclic methyl group at C(24) is in a quasi-axial orientation. The bond lengths and angles in the lactone ring are normal. The torsion angles differ considerably from those observed previously (see Table 4). The ring has a very flat envelope conformation. Atom C(14) is displaced by −0·25 (1) Å from mean plane C(13), O(22), C(23), C(24), O(25), which is planar to within 0·06 (1) Å. The folding angle, defined by the dihedral angle between the above plane and plane C(13), C(14), C(24), is 15·0 (2)°. Angles of between 20 and 60° have been observed previously (Lere-Porte *et al.*, 1981, and references therein).

In the crystal the only short intermolecular contact between non-H atoms is that between atom O(22) of the lactone ring and the hydroxyl substituent at atom C(12) of an adjacent symmetry-related molecule [3·19 (1) Å].

DJR wishes to thank the SERC for financial support.

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* An error in the published atomic coordinates of trichodesmine did not allow its inclusion in this table.

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Structure of Jacobine Methanol Solvate, $C_{18}H_{25}NO_6.CH_4O$

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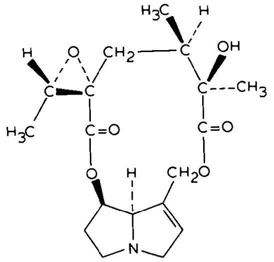
(*Received* 7 *February* 1984; *accepted* 4 *April* 1984)

Abstract. $M_r = 383{\cdot}44$, orthorhombic, $P2_12_12_1$, $a = 10{\cdot}9903\,(8)$, $b = 20{\cdot}530\,(1)$, $c = 8{\cdot}9550\,(6)$ Å, $V = 2020{\cdot}5$ Å^3, $Z = 4$, $D_x = 1{\cdot}260$ g cm^{-3}, Ni-filtered Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 7{\cdot}59$ cm^{-1}, $F(000) = 824$, $T = 257$ K, $R = 0{\cdot}044$ for 2373 unique reflections. The conformations of the pyrrolizidine ring system and the 12-membered macrocyclic ring in this structure are surprisingly similar to the conformations observed in three other pyrrolizidine alkaloids containing a 12-membered macrocyclic ring. This structural consistency suggests that this is a preferred conformation for this type of molecule.

Introduction. Large numbers of people have been poisoned when plants containing hepatotoxic pyrrolizidine† alkaloids, such as jacobine, have been harvested with cereal or grain crops (Mohabbat, Younos, Merzad, Srivastava, Sediq & Aram, 1976). Human exposure to these pyrrolizidine alkaloids can also occur through consumption of herbal teas or indirectly from honey or milk when foraging of plants containing these alkaloids occurs (Deinzer, Thomson, Burgett & Isaacson, 1977; Culvenor, Edgar & Smith, 1981). Some concern has also arisen over the possibility that low levels of these alkaloids in food may produce tumors (Culvenor & Jago, 1979).

Crystallographic studies on jacobine were undertaken to explore the structural and hydrogen-bonding characteristics of the molecule. These results have been used as an aid to understanding the results of positive and negative ion methane chemical ionization mass spectrometry studies of a series of pyrrolizidine alkaloid derivatives (Karchesy, Deinzer, Griffin & Rohrer, 1984).



Experimental. Colorless rod-shaped crystals grown by slow evaporation of a methanol solution yielding a crystal 0·4 × 0·4 × 0·8 mm. CAD-4 diffractometer equipped with a cool stream, 257 K, 2373 independent intensities, 2θ limit 150°, θ–2θ scan. Intensity data measured and saved as profiles of 96 intervals for each scan. 4 standard intensities used to monitor variations in intensity data, <3% variation observed. Least-squares procedure based on centered 2θ values of 25 reflections in range 70 to 80° used to refine lattice parameters. Profile intensity data converted into integrated net intensities (Blessing, 1980) and structure-factor amplitudes. h 0–13, k 0–25, l 0–11. Structure determined using direct-methods program *MULTAN* (Main, Lessinger, Woolfson, Germain & Declercq, 1977) in conjunction with the NQEST figure-of-merit

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† Pyrrolizidine is 5,6,7,7a-tetrahydro-3*H*-pyrrolizine.

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