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Junceine: a Pyrrolizidine Alkaloid

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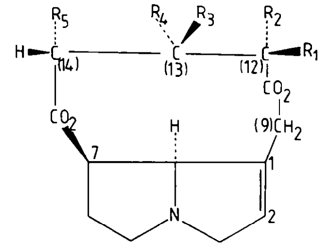
Abstract. $C_{18}H_{27}NO_7$, orthorhombic, $C222_1$, a = 12·285 (7), b = 16·861 (8), c = 17·502 (9) Å, from diffractometer measurements (Mo $K\alpha$ radiation), V = 3625·3 Å^3, M_r = 369, D_m = 1·34 Mg m^{-3}, Z = 8, D_c = 1·352 Mg m^{-3}, μ(Mo $K\alpha$) = 0·06 mm^{-1}. The structure was solved by multisolution direct methods and refined by the blocked full-matrix least-squares method to R = 0·050 for 1011 reflections. Junceine, a pyrrolizidine alkaloid derived from retronecine, has an 11-membered macrocycle with the ester carbonyls synparallel and directed below the plane of the macrocycle.

Introduction. The present analysis continues our structural studies of pyrrolizidine alkaloids (PA's) whose structure and/or toxicity are of particular interest (Stoeckli-Evans & Crout, 1976; Stoeckli-Evans, 1979*a*,*b*, 1980). The PA's are responsible for widespread losses of livestock in countries where plants containing these alkaloids occur in pasture and grazing lands (Bull, Culvenor & Dick, 1968). Structural requirements for toxicity are the presence of ester functions at C(7) and C(9) and a double bond in the pyrrolizidine nucleus between atoms C(1) and C(2) (Mattocks, 1972). Junceine (I), a PA derived from retronecine, is rare and to date has only been found in two species of the genus *Crotalaria* (Robins, 1981). It contains an 11-membered macrocycle like fulvine (V) (Sussman & Wodak, 1973), axillarine (IV) (Stoeckli-Evans & Crout, 1976), monocrotaline (VI) (Stoeckli-Evans, 1979*b*; Wang, 1980), incanine (III) (Tashkhodzhaev, Telezhenetskaya & Yunusov, 1979) and trichodesmine (II) (Tashkhodzhaev, Yagudaev & Yunusov, 1979). In trichodesmine (II) the ester carbonyls are antiparallel rather than synparallel as in alkaloids (III) to (VI). This antiparallel arrangement is more common to the 12-membered macrocycle retronecine-derived PA's, such as jacobine (Pérez-Salazar, Cano & García-Blanco, 1978), and retrorsine (Stoeckli-Evans, 1979*a*; Coleman, Coucourakis & Pretorius, 1980). As junceine (I) differs only slightly chemically from trichodesmine (II), an hydroxymethylene group in place of the methyl group at C(12), a structural analysis was carried out to determine the conformation of the macrocycle and to elucidate the configuration at asymmetric centers C(12), C(13) and C(14).



		R_1	R_2	R_3	R_4	R_5
(I)	Junceine	OH	CH_2OH	OH	CH_3	$CH(CH_3)_2$
(II)	Trichodesmine	OH	CH_3	OH	CH_3	$CH(CH_3)_2$
(III)	Incanine	OH	CH_3	H	CH_3	$CH(CH_3)_2$
(IV)	Axillarine	OH	$CH(OH)CH_3$	OH	H	$CH(CH_3)_2$
(V)	Fulvine	H	CH_3	OH	CH_3	CH_3
(VI)	Monocrotaline	OH	CH_3	OH	CH_3	CH_3

Junceine (I) was isolated from *Crotalaria juncea* L. Crystals were grown from a methanol solution. Two crystals of similar shape and size were used to collect data for layers 0–12kl and hk0–10 with θ_{max} = 25° on a Stoe Stadi-2 two-circle diffractometer (graphite-monochromated Mo $K\bar{\alpha}$ radiation) using the variable ω-scan technique (Freeman, Guss, Nockolds, Page & Webster, 1970); 1015 unique reflections [$I > 2\sigma(I)$], corrected for Lorentz and polarization effects, were obtained and used in subsequent calculations. Systematic absences indicated space group $C222_1$. The structure was solved using *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). Refinement and all other calculations were carried out using *SHELX* 76 (Sheldrick, 1976). Complex neutral-atom scattering factors were taken from *International Tables for X-ray Crystallography* (1974). All 27 H-atom positions were located from difference Fourier syntheses. Weighted anisotropic (isotropic for H atoms) blocked full-matrix least-squares refinement converged at R = 0·050 for 1011 reflections (four reflections suffering from extinction were removed from the final cycles of refinement); R_w = 0·053 {$R = \sum ||F_o| - |F_c||/\sum |F_o|$; $R_w = \sum ||F_o| - |F_c||w^{1/2}/\sum |F_o| w^{1/2}$; $w = 0{\cdot}498/[\sigma^2(F_o) + 0{\cdot}0079 F_o^2]$}. In the final cycle the average parameter shift was <0·5 e.s.d. A final difference Fourier synthesis showed no significant

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Table 1. *Final positional parameters* ($\times 10^4$) *and equivalent isotropic thermal parameters* ($\times 10^3$), *with e.s.d.'s in parentheses*

$$U_{eq} = (U_{11}U_{22}U_{33})^{1/3}.$$

	x	y	z	U_{eq} (Å^2)
C(1)	−2049 (4)	3360 (4)	7662 (3)	40 (3)
C(2)	−1311 (5)	3830 (6)	7984 (4)	66 (5)
C(3)	−1513 (5)	4683 (5)	7834 (5)	72 (5)
N(4)	−2529 (4)	4690 (3)	7383 (3)	44 (3)
C(5)	−2454 (5)	5092 (4)	6625 (4)	65 (5)
C(6)	−3123 (6)	4583 (4)	6098 (4)	54 (4)
C(7)	−2909 (4)	3754 (4)	6360 (3)	34 (3)
C(8)	−2853 (5)	3848 (4)	7228 (3)	41 (4)
C(9)	−2086 (6)	2465 (5)	7725 (4)	66 (5)
O(10)	−1315 (3)	2117 (3)	7184 (2)	51 (3)
C(11)	−1741 (5)	1786 (4)	6562 (3)	47 (4)
C(12)	−835 (4)	1427 (3)	6057 (3)	36 (3)
C(13)	−856 (4)	1795 (3)	5226 (3)	29 (3)
C(14)	−719 (4)	2718 (3)	5281 (3)	29 (3)
C(15)	−1805 (4)	3127 (3)	5393 (3)	71 (3)
O(16)	−1843 (3)	3455 (2)	6113 (2)	34 (2)
O(17)	−2538 (3)	3204 (2)	4941 (2)	40 (2)
O(18)	−2694 (3)	1742 (3)	6431 (3)	57 (3)
O(19)	217 (2)	1584 (2)	6337 (2)	39 (2)
C(20)	−1015 (5)	525 (3)	6043 (4)	52 (4)
O(21)	−717 (3)	222 (3)	6765 (3)	74 (3)
O(22)	63 (3)	1465 (2)	4853 (2)	36 (2)
C(23)	−1848 (5)	1504 (3)	4763 (3)	47 (4)
C(24)	−72 (4)	3107 (3)	4629 (3)	33 (3)
C(25)	101 (5)	3984 (3)	4773 (4)	52 (4)
C(26)	−514 (5)	2988 (4)	3817 (3)	50 (4)

residual electron density. Final positional and thermal parameters are given in Table 1.*

Discussion. Bond distances and angles and their standard deviations are given in Table 2. Within experimental error they differ little from those observed in other retronecine-derived PA's (Stoeckli-Evans, 1979*a,b*). The torsion angles in the macrocycle are given in Table 3. The numbering scheme used is apparent from Fig. 1, a projection of the molecule onto the least-squares plane of the macrocycle. Fig. 1 also shows the configuration at asymmetric centers C(12), C(13) and C(14), which are similar to those found in trichodesmine (II).

The absolute configuration of junceine was assigned by comparison with that of jacobine bromohydrin (Fridrichsons, Mathieson & Sutor, 1963), as both are derived from the same pyrrolizidine nucleus retronecine (Bull *et al.*, 1968).

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

C(1)–C(2)	1·331 (10)	C(12)–C(13)	1·582 (7)
C(2)–C(3)	1·482 (13)	C(12)–O(19)	1·408 (6)
C(3)–N(4)	1·476 (8)	C(12)–C(20)	1·536 (8)
N(4)–C(5)	1·492 (9)	C(20)–O(21)	1·411 (8)
N(4)–C(8)	1·500 (8)	C(13)–C(14)	1·568 (7)
C(5)–C(6)	1·505 (10)	C(13)–O(22)	1·418 (6)
C(6)–C(7)	1·495 (9)	C(13)–C(23)	1·544 (7)
C(7)–C(8)	1·528 (8)	C(14)–C(15)	1·514 (7)
C(8)–C(1)	1·493 (8)	C(14)–C(24)	1·537 (7)
C(1)–C(9)	1·513 (11)	C(24)–C(25)	1·515 (8)
C(9)–O(10)	1·463 (8)	C(24)–C(26)	1·535 (8)
O(10)–C(11)	1·330 (7)	C(15)–O(16)	1·377 (7)
C(11)–O(18)	1·196 (7)	C(15)–O(17)	1·205 (6)
C(11)–C(12)	1·545 (8)	O(16)–C(7)	1·468 (6)

C(8)–C(1)–C(2)	109·8 (7)	O(19)–C(12)–C(11)	112·9 (4)
C(9)–C(1)–C(2)	125·7 (6)	O(19)–C(12)–C(13)	105·1 (4)
C(9)–C(1)–C(8)	124·5 (5)	C(20)–C(12)–C(11)	107·1 (5)
C(3)–C(2)–C(1)	112·8 (6)	C(20)–C(12)–C(13)	111·8 (4)
N(4)–C(3)–C(2)	104·2 (6)	C(20)–C(12)–O(19)	108·9 (4)
C(5)–N(4)–C(3)	115·3 (5)	C(14)–C(13)–C(12)	109·4 (4)
C(8)–N(4)–C(3)	108·3 (5)	O(22)–C(13)–C(12)	104·8 (4)
C(8)–N(4)–C(5)	106·6 (5)	O(22)–C(13)–C(14)	109·4 (4)
C(6)–C(5)–N(4)	104·6 (5)	C(23)–C(13)–C(12)	111·7 (4)
C(7)–C(6)–C(5)	104·4 (5)	C(23)–C(13)–C(14)	115·6 (4)
C(8)–C(7)–C(6)	102·5 (5)	C(23)–C(13)–O(22)	105·2 (4)
O(16)–C(7)–C(6)	112·9 (5)	C(15)–C(14)–C(13)	111·5 (4)
O(16)–C(7)–C(8)	106·8 (4)	C(24)–C(14)–C(13)	115·7 (4)
N(4)–C(8)–C(1)	104·7 (5)	C(24)–C(14)–C(15)	110·9 (4)
C(7)–C(8)–C(1)	118·5 (5)	O(16)–C(15)–C(14)	109·3 (4)
C(7)–C(8)–N(4)	106·8 (5)	O(17)–C(15)–C(14)	128·5 (5)
O(10)–C(9)–C(1)	109·5 (5)	O(17)–C(15)–O(16)	122·1 (5)
C(11)–O(10)–C(9)	116·3 (5)	C(15)–O(16)–C(7)	116·0 (4)
C(12)–C(11)–O(10)	110·4 (5)	O(21)–C(20)–C(12)	107·8 (5)
O(18)–C(11)–O(10)	124·7 (6)	C(25)–C(24)–C(14)	111·5 (4)
O(18)–C(11)–C(12)	124·8 (5)	C(26)–C(24)–C(14)	116·7 (4)
C(13)–C(12)–C(11)	111·1 (4)	C(26)–C(24)–C(25)	109·3 (5)

Table 3. *Torsion angles* (°) *in the macrocycle* (*e.s.d.* ~0·6°)

C(8)–C(1)–C(9)–O(10)	99·8	C(14)–C(15)–O(16)–C(7)	−169·9
C(1)–C(9)–O(10)–C(11)	−105·2	C(15)–O(16)–C(7)–C(8)	163·0
C(9)–O(10)–C(11)–C(12)	−178·6	O(16)–C(7)–C(8)–C(1)	−24·2
O(10)–C(11)–C(12)–C(13)	−122·4	C(7)–C(8)–C(1)–C(9)	−65·4
C(11)–C(12)–C(13)–C(14)	57·9	C(2)–C(1)–C(9)–O(10)	−80·9
C(12)–C(13)–C(14)–C(15)	−86·9	O(19)–C(12)–C(13)–O(22)	52·8
C(13)–C(14)–C(15)–O(16)	112·0		

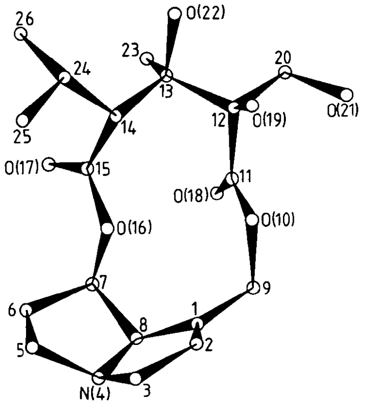

Fig. 1. A perspective view of the molecule showing the numbering scheme.

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(*a*) The pyrrolizidine nucleus exists in the *exo*-puckered form, with atom C(6) and the unsaturated five-membered ring on opposite sides of the plane defined by atoms N(4), C(5) and C(7). The puckering angle between planes defined by atoms C(5),C(6),C(7) and C(5),N(4),C(8) is 36·7 (6)°. In fulvine this angle is 46°, in axillarine 42°, in monocrotaline 37°, in incanine 42° and in trichodesmine 35°; all exist in the *exo*-puckered form.

(*b*) The angle between the least-squares planes defined by atoms C(1),C(2),C(3),N(4),C(8) and C(5),N(4),C(8),C(7) of the pyrrolizidine nucleus is 125·7 (5)°, equal to the average value for retronecine-derived PA's.

(*c*) The pyrrolizidine ring-fusion distance N(4)—C(8) is 1·500 (8) Å, equal to the average distance for these alkaloids.

(*d*) It is seen from Fig. 1 that the C(7) and C(9) ester carbonyl bonds are synparallel and directed below the plane of the macrocycle. Hence junceine (I) and trichodesmine (II) do not have the same macrocycle conformation. Torsion angles around the macrocycle (Table 3) are similar to those found in alkaloids (III) to (VI).

Hydrogen-bond distances and bond angles are given in Table 4(*a*). Short intra- and intermolecular distances are given in Table 4(*b*). The most important hydrogen bond is that linking molecules related by a screw axis in the **b** direction. Distance O(21)—N(4$^{\rm ii}$) is 2·77 (1) Å, and H(21)—N(4$^{\rm ii}$) is 1·87 (6) Å. Hydroxyls O(19) and O(22) are in the *gauche* conformation with a torsion angle [O(19)—C(12)—C(13)—O(22)] of 52·8 (6)°. They form a weak asymmetric hydrogen bond; O(22)—O(19) is 2·61 (1) Å, and H(22)—O(19) is 2·39 (5) Å. Hydroxyl O(19) forms a weak asymmetric hydrogen bond with atom O(21). O(19)—O(21) is 2·67 (1) Å and H(19)—O(21) is 2·36 (8) Å. Hydroxyl O(22) also appears to be hydrogen bonded to the carbonyl O atom O(17$^{\rm i}$) of the molecule related by the screw axis in the **a** direction. O(22)—O(17$^{\rm i}$) is 3·02 (1) Å and H(22)—O(17$^{\rm i}$) is 2·28 (5) Å. Atom O(19) is also 2·56 (1) Å from atom O(10) of the same molecule and 3·05 (1) Å from atom O(10$^{\rm iii}$) of the molecule related by the twofold axis in the **b** direction.

Table 4. *Hydrogen bonding and short contacts*

(*a*) Hydrogen-bond lengths (Å) and angles (°)

D—H···*A*	*D*—H	*D*···*A*	H···*A*	*D*—H···*A*
O(21)—H(21)···N(4$^{\rm ii}$)	0·91 (6)	2·77 (1)	1·87 (6)	174·5 (3·9)
O(22)—H(22)···O(19)	0·85 (5)	2·61 (1)	2·39 (5)	95·3 (5·1)
O(19)—H(19)···O(21)	0·78 (9)	2·67 (1)	2·36 (8)	105·3 (4·8)
O(22)—H(22)···O(17$^{\rm i}$)	0·85 (5)	3·02 (1)	2·28 (5)	145·1 (3·4)

(*b*) Short intra- and intermolecular distances (Å)

O(19)—O(10)	2·559 (5)	C(11)—C(15)	3·051 (8)
O(19)—O(10$^{\rm iii}$)	3·054 (6)	O(10)—O(16)	3·004 (6)
C(11)—O(16)	2·924 (7)		

Symmetry code: (i) $0·5 + x,\ 0·5 - y,\ 1 - z$; (ii) $-0·5 - x,\ -0·5 + y,\ 1·5 - z$; (iii) $-x,\ y,\ 1·5 - z$.

The shortest transannular distance in the macrocycle of junceine is that between atoms C(11) and O(16). This distance is 2·92 (1) Å in junceine and 2·88 Å for the same distance in axillarine. In fulvine, monocrotaline, incanine and trichodesmine, transannular distance C(15)—O(10) is the shortest, ranging from 2·78 to 2·87 Å.

The torsion angle C(2)—C(1)—C(9)—O(10) in junceine is −81 (1)° compared to −88° in axillarine, −63° in monocrotaline, −64° in fulvine, and −80° in incanine. In 12-membered macrocyclic PA's and trichodesmine, where the C(9) ester carbonyl bond is directed above the plane of the macrocycle, this angle is generally larger; for example, −106° in jacobine and −108° in swazine (Laing & Sommerville, 1972). It has been suggested that the toxicity of the PA's depends, in part, on the susceptibility to attack of the C(1)—C(2) double bond – regarded in terms of the magnitude of this torsion angle. However, a systematic toxicological study must be carried out before further conclusions may be drawn.

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2,2'-(*p*-Phenylene)di-2-propanol

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Abstract. $C_{12}H_{18}O_2$ (PDHIPB), $M_r = 194\cdot26$, triclinic, $P\bar{1}$, $a = 10\cdot269\,(4)$, $b = 14\cdot369\,(4)$, $c = 6\cdot276\,(6)$ Å, $\alpha = 98\cdot21\,(3)$, $\beta = 96\cdot62\,(4)$, $\gamma = 70\cdot15\,(10)^\circ$, $Z = 3$, $D_x = 1\cdot125$, $D_m = 1\cdot10\,(3)$ g cm^{-3} (by flotation), $\mu = 0\cdot807$ cm^{-1} for Mo $K\alpha$ radiation; $R = 0\cdot068$ for 1211 observed reflexions. A hydrogen-bonding system connects the O atoms of three adjacent molecules and produces spirals parallel to the **c** direction. The spirals link the molecules into sheets parallel to the (110) plane.

Introduction. The aim of the structure determination was (*a*) a comparison of the structure with that of the Si-analogue compound 1,1'-(*p*-phenylene)bis(dimethylsilanol) (DHMSB), which is the monomer of disilanol type of poly[oxy(dimethylsilyl)-*p*-phenylene-(dimethylsilyl)] (Alexander, Northolt & Engmann, 1967), and (*b*) to obtain a key to the interpretation of the vibration spectra of PDHIPB (Zelei & Dobos, 1979). The sample was prepared by Dr B. Zelei in the Institute of Inorganic Chemistry of the Hungarian Academy of Sciences by the method of Mitin (1958). The crystals form plates elongated in the **c** direction. One of the linear dimensions of the specimen was about 0·01 mm and so only 1746 independent reflexions could be collected on an Enraf–Nonius CAD-4 diffractometer; 535 of these with zero intensities were excluded from the final data set. No absorption corrections were made. The phases for 196 reflexions having $E \geq 1\cdot7$ were obtained by *MULTAN* (Germain, Main & Woolfson, 1971). The E map calculated with these signs revealed the positions of all non-hydrogen atoms ($R = 0\cdot37$). A full-matrix least-squares refinement procedure resulted in $R = 0\cdot072$ for the observed reflexions. At the stage when anisotropic temperature factors were used the refinement proceeded separately for the two parts of the asymmetric unit. A difference Fourier map gave the positions of all H atoms and the subsequent refinement cycles resulted in a final $R = 0\cdot068$ for the 1211 observed and $R = 0\cdot103$ for all reflexions.* All calculations were performed on a PDP

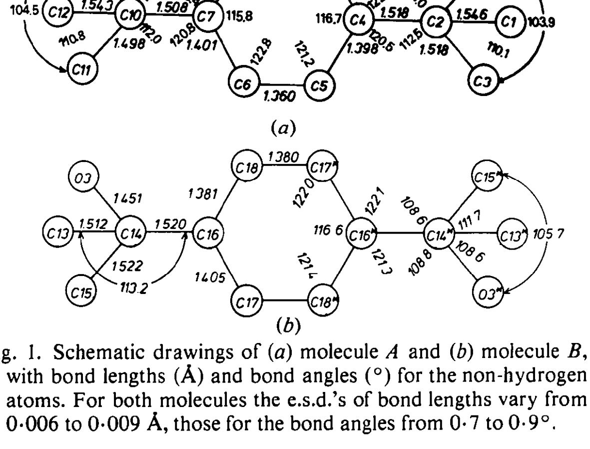

Fig. 1. Schematic drawings of (*a*) molecule *A* and (*b*) molecule *B*, with bond lengths (Å) and bond angles (°) for the non-hydrogen atoms. For both molecules the e.s.d.'s of bond lengths vary from 0·006 to 0·009 Å, those for the bond angles from 0·7 to 0·9°.

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* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36591 (10 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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