Acta Cryst. (1984). C**40**, 1073–1077

Ethanol–Water Solvates of Anacrotine and Madurensine, $C_{18}H_{25}NO_6.\frac{1}{2}C_2H_6O.\frac{1}{2}H_2O$. Isomeric Pyrrolizidine Alkaloids

BY M. F. MACKAY AND M. SADEK

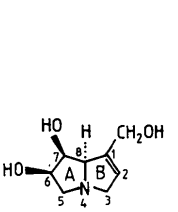
Department of Physical Chemistry, La Trobe University, Bundoora, Victoria 3083, *Australia*

AND C. C. J. CULVENOR

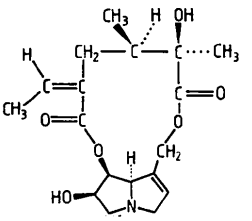
Division of Animal Health, CSIRO, Parkville, Victoria 3052, *Australia*

(*Received* 16 *November* 1983; *accepted* 8 *February* 1984)

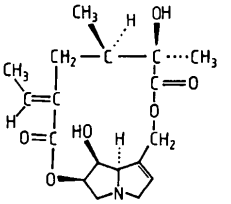
Abstract. $M_r = 383{\cdot}4$, orthorhombic, $Z = 4$, D_m (flotation) = 1·28 (1), $D_x = 1{\cdot}279$ Mg m^{-3}, Cu $K\alpha$, $\lambda = 1{\cdot}5418$ Å, $\mu = 0{\cdot}72$ mm^{-1}, $F(000) = 824$, $T = 289$ (1) K. Anacrotine solvate: $P2_12_12$, $a = 19{\cdot}810$ (2), $b = 11{\cdot}256$ (1), $c = 8{\cdot}931$ (1) Å, $U = 1991{\cdot}4$ (3) Å^3. Madurensine solvate: $P2_12_12_1$, $a = 17{\cdot}418$ (2), $b = 16{\cdot}074$ (1), $c = 7{\cdot}111$ (1) Å, $U = 1990{\cdot}9$ (4) Å^3. Least-squares refinement converged at R values of 0·068 and 0·072 for 1848 and 1676 reflections for the anacrotine and madurensine solvates respectively. The alkaloids are diesters of stereoisomeric diprotic acids and the aminotriol crotanecine. The position of linkage of the secondary ester on the pyrrolizidine nucleus is at C(7) in anacrotine, forming a 12-membered macro-ring; and at C(6) in madurensine, forming a 13-membered macro-ring. This change in linkage has little effect on the general conformation of the macro-ring and the secondary ester group.



(I)



(II)



(III)

Introduction. The isomeric alkaloids anacrotine and madurensine have been isolated from species of *Crotalaria*, madurensine from *C. madurensis* and *C. agatiflora* and anacrotine from *C. anagyroides* and *C. agatiflora* (Atal, Kapur, Culvenor & Smith, 1966; Culvenor & Smith, 1972). The alkaloids are diesters derived from the stereoisomers of the diprotic acid 5-ethylidene-2-hydroxy-2,3-dimethylhexanedioic acid, and the aminotriol crotanecine (I). The structures (II) and (III) have been proposed for anacrotine (Atal, Kapur, Culvenor & Smith, 1966) and madurensine (Culvenor, Smith & Willing, 1970), respectively, based mainly on NMR data. The analyses reported here were carried out to define the effect on conformation of closing the macro-ring through C(6), and form part of a conformational study of hepatotoxic pyrrolizidine alkaloids.

Experimental. Both compounds formed prismatic crystals from ethanol; crystals of anacrotine solvate *ca* 0·22 × 0·35 × 0·55 mm, madurensine solvate *ca* 0·22 × 0·39 × 0·32 mm aligned on a Rigaku-AFC diffractometer; cell parameters determined by least squares from 2θ values for 25 strong reflections, 3 standard reflections, no intensity variation for madurensine, gradual 2% decrease in intensities for anacrotine and data scaled accordingly, Cu $K\alpha$ radiation (graphite-crystal monochromator); ω–2θ scan, 2θ scan rate 2° min^{-1}, scan range ($\Delta\omega$) $1{\cdot}2° + 0{\cdot}5°\tan\theta$, $2\theta_{max} = 130°$; 1935 non-equivalent terms for anacrotine, h 0–23, k −13–0, l 0–10, 1873 with $|F_o| \geq 2\sigma(|F_o|)$ used for structure refinement; 1899 non-equivalent terms for madurensine, h 0–20, k 0–18, l 0–7 and h 0–14, k −9–0, l 6–8, 1676 with $|F_o| \geq 3\sigma(|F_o|)$ used; intensities not corrected for absorption; six large terms apparently seriously affected by extinction omitted from final refinement of anacrotine; scattering factors for O, N and C from Cromer & Mann (1968), for H from Stewart, Davidson & Simpson (1965); anomalous-dispersion corrections with values of Cromer & Liberman (1970). Structures solved by direct methods with *SHELX*76 (Sheldrick, 1976). In both crystals there was disorder of solvent molecules: in

0108-2701/84/061073-05$01.50

Table 1. *Final atomic coordinates for the non-hydrogen atoms* ($\times 10^4$) *and equivalent isotropic temperature factors for the ethanol–water solvate of anacrotine*

E.s.d.'s are given in parentheses.

	x	y	z	B^*_{eq}(Å^2)
C(1)	2559 (2)	921 (4)	−414 (6)	3·2 (1)
C(2)	2769 (3)	1594 (5)	−1543 (6)	3·8 (2)
C(3)	3521 (3)	1591 (6)	−1693 (8)	4·1 (2)
N(4)	3745 (2)	702 (4)	−568 (5)	2·9 (1)
C(5)	4278 (3)	1142 (5)	431 (6)	3·4 (1)
C(6)	4112 (2)	601 (5)	1951 (6)	2·9 (1)
C(7)	3336 (2)	666 (4)	1977 (6)	2·4 (1)
C(8)	3150 (3)	346 (4)	364 (6)	2·7 (1)
C(9)	1835 (3)	603 (6)	−157 (8)	4·0 (2)
O(10)	1556 (2)	1158 (3)	1189 (5)	3·6 (1)
C(11)	1245 (2)	2212 (5)	984 (6)	3·0 (1)
C(12)	969 (2)	2688 (4)	2467 (6)	2·8 (1)
C(13)	1544 (2)	2722 (5)	3629 (6)	2·8 (1)
C(14)	2104 (2)	3591 (4)	3098 (6)	3·1 (1)
C(15)	2766 (2)	3380 (4)	3894 (6)	2·7 (1)
C(16)	3031 (2)	2153 (4)	3746 (6)	2·5 (1)
O(17)	3122 (2)	1870 (3)	2281 (4)	2·6 (1)
C(18)	373 (3)	1893 (5)	2944 (8)	3·9 (1)
C(19)	1314 (3)	3048 (6)	5222 (6)	4·6 (2)
C(20)	3082 (3)	4196 (5)	4701 (6)	3·9 (1)
C(21)	3743 (4)	4046 (6)	5490 (12)	5·2 (2)
O(22)	1202 (2)	2709 (4)	−216 (5)	4·0 (1)
O(23)	688 (2)	3842 (3)	2239 (4)	3·1 (1)
O(24)	3121 (2)	1456 (3)	4758 (5)	3·6 (1)
O(25)	4441 (2)	1266 (4)	3077 (4)	4·1 (1)
O(*W*)	0	5000	4491 (6)	4·3 (2)
C(Et)	4884	4341	1778	12·8 (3)†
O(Et)	5154	3734	2902	12·8 (3)†

* Calculated from the refined anisotropic thermal parameters $B_{eq} = 8\pi^2 U_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a^*_i a^*_j \mathbf{a}_i . \mathbf{a}_j$.
† Overall isotropic temperature factor B_{iso}.

Table 2. *Final atomic coordinates of the non-hydrogen atoms* ($\times 10^4$) *and equivalent isotropic temperature factors for the ethanol–water solvate of madurensine*

E.s.d.'s are given in parentheses.

	x	y	z	B^*_{eq}(Å^2)
C(1)	5306 (4)	586 (4)	12224 (10)	2·6 (2)
C(2)	5301 (4)	928 (4)	13893 (11)	3·1 (2)
C(3)	5073 (5)	338 (4)	15419 (10)	3·8 (2)
N(4)	4855 (3)	−444 (3)	14382 (8)	2·8 (1)
C(5)	4017 (4)	−636 (4)	14446 (11)	3·1 (2)
C(6)	3703 (4)	−470 (4)	12497 (11)	3·3 (2)
C(7)	4377 (4)	−643 (4)	11246 (10)	2·8 (2)
C(8)	5081 (4)	−336 (4)	12357 (9)	2·6 (2)
C(9)	5569 (4)	990 (4)	10414 (10)	3·1 (2)
O(10)	4927 (2)	1432 (3)	9493 (6)	3·1 (1)
C(11)	4816 (4)	2226 (4)	10060 (11)	3·0 (2)
C(12)	4118 (4)	2589 (4)	9081 (11)	2·9 (2)
C(13)	3401 (4)	2083 (4)	9670 (11)	2·7 (2)
C(14)	3318 (4)	2081 (4)	11846 (11)	3·0 (2)
C(15)	2683 (3)	1561 (4)	12573 (10)	2·9 (2)
C(16)	2800 (4)	633 (5)	12759 (11)	3·3 (2)
O(17)	3519 (2)	412 (3)	12313 (6)	3·1 (1)
C(18)	4258 (5)	2602 (5)	6952 (11)	4·6 (2)
C(19)	2671 (4)	2416 (5)	8717 (12)	4·3 (2)
C(20)	1990 (4)	1834 (5)	13194 (12)	4·3 (2)
C(21)	1740 (5)	2724 (5)	13233 (15)	6·2 (3)
O(22)	5204 (3)	2592 (3)	11192 (8)	4·3 (2)
O(23)	4001 (2)	3418 (3)	9700 (8)	4·0 (1)
O(24)	2317 (3)	139 (3)	13271 (9)	5·1 (2)
O(25)	4344 (3)	−320 (3)	9424 (6)	3·8 (1)
O(*W*)	1900	5510	1460	19·1 (6)†
C(1Et)	2520	5100	170	19·1 (6)†
C(2Et)	2750	4770	2100	19·1 (6)†
O(Et)	2240	5250	3470	19·1 (6)†

* Calculated from the refined anisotropic thermal parameters $B_{eq} = 8\pi^2 U_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a^*_i a^*_j \mathbf{a}_i . \mathbf{a}_j$.
† Overall isotropic temperature factor B_{iso}.

anacrotine they lie on twofold axes so that ethanol molecules are subject to twofold disorder. Difference map calculated for madurensine after inclusion of alkaloid atoms contained a column of electron density of elliptical cross section about the screw axis along c extending the length of the c axis. An estimate of this residual density (Cochran, 1951) is consistent with the presence of half an ethanol and half a water molecule per asymmetric unit as in the anacrotine solvate, and is in accord with the measured crystal density.* As an approximate model for the solvent of crystallization in the madurensine crystal, four sites feasible for the C and O atoms of ethanol and water were derived; these atoms were included at fixed positions with an occupancy factor 0·5 and an overall isotropic temperature factor which refined to $B = 19{\cdot}2\ (5)$ Å^2. Refinement by full-matrix least squares, anisotropic temperature factors for C, N and O atoms of alkaloid molecules (O of water in anacrotine), $R = 0{\cdot}068$, $R_w = 0{\cdot}078$ for anacrotine solvate and $R = 0{\cdot}072$, $R_w = 0{\cdot}084$ for madurensine solvate. Apart from H atom of hydroxyl substituent on pyrrolizidine nucleus in anacrotine which was not located, H atoms of alkaloid molecules were included in analyses; for anacrotine their coordinates were refined and atoms given isotropic temperature factors; for madurensine H-atom coordinates were not refined and atoms given overall isotropic temperature factor which refined to $B = 5{\cdot}4\ (4)$ Å^2; mean Δ/σ 0·04:1 for H atoms and 0·02:1 for all other parameters for anacrotine, for madurensine Δ/σ 0·04:1; largest peaks on final difference maps +0·48 and −0·48 e Å^{-3} (anacrotine) and +0·80 and −0·27 e Å^{-3} (madurensine); the function minimized was $\sum w(|F_o| - |F_c|)^2$, $w = (\sigma^2 |F_o| + 0{\cdot}00005 |F_o|^2)^{-1}$.

Discussion. Final atomic coordinates of the non-hydrogen atoms are given in Tables 1 and 2.* Fig. 1, which contains the atom numbering, and Fig. 2 have been prepared from the output of *ORTEP* (Johnson, 1965). The molecular conformations are illustrated in Fig. 1, bond lengths and angles being given in Table 3 and selected torsional angles in Table 4.

* NMR data also indicated the presence of ethanol.

* Lists of structure amplitudes, anisotropic temperature factors, H-atom parameters and short intermolecular contact distances have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39258 (43 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

	Anacrotine	Madurensine
C(1)–C(2)	1·328 (8)	1·308 (10)
C(1)–C(8)	1·507 (7)	1·536 (9)
C(1)–C(9)	1·496 (7)	1·513 (10)
C(2)–C(3)	1·496 (8)	1·495 (10)
C(3)–N(4)	1·486 (8)	1·506 (8)
N(4)–C(5)	1·468 (7)	1·493 (9)
N(4)–C(8)	1·498 (7)	1·503 (9)
C(5)–C(6)	1·524 (8)	1·514 (11)
C(6)–C(7)	1·539 (6)	1·499 (10)
C(6)–O(17)		1·459 (8)
C(6)–O(25)	1·413 (7)	
C(7)–C(8)	1·530 (7)	1·540 (10)
C(7)–O(17)	1·446 (6)	
C(7)–O(25)		1·397 (9)
C(9)–O(10)	1·463 (8)	1·478 (8)
O(10)–C(11)	1·349 (6)	1·352 (8)
C(11)–C(12)	1·530 (8)	1·518 (10)
C(11)–O(22)	1·212 (8)	1·204 (9)
C(12)–C(13)	1·541 (7)	1·548 (10)
C(12)–C(18)	1·542 (7)	1·534 (11)
C(12)–O(23)	1·428 (6)	1·418 (8)
C(13)–C(14)	1·553 (7)	1·554 (11)
C(13)–C(19)	1·538 (8)	1·537 (10)
C(14)–C(15)	1·511 (6)	1·480 (9)
C(15)–C(16)	1·483 (6)	1·511 (10)
C(15)–C(20)	1·325 (8)	1·358 (9)
C(16)–O(17)	1·359 (6)	1·340 (8)
C(16)–O(24)	1·210 (6)	1·213 (9)
C(20)–C(21)	1·497 (11)	1·496 (11)
C(2)–C(1)–C(8)	110·6 (5)	110·4 (6)
C(2)–C(1)–C(9)	123·6 (5)	126·4 (6)
C(8)–C(1)–C(9)	124·8 (5)	123·0 (6)
C(1)–C(2)–C(3)	112·3 (5)	113·2 (6)
C(2)–C(3)–N(4)	103·8 (5)	103·9 (6)
C(3)–N(4)–C(5)	113·5 (4)	113·8 (5)
C(3)–N(4)–C(8)	108·7 (4)	107·9 (5)
C(5)–N(4)–C(8)	108·6 (4)	108·0 (5)
N(4)–C(5)–C(6)	104·6 (4)	106·8 (6)
C(5)–C(6)–C(7)	102·1 (4)	103·2 (6)
C(5)–C(6)–O(17)		109·4 (6)
C(5)–C(6)–O(25)	108·8 (4)	
C(7)–C(6)–O(17)		107·4 (5)
C(7)–C(6)–O(25)	115·1 (4)	
C(6)–C(7)–C(8)	102·4 (4)	105·1 (6)
C(6)–C(7)–O(17)	109·9 (4)	
C(6)–C(7)–O(25)		116·7 (6)
C(8)–C(7)–O(17)	109·1 (4)	
C(8)–C(7)–O(25)		112·9 (6)
C(1)–C(8)–N(4)	103·9 (4)	103·7 (5)
C(1)–C(8)–C(7)	121·3 (4)	118·7 (6)
N(4)–C(8)–C(7)	105·7 (4)	104·2 (5)
C(1)–C(9)–O(10)	112·7 (5)	110·8 (5)
C(9)–O(10)–C(11)	115·9 (4)	115·5 (5)
O(10)–C(11)–C(12)	110·7 (4)	109·9 (6)
O(10)–C(11)–O(22)	123·9 (5)	125·4 (6)
C(12)–C(11)–O(22)	125·4 (5)	124·6 (7)
C(11)–C(12)–C(13)	109·1 (4)	108·7 (6)
C(11)–C(12)–C(18)	108·0 (4)	109·3 (6)
C(11)–C(12)–O(23)	109·5 (4)	109·5 (6)
C(13)–C(12)–C(18)	113·2 (4)	113·7 (6)
C(13)–C(12)–O(23)	111·2 (4)	107·1 (6)
C(18)–C(12)–O(23)	105·6 (4)	108·5 (6)
C(12)–C(13)–C(14)	109·8 (4)	110·2 (6)
C(12)–C(13)–C(19)	114·2 (4)	111·4 (6)
C(14)–C(13)–C(19)	110·1 (4)	111·3 (6)
C(13)–C(14)–C(15)	112·2 (4)	114·7 (6)
C(14)–C(15)–C(16)	114·3 (4)	119·2 (6)
C(14)–C(15)–C(20)	123·9 (5)	126·5 (6)
C(16)–C(15)–C(20)	121·8 (5)	114·2 (6)
C(15)–C(16)–O(17)	110·6 (4)	111·5 (6)
C(15)–C(16)–O(24)	126·1 (4)	125·4 (7)
O(17)–C(16)–O(24)	123·2 (4)	123·1 (7)

Table 3 (*cont.*)

	Anacrotine	Madurensine
C(6)–O(17)–C(16)		116·2 (5)
C(7)–O(17)–C(16)	116·1 (4)	
C(15)–C(20)–C(21)	126·3 (6)	125·0 (7)

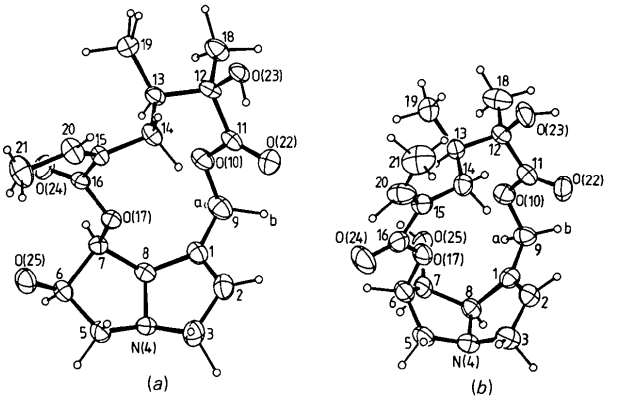


Fig. 1. Perspective view of the molecules with thermal ellipsoids scaled to 40% probability. The C atoms are denoted by numerals only. (*a*) Anacrotine, (*b*) madurensine.

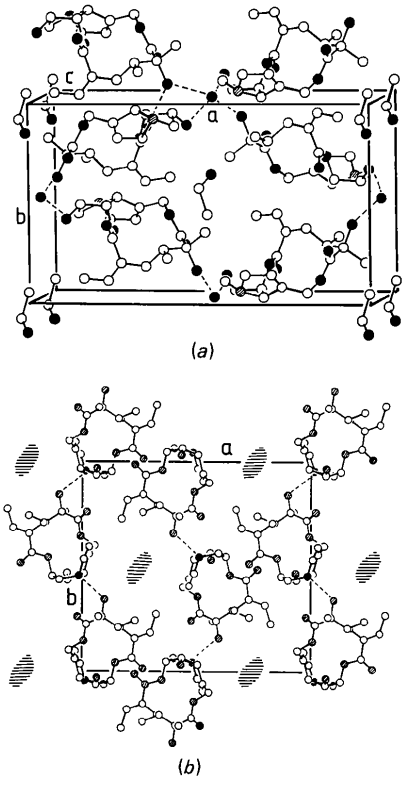


Fig. 2. The crystal packing: (*a*) anacrotine solvate; the ethanol molecules are included with one of the two alternate orientations; (*b*) madurensine solvate; projection of the structure down the *c* axis. The approximate sites of the solvent of crystallization are included as shaded areas.

Table 4. *Selected torsional angles* (°); *e.s.d.'s range from* 0·5 *to* 0·6°

Atoms are represented by their identification number.

	Anacrotine	Madurensine		Anacrotine	Madurensine
1–8–7–6	−144·3	−85·4	9–10–11–22	−1·6	1·9
1–8–7–17	−27·9		10–11–12–13	53·7	62·7
1–9–10–11	92·6	87·0	10–11–12–23	175·7	179·3
2–1–9–10	−111·8	−88·8	11–12–13–14	62·6	56·3
6–7–17–16	−90·6		12–13–14–15	−161·6	−175·6
6–17–16–15		178·3	13–14–15–16	56·8	80·8
7–6–17–16		157·3	13–14–15–20	−121·1	−102·4
7–8–1–9	−77·3	−64·3	14–15–16–17	58·5	3·8
7–17–16–15	−176·0		16–15–20–21	3·4	177·7
8–1–9–10	80·7	97·7	17–6–7–25		−46·4
8–7–6–17		79·5	17–7–6–25	41·3	
8–7–17–16	157·9		20–15–16–24	60·6	5·5
9–10–11–12	179·3	−177·1	22–11–12–23	−3·4	0·3

Anacrotine solvate. The molecular structure of (+)-anacrotine (12*R*, 13*R*) illustrated in Fig. 1(*a*) [see also Table 4] is similar to that of senecionine (Mackay & Culvenor, 1982); the latter only differs from anacrotine in having an H atom at C(6) in place of a hydroxyl substituent. The pyrrolizidine nucleus is *exo* buckled with a pucker angle 37·9 (6)°, and an angle of 127·1 (7)° between the mean planes defined by ring *B* atoms and atoms C(5), N(4), C(8), C(7) of ring *A* compared with the respective values of 35·3 (4) and 127·9 (4)° in senecionine.

Atoms in the primary ester group, C(9), O(10), C(11), O(22), C(12), are coplanar within ±0·01 (1) Å. One H atom at C(9) lies much closer to the plane of the unsaturated ring than the other [torsional angle H(9*b*)–C(9)–C(1)–C(2) 22(5)°, 13 (3)° in senecionine]; the α-OH at C(12) lies close to the ester plane, which is reflected in the torsional angle O(22)–C(11)–C(12)–O(23) −3·4 (5)° [*cf.* −3·8 (3)° in senecionine]. Atoms in the secondary ester system C(7), O(17), C(16), O(24), C(15) are coplanar within ± 0·03 (1) Å [torsional angle C(7)–O(17)–C(16)–C(15) −176·0 (5)°]. There is an angle of 34 (3)° [68 (1)° in senecionine] between the planes defined by the atoms H(7), C(7), O(17) and O(17), C(16), O(24), C(15), and the hydrogen at C(7) lies adjacent to the carbonyl group, the H(7)···O(24) distance being 2·39 (7) Å. The unsaturated side chain C(15)=C(20)–C(21) is in a nearly *cis* arrangement with the carbonyl group [atoms C(14), C(15), C(20), C(21), C(16) coplanar within ±0·02 (1) Å as also observed in madurensine]. The torsional angle C(20)–C(15)–C(16)–O(24) of 60·6 (5)°, compared with the value 46·2 (3)° in senecionine, illustrates a greater twist about the C(15)–C(16) bond than in the latter. The differences between anacrotine and senecionine in torsional angles around the secondary ester system appear to be due to the close approach of the carbonyl oxygen, O(24), to the hydroxyl substituent at C(6), the O(24)···O(25) distance being 3·023 (5) Å.

The carbonyl bonds of the ester functions are antiparallel as observed in the other pyrrolizidine alkaloids which have a 12-membered macrocycle. The angle between the bonds is 14·0 (5)° compared with 16·8 (3)° in senecionine, 17·2 (7)° in retrorsine (Coleman, Coucourakis & Pretorius, 1980) and 18·3 (3)° in jacobine (Pérez-Salazar, Cano & Garcia-Blanco, 1978). The transannular distance O(10)···O(17) of 3·349 (6) Å is slightly longer than the values 3·293 (3) Å in senecionine, 3·28 (1) Å in retrorsine and 3·255 (4) Å in jacobine; other close contacts within the macro-ring, O(10)···C(13) 2·802 (7) Å, O(10)···C(14) 3·404 (6) Å and C(11)···C(14) 2·978 (7) Å, are similar in value to the corresponding distances, 2·837 (4), 3·406 (4) and 2·986 (5) Å, in senecionine.

The crystal packing is illustrated in Fig. 2(*a*). An intermolecular hydrogen bond involving the hydroxyl substituent at C(12) and the N atom of an adjacent molecule related by the twofold screw axis [$x = \frac{1}{4}$, $z = \frac{1}{2}$] links the alkaloid molecules into helices along **b**. The O(23)···N(4), O(23)–H(23) and H(23)···N(4) distances are 2·806 (6), 1·06 (7) and 1·81 (6) Å, respectively, and the N(4)···H(23)–O(23) angle is 155 (4)°. Similar interactions were noted in the senecionine crystal [*cf.* distances 2·827 (4), 0·77 (5), 2·07 (5) Å and angle 167 (3)°]. The water molecules, which are situated on twofold axes [$x = 0$, $y = \frac{1}{2}$], link the two anacrotine molecules related by the twofold symmetry by hydrogen bonds which involve both hydroxyl substituents. For the interaction with O(23), the water oxygen is the donor and for the interaction with the hydroxyl substituent at C(6) it is presumed to be the acceptor [H atom at O(25) was not located]. The O(23)···O(*W*), H(O*W*)–O(*W*) and O(23)···H(O*W*) distances have the respective values 2·757 (6), 1·00 and 1·78 Å and the angle O(23)···O(*W*)–H(O*W*) is 165°, while the O(25)···O(*W*) distance is 2·824 (6) Å. The disordered ethanol molecules which also lie on twofold axes [$x = \frac{1}{2}$, $y = \frac{1}{4}$] do not appear to enter into hydrogen bonding although there is a short approach O(25)···O(Et) of 3·12 Å with the alkaloid molecule.

Madurensine solvate. The molecular structure of madurensine (12*R*, 13*R*) is illustrated in Fig. 1(*b*) [see also Tables 3 and 4]. The pyrrolizidine nucleus is *endo* buckled, as was indicated by the nuclear magnetic studies of Atal, Kapur, Culvenor & Smith (1966), with pucker angle 28·2 (7)° and an angle of 123·1 (7)° between the mean planes defined by the ring *B* atoms and atoms C(5), N(4), C(8), C(7) of ring *A*. The *endo* pucker probably arises from the involvement of the hydroxyl substituent at C(6) in the secondary ester instead of the C(7) hydroxyl group as in anacrotine, for which the more usual *exo* pucker is observed. *endo* puckering has also been observed in crystals of

heliotrine (Wodak, 1975) and lasiocarpine (Hay, Mackay & Culvenor, 1982), both alkaloids derived from the aminodiol heliotrine and monoprotic acids.

Atoms in the primary ester grouping, C(9), O(10), C(11), O(22), C(12) are coplanar within ± 0·02 (1) Å, and as in anacrotine the hydroxyl substituent at C(12) lies close to the plane, the torsional angle O(22)–O(11)–C(12)–O(23) being −3·4 (6)° in each case. Atom H(9*a*) at C(9) lies closer to the plane of the unsaturated ring and the ester plane than H(9*b*). This is reflected in the torsional angles H(9*a*)–C(9)–C(1)–C(2) and H(9*a*)–C(9)–O(10)–C(11), which have the respective values 165 and −165°, compared with H(9*b*)–C(9)–C(1)–C(2) of 37° and H(9*b*)–C(9)–O(10)–C(11) of −49°. In the secondary ester system at C(6), atoms C(6), O(17), C(16), O(24), C(15) are coplanar within ±0·01 (1) Å but H(6) lies out of plane [torsional angle H(6)–C(6)–O(17)–C(16) 37°] and adjacent to the carbonyl group, the H(6)···O(24) distance being 2·35 Å. Apparently, closure of the macro-ring through C(6) in madurensine, rather than through C(7) as in anacrotine, has not significantly altered the configuration of the secondary ester grouping [*cf.* torsional angle H(6)–C(6)–O(17)–C(16) 34 (5)° in anacrotine]. However, with C(21) *trans* to the carbonyl group, in contrast to the near *cis* arrangement in anacrotine, the atoms associated with the C(15)–C(20) double bond lie close to the ester plane [torsional angles C(20)–C(15)–C(16)–O(24), C(14)–C(15)–C(16)–O(17), C(21)–C(20)–C(15)–C(16) 5·5 (5), 3·8 (6), 177·7 (6)°, respectively]. The two carbonyl bonds in the macrocyclic system are directed away from each other with an angle between the bonds of 120·6 (6)°. The intramolecular distances within the macro-ring, O(17)···O(10), O(17)···C(13), O(17)···C(14) and C(13)···C(16), have the respective values 3·567 (6), 3·285 (8), 2·726 (8) and 3·369 (11) Å, and O(25) lies 2·994 (7) Å from O(10).

Termination of the macro-ring at C(6) in madurensine rather than the usual C(7) position has had surprisingly little effect on the general conformation of the ring from C(9) to C(15). It is evident that no exceptional strain is involved, an important factor in this being the ability of the pyrrolizidine ring to adjust into an *endo* buckled position.

Fig. 2(*b*) shows a projection of the structure down the *c* axis. As in the anacrotine crystal, an intermolecular hydrogen bond involving the hydroxyl substituent at C(12) and the N atom of an adjacent molecule related by the twofold screw axis at $x = \frac{1}{2}$, $z = \frac{1}{4}$ links the alkaloid molecules into helices along **b**. The O(23)···N(4), O(23)–H(23), H(23)···N(4) distances have the respective values 2·783 (7), 0·89 and 1·92 Å and the angle O(23)–H(23)···N(4) is 163°. It is likely that O(23) also is involved in H bonding with the solvents of crystallization, but no other oxygen atoms of the alkaloid molecule are close enough to the solvent molecules to enter into such interactions. The disordering of the solvent molecules in the madurensine crystal in cavities down the short 7·111 (1) Å axis is somewhat similar to situations noted in other crystals when there is not enough space to accommodate the appropriate intermolecular bonding. For example, in a hydrate of caffeine (Sutor, 1958), a disorder of the water molecule down a short 3·97 Å axis with a departure from the crystallographic symmetry was reported. More recently, columns running the length of a short 7·25 (1) Å axis in a hydrate of a copper(II) complex (Beckett & Hoskins, 1972) were found to contain randomly distributed water molecules.

Financial support from the Australian Research Grants Scheme is gratefully acknowledged, and we express our appreciation to Dr A. McL. Mathieson for valuable discussion.

References

ATAL, C. K., KAPUR, K. K., CULVENOR, C. C. J. & SMITH, L. W. (1966). *Tetrahedron Lett.* pp. 537–544.

BECKETT, R. & HOSKINS, B. F. (1972). *J. Chem. Soc. Dalton Trans.* pp. 291–295.

COCHRAN, W. (1951). *Acta Cryst.* **4**, 81–92.

COLEMAN, P. C., COUCOURAKIS, E. D. & PRETORIUS, J. A. (1980). *S. Afr. J. Chem.* **33**, 116–119.

CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.

CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* A**24**, 321–324.

CULVENOR, C. C. J. & SMITH, L. W. (1972). *An. R. Soc. Esp. Fís. Quím.* **68**, 883–892.

CULVENOR, C. C. J., SMITH, L. W. & WILLING, R. I. (1970). *Chem. Commun.* pp. 65–66.

HAY, D. G., MACKAY, M. F. & CULVENOR, C. C. J. (1982). *Acta Cryst.* B**38**, 155–159.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

MACKAY, M. F. & CULVENOR, C. C. J. (1982). *Acta Cryst.* B**38**, 2754–2758.

PÉREZ-SALAZAR, A., CANO, F. H. & GARCÍA-BLANCO, S. (1978). *Cryst. Struct. Commun.* **7**, 105–109.

SHELDRICK, G. M. (1976). *SHELX*76. Program for crystal structure determination. Univ. of Cambridge, England.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

SUTOR, D. J. (1958). *Acta Cryst.* **11**, 453–458.

WODAK, S. J. (1975). *Acta Cryst.* B**31**, 569–573.