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Lycopsamine and Intermedine, $C_{15}H_{25}NO_5$: Diastereoisomeric Pyrrolizidine Alkaloids

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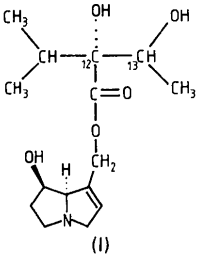
Abstract. $M_r = 299{\cdot}4$, orthorhombic, $P2_12_12_1$, $Z = 4$, $F(000) = 648$, $\lambda(\text{Cu } K\alpha) = 1{\cdot}5418$ Å, $T = 288$ K. Lycopsamine: $a = 10{\cdot}183$ (2), $b = 12{\cdot}312$ (1), $c = 12{\cdot}769$ (1) Å, $U = 1600{\cdot}9$ (4) Å^3, $D_m = 1{\cdot}237$ (5), $D_x = 1{\cdot}242$ Mg m^{-3}, $\mu(\text{Cu } K\alpha) = 0{\cdot}68$ mm^{-1}. Intermedine: $a = 11{\cdot}245$ (3), $b = 11{\cdot}762$ (1), $c = 11{\cdot}842$ (2) Å, $U = 1566{\cdot}3$ (5) Å^3, $D_m = 1{\cdot}269$ (5), $D_x = 1{\cdot}269$ Mg m^{-3}, $\mu(\text{Cu } K\alpha) = 0{\cdot}69$ mm^{-1}. The structures were solved by direct methods with diffractometer data measured with Cu $K\alpha$ radiation. Full-matrix least-squares refinement converged at R values of 0·043 and 0·045 for 1529 and 1432 reflections for lycopsamine and intermedine respectively. The absolute configuration of the two diastereoisomeric alkaloids which are monoesters of (+)-retronecine is defined by reference to the absolute configuration of the latter. In each molecule, the hydroxyl substitutent on the pyrrolizidine nucleus forms an intramolecular hydrogen bond with an hydroxyl group on the esterifying acid moiety. An intermolecular hydrogen-bonding system which involves the N atom and three hydroxyl groups links the molecules into a three-dimensional network in each crystal.

Introduction. The diastereoisomeric alkaloids lycopsamine and intermedine, represented as (I), occur singly or together in a number of genera of the Boraginaceae (*e.g.* Culvenor & Smith, 1966; Culvenor, Edgar, Frahn & Smith, 1980), in the genera *Eupatorium* and *Conoclinium* of the Compositae (Herz, Kulanthaivel, Subramanian, Culvenor & Edgar, 1981) and in the genus *Parsonsia* of the Apocynaceae (Edgar & Culvenor, 1975). Separation of the two alkaloids as their borate complexes has been achieved by partition and ion-exchange chromatography (Frahn, Culvenor & Mills, 1980). The two alkaloids are monoesters of the aminodiol (+)-retronecine, and the monoprotic acid 2,3-dihydroxy-2-isopropylbutanoic acid, and contain vicinal glycol groups of different configuration at C(13). The crystallographic analyses reported here form parts of the study of the conformational aspects of the hepatotoxic pyrrolizidine alkaloids which currently we are undertaking.



(I)

Experimental. Both compounds formed thick prismatic crystals from acetone. Specific rotations $[\alpha]_D^{20°C} = +5{\cdot}7°$ ($c = 0{\cdot}89$ g dm^{-3} in ethanol) and $+9{\cdot}8°$ ($c = 1{\cdot}49$ g dm^{-3} in ethanol) for lycopsamine and intermedine respectively (Frahn, Culvenor & Mills, 1980). Weissenberg photographs showed the crystals to be orthorhombic, and systematic extinctions indicated space group $P2_12_12_1$; cell parameters determined by least squares from 2θ values measured for 25 strong reflections with Cu $K\alpha$ radiation on a diffractometer; crystal densities determined by flotation. Integrated intensities measured with Cu $K\alpha$ radiation (graphite-crystal monochromator) from crystals *ca* 0·22 × 0·29 × 0·32 mm (lycopsamine) and *ca* 0·32 × 0·39 × 0·45 mm (intermedine) aligned on a Rigaku-*AFC* diffractometer; ω–2θ scan, 2θ scan rate 2° min^{-1}, scan range ($\Delta\omega$) 1·2° + 0·5° tan θ, 10s stationary background counts; three reference reflections monitored every 50 reflections showed no significant variation in intensity during data collection; $2\theta_{max} = 130°$; of the 1560 non-equivalent terms for lycopsamine, 1529 for which $|F_o| > 2\sigma|F_o|$ were used for structure refinement, and for intermedine 1432 terms of a total 1524 were used; no correction for absorption or extinction; scattering factors for O, N and C from Cromer & Mann (1968), for H from Stewart, Davidson & Simpson (1965); anomalous-dispersion corrections made with the values of Cromer & Liberman (1970). The structures were solved by direct methods with *SHELX*76 (Sheldrick, 1976); full-matrix least-squares refinement and all H-atom sites located on difference maps; refinement with anisotropic temperature factors given to the C, N and O atoms and isotropic for the H atoms converged at $R = 0{\cdot}043$ and $R_w = 0{\cdot}053$ for lycopsamine and $R = 0{\cdot}045$ and $R_w = 0{\cdot}050$ for

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intermedine; temperature factors and positional coordinates of the H atoms were allowed to vary. At convergence the mean parameter shift-to-error ratios were 0·02:1 for the H atoms and 0·01:1 for all other parameters for lycopsamine; the values for intermedine were 0·12:1 and 0·05:1. The largest peaks on the final difference map were of heights + 0·24 and −0·31 e Å^{-3} (lycopsamine) and + 0·18 and −0·35 e Å^{-3} (intermedine). The function minimized in the refinements was $\sum w(|F_o| - |F_c|)^2$ with weights $(\sigma^2|F_o| + m|F_o|^2)^{-1}$ for which values of m were 5×10^{-4} and 5×10^{-5} for lycopsamine and intermedine respectively.

Discussion. Final atomic coordinates are given in Tables 1 and 2;* Fig. 1 which contains the atom numbering and Fig. 2 which shows the crystal packing have been prepared from the output of *ORTEP* (Johnson, 1965).

The absolute molecular structures of the two alkaloids illustrated in Fig. 1 have been assigned by comparison with that of retronecine. Consequently, the absolute configuration of (+)-lycopsamine is (12*S*,13*S*) and of (+)-intermedine is(12*S*,13*R*) in agreement with the absolute configuration established by Kochetkov, Likhosherstov & Kulakov (1969) for (–)-viridifloric (2*S*,3*S*) and (+)-trachelanthic (2*S*,3*R*) acids, the acid moieties in lycopsamine and intermedine respectively. The relative and absolute configurations of (+)-trachelanthic acid are the same as in heliotric and lasiocarpic acids, whose parent alkaloids have also been the subject of crystallographic studies (Wodak, 1975; Hay, Mackay & Culvenor, 1982).

* Lists of structure factors, anisotropic thermal parameters, intermolecular approach distances and details of hydrogen bonds for both compounds have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38399 (36 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* (× 10^4, *for* H × 10^3) *and isotropic temperature factors for lycopsamine, with e.s.d.'s in parentheses*

H atoms are numbered according to the atom to which they are attached. For non-H atoms $B_{eq} = \frac{4}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq} or B_{iso} (Å^2)
C(1)	6322 (2)	−1111 (2)	11220 (2)	2·2 (1)
C(2)	6736 (3)	−1041 (2)	12198 (2)	2·8 (1)
C(3)	6734 (3)	−2116 (2)	12743 (2)	3·1 (1)
N(4)	6239 (2)	−2885 (2)	11944 (2)	2·5 (1)
C(5)	5014 (3)	−3443 (2)	12243 (2)	2·9 (1)
C(6)	4314 (3)	−3615 (2)	11210 (2)	3·2 (1)
C(7)	4551 (2)	−2546 (2)	10634 (2)	2·3 (1)
C(8)	5981 (2)	−2272 (2)	10947 (2)	2·1 (1)
C(9)	6330 (3)	−214 (2)	10432 (2)	2·6 (1)
O(10)	5136 (2)	−331 (2)	9831 (2)	2·8 (1)
C(11)	4870 (3)	403 (2)	9101 (2)	2·5 (1)
C(12)	3609 (3)	134 (2)	8509 (2)	2·2 (1)
C(13)	2695 (3)	1143 (2)	8526 (2)	2·9 (1)
C(14)	2362 (5)	1484 (4)	9633 (3)	4·8 (2)
C(15)	3972 (3)	−233 (2)	7382 (2)	2·8 (1)
C(16)	4493 (3)	668 (3)	6677 (2)	3·6 (1)
C(17)	4932 (4)	−1186 (3)	7396 (3)	4·4 (2)
O(18)	5556 (2)	1179 (2)	8937 (2)	3·8 (1)
O(19)	2981 (2)	−734 (1)	9046 (2)	2·4 (1)
O(20)	1505 (2)	869 (2)	8009 (2)	3·7 (1)
O(21)	3600 (2)	−1778 (2)	10993 (1)	2·6 (1)
H(2)	696 (3)	−38 (3)	1251 (2)	3·2 (6)
H(3*a*)	616 (4)	−214 (3)	1337 (3)	4·7 (8)
H(3*b*)	771 (5)	−238 (4)	1295 (4)	6·3 (10)
H(5*a*)	453 (3)	−299 (2)	1275 (2)	2·0 (5)
H(5*b*)	524 (4)	−413 (3)	1258 (3)	3·6 (7)
H(6*a*)	327 (5)	−327 (3)	1130 (3)	5·3 (9)
H(6*b*)	468 (4)	−422 (3)	1089 (3)	4·8 (8)
H(7)	445 (4)	−256 (3)	987 (3)	4·2 (7)
H(8)	663 (3)	−255 (2)	1038 (2)	2·1 (5)
H(9*a*)	703 (3)	−28 (2)	998 (2)	2·0 (5)
H(9*b*)	636 (4)	52 (3)	1081 (3)	3·7 (7)
H(13)	320 (3)	176 (3)	826 (3)	3·2 (6)
H(14*a*)	308 (5)	168 (4)	999 (4)	5·6 (10)
H(14*b*)	178 (5)	218 (4)	963 (4)	5·9 (10)
H(14*c*)	203 (5)	87 (4)	1005 (4)	6·8 (12)
H(15)	322 (4)	−45 (3)	713 (3)	3·2 (6)
H(16*a*)	387 (5)	134 (3)	660 (3)	5·5 (9)
H(16*b*)	531 (5)	95 (3)	696 (3)	5·0 (9)
H(16*c*)	469 (4)	34 (3)	611 (4)	5·2 (9)
H(17*a*)	466 (5)	−180 (4)	785 (4)	6·5 (11)
H(17*b*)	517 (5)	−149 (4)	677 (4)	6·9 (11)
H(17*c*)	577 (5)	−89 (3)	760 (4)	5·4 (10)
H(19)	247 (4)	−107 (3)	867 (3)	3·5 (7)
H(20)	136 (5)	121 (4)	747 (4)	7·0 (12)
H(21)	348 (4)	−127 (3)	1053 (3)	4·2 (8)

Table 2. *Final atomic coordinates* (× 10^4, *for* H × 10^3) *and isotropic temperature factors for intermedine, with e.s.d.'s in parentheses*

H atoms are numbered according to the atom to which they are attached. For non-H atoms $B_{eq} = \frac{4}{3}\sum_i\sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq} or B_{iso} (Å^2)
C(1)	3926 (3)	5112 (3)	11051 (3)	2·2 (2)
C(2)	4248 (4)	6049 (4)	11583 (4)	3·4 (2)
C(3)	3330 (5)	6947 (4)	11540 (5)	3·8 (2)
N(4)	2292 (3)	6388 (3)	11005 (3)	2·5 (1)
C(5)	1747 (5)	7001 (4)	10048 (4)	3·3 (2)
C(6)	1425 (4)	6071 (5)	9208 (4)	3·5 (2)
C(7)	2491 (4)	5270 (4)	9301 (4)	2·5 (2)
C(8)	2684 (4)	5238 (3)	10578 (3)	2·1 (2)
C(9)	4620 (4)	4039 (4)	10981 (3)	2·6 (2)
O(10)	5111 (2)	3987 (2)	9841 (2)	2·3 (1)
C(11)	5845 (3)	3113 (3)	9615 (3)	2·2 (1)
C(12)	6240 (3)	3177 (3)	8384 (3)	1·8 (1)
C(13)	5145 (3)	2986 (3)	7600 (4)	2·1 (1)
C(14)	4365 (4)	2023 (4)	8006 (5)	3·3 (2)
C(15)	6878 (3)	4313 (3)	8176 (3)	2·3 (2)
C(16)	7957 (5)	4434 (5)	8947 (5)	3·5 (2)
C(17)	7242 (5)	4452 (4)	6938 (4)	3·1 (2)
O(18)	6124 (3)	2417 (3)	10300 (2)	3·5 (1)
O(19)	7048 (3)	2260 (2)	8209 (3)	2·3 (1)
O(20)	4494 (2)	4025 (2)	7501 (2)	2·2 (1)
O(21)	3460 (3)	5787 (3)	8702 (2)	2·5 (1)
H(2)	503 (4)	617 (4)	1196 (4)	4·6 (11)
H(3*a*)	350 (6)	766 (5)	1108 (5)	7·2 (16)
H(3*b*)	316 (6)	721 (6)	1241 (6)	9·9 (20)
H(5*a*)	240 (5)	760 (4)	971 (4)	5·1 (12)
H(5*b*)	113 (4)	751 (4)	1028 (4)	3·9 (10)
H(6*a*)	131 (4)	642 (3)	842 (4)	3·7 (9)
H(6*b*)	68 (5)	563 (4)	944 (5)	5·5 (13)
H(7)	235 (4)	447 (3)	896 (3)	2·6 (9)
H(8)	214 (4)	463 (3)	1086 (3)	2·1 (8)
H(9*a*)	415 (4)	335 (4)	1110 (4)	3·5 (10)
H(9*b*)	529 (4)	408 (4)	1152 (4)	3·7 (10)
H(13)	552 (4)	274 (4)	678 (4)	2·7 (9)
H(14*a*)	481 (4)	137 (4)	820 (4)	4·1 (11)
H(14*b*)	368 (7)	178 (6)	741 (6)	8·9 (18)
H(14*c*)	393 (5)	216 (5)	879 (5)	7·4 (16)
H(15)	626 (3)	493 (3)	840 (3)	2·2 (8)
H(16*a*)	858 (5)	392 (4)	876 (4)	5·5 (13)
H(16*b*)	832 (6)	513 (5)	880 (5)	6·4 (16)
H(16*c*)	772 (4)	444 (4)	981 (5)	4·8 (12)
H(17*a*)	782 (4)	382 (4)	676 (4)	3·4 (10)
H(17*b*)	779 (5)	520 (5)	684 (5)	5·9 (13)
H(17*c*)	657 (5)	446 (5)	640 (5)	5·9 (14)
H(19)	688 (4)	196 (4)	773 (4)	2·0 (10)
H(20)	397 (5)	392 (4)	699 (5)	5·4 (14)
H(21)	391 (4)	534 (4)	856 (4)	2·3 (11)

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

	Lycopsamine	Intermedine		Lycopsamine	Intermedine		Lycopsamine	Intermedine
C(1)–C(2)	1·321 (4)	1·320 (6)	C(6)–C(7)	1·527 (4)	1·529 (7)	C(12)–C(13)	1·552 (4)	1·558 (5)
C(1)–C(8)	1·512 (3)	1·512 (6)	C(7)–C(8)	1·547 (3)	1·528 (6)	C(12)–C(15)	1·553 (4)	1·536 (5)
C(1)–C(9)	1·494 (4)	1·486 (6)	C(7)–O(21)	1·429 (3)	1·435 (6)	C(12)–O(19)	1·422 (3)	1·425 (4)
C(2)–C(3)	1·495 (4)	1·478 (7)	C(9)–O(10)	1·445 (4)	1·460 (4)	C(13)–C(14)	1·513 (5)	1·511 (6)
C(3)–N(4)	1·480 (4)	1·482 (6)	O(10)–C(11)	1·326 (4)	1·345 (4)	C(13)–O(20)	1·421 (4)	1·429 (4)
N(4)–C(5)	1·474 (4)	1·476 (6)	C(11)–C(12)	1·526 (4)	1·526 (5)	C(15)–C(16)	1·524 (4)	1·525 (7)
N(4)–C(8)	1·503 (4)	1·510 (5)	C(11)–O(18)	1·202 (4)	1·194 (5)	C(15)–C(17)	1·527 (5)	1·531 (6)
C(5)–C(6)	1·514 (4)	1·522 (7)						
C(2)–C(1)–C(8)	110·7 (2)	110·4 (3)	C(6)–C(7)–O(21)	108·0 (2)	107·4 (4)	C(11)–C(12)–C(15)	108·8 (2)	109·4 (3)
C(2)–C(1)–C(9)	125·9 (2)	126·3 (4)	C(8)–C(7)–O(21)	114·3 (2)	113·1 (4)	C(11)–C(12)–O(19)	107·6 (2)	106·7 (3)
C(8)–C(1)–C(9)	123·0 (2)	123·2 (3)	C(1)–C(8)–N(4)	103·9 (2)	103·5 (3)	C(13)–C(12)–C(15)	112·9 (2)	113·5 (3)
C(1)–C(2)–C(3)	112·5 (2)	112·9 (4)	C(1)–C(8)–C(7)	118·8 (2)	120·0 (3)	C(13)–C(12)–O(19)	109·0 (2)	107·9 (3)
C(2)–C(3)–N(4)	104·2 (2)	104·4 (4)	N(4)–C(8)–C(7)	105·9 (2)	105·5 (3)	C(15)–C(12)–O(19)	109·6 (2)	109·7 (3)
C(3)–N(4)–C(5)	114·1 (2)	116·0 (4)	C(1)–C(9)–O(10)	106·2 (2)	106·6 (3)	C(12)–C(13)–C(14)	111·7 (3)	112·2 (3)
C(3)–N(4)–C(8)	108·8 (2)	108·1 (3)	C(9)–O(10)–C(11)	118·5 (2)	116·6 (3)	C(12)–C(13)–O(20)	108·4 (2)	109·3 (3)
C(5)–N(4)–C(8)	107·8 (2)	107·6 (3)	O(10)–C(11)–C(12)	111·8 (2)	109·3 (3)	C(14)–C(13)–O(20)	108·0 (3)	110·9 (3)
N(4)–C(5)–C(6)	103·8 (2)	104·4 (4)	O(10)–C(11)–O(18)	123·1 (3)	123·4 (3)	C(12)–C(15)–C(16)	114·7 (2)	110·9 (3)
C(5)–C(6)–C(7)	103·0 (2)	102·1 (4)	C(12)–C(11)–O(18)	125·1 (3)	127·3 (3)	C(12)–C(15)–C(17)	111·4 (2)	111·8 (3)
C(6)–C(7)–C(8)	102·3 (2)	101·4 (4)	C(11)–C(12)–C(13)	108·9 (2)	109·4 (3)	C(16)–C(15)–C(17)	110·1 (3)	110·5 (4)

Table 4. *Selected torsional angles* (°)

E.s.d.'s are about 0·3°. Atoms are represented by their identification number.

	Lycopsamine	Intermedine		Lycopsamine	Intermedine
1–8–7–21	−21·8	−32·4	11–12–13–14	−58·9	−43·4
1–9–10–11	176·9	175·6	11–12–13–20	−177·3	81·1
2–1–8–7	118·3	112·9	11–12–15–16	−70·1	59·0
2–1–9–10	−142·1	−105·3	11–12–15–17	55·8	−177·2
9–10–11–12	177·5	178·4	13–12–11–18	−52·5	114·6
9–10–11–18	−2·3	−1·9	14–13–12–15	−179·8	−165·8
10–11–12–13	127·7	−65·7	15–12–11–18	70·9	−120·5
10–11–12–15	−108·9	59·2	19–12–11–18	−170·5	−1·9
10–11–12–19	9·7	177·8	19–12–13–20	−60·6	−163·2

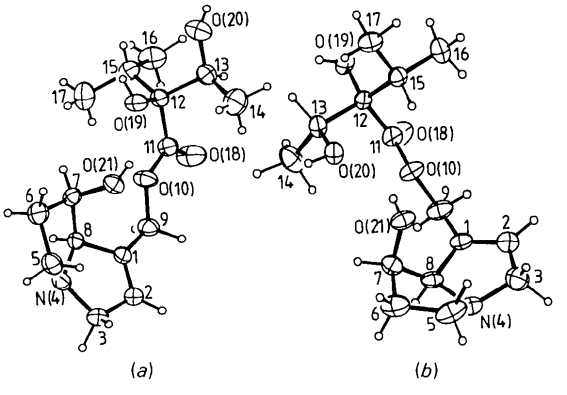

Fig. 1. Perspective views of the molecules with thermal ellipsoids scaled to 40% probability: (*a*) lycopsamine, (*b*) intermedine.

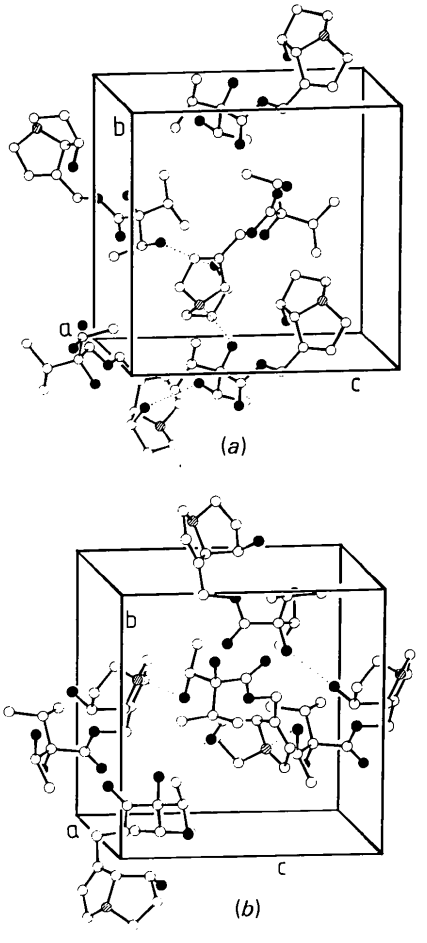

Fig. 2. The molecular packing: (*a*) lycopsamine, (*b*) intermedine.

Bond lengths and angles are given in Table 3 and selected torsional angles are given in Table 4.

As generally observed for the retronecine alkaloids, the pyrrolizidine nucleus is *exo*-buckled; the puckering angles are 40·2 (4) and 38·5 (5)° in lycopsamine and intermedine respectively, while the angles between the mean planes defined by the atoms C(1), C(2), C(3), N(4), C(8), and C(5), N(4), C(8), C(7) are 125·4 (3) and 127·2 (4)°. In lycopsamine the unsaturated ring atoms are coplanar within ±0·008 (3) Å with C(9) lying 0·136 (3) Å from the plane; in intermedine the atoms are only coplanar within ±0·055 (6) Å and C(9) lies 0·178 (4) Å out-of-plane. It has also been noted that C(9) lies significantly from the plane of the unsaturated ring in the two retronecine alkaloids senecionine (Mackay & Culvenor, 1982) and jacobine (Pérez-Salazar, Cano & García-Blanco, 1978).

Although the torsional angle C(2)–C(1)–C(9)–O(10) in the two diastereoisomeric alkaloids differs by 36·8 (4)° [−142·1 (4)° in lycopsamine and −105·3 (4)° in intermedine] one H atom at C(9), H(9*b*), lies close to the plane of the unsaturated ring, the torsional angle C(2)–C(1)–C(9)–H(9*b*) being −22 (3) and 11 (4)° in the respective alkaloids [*cf.* the value 13 (3)° in senecionine].

In each alkaloid molecule the esterifying acid moiety adopts an extended conformation with the atoms C(1), C(9), O(10), C(11), C(12), O(18), O(19) almost coplanar [see torsional angles C(1)–C(9)–O(10)–C(11), C(9)–O(10)–C(11)–C(12), and O(18)–C(11)–C(12)–O(19)]. The monoprotic esterifying acid moieties, lasiocarpic and heliotric acids in the heliotridine alkaloids lasiocarpine (Hay, Mackay & Culvenor, 1982) and heliotrine (Wodak, 1975) respectively, adopt a similar extended conformation. The five atoms of the ester group, C(9), O(10), C(11), C(12), O(18), are coplanar within ±0·020 (3) Å in lycopsamine and within ±0·015 (3) Å in intermedine, and in each molecule the O–H bond of the hydroxyl substituent at C(12) is directed away from the carbonyl oxygen, O(18).

A comparison of the conformations adopted by the esterifying acids in the two alkaloids is of interest in relation to the differential complexing of the alkaloids with borate. Lycopsamine complexes more strongly than intermedine (Frahn, Culvenor & Mills, 1980). These authors have pointed out that eclipsing of the vicinal hydroxyl groups (as ideally required for the formation of the borate complex) results, in intermedine, in the energetically unfavourable eclipsing of the methyl at C(13) and the isopropyl group at C(12), whereas in lycopsamine the methyl at C(13) eclipses the carbonyl group at C(12), a much less unfavourable situation. In the crystal structures, the methyl–isopropyl interaction is minimized [torsional angle C(14)–C(13)–C(12)–C(15) is −165·8 (4)° in intermedine, and −179·8 (4)° in lycopsamine] and the vicinal hydroxyl groups are *anti* in intermedine [torsional angle O(19)–C(12)–C(13)–O(20) −163·2 (4)°] and *syn* in lycopsamine [torsional angle O(19)–C(12)–C(13)–O(20) −60·6 (4)°]. Lycopsamine will clearly require less energy than intermedine to change to the conformation required for complexing.

The conformations adopted by the alkaloids might also be expected to clarify reasons for the characteristic differences in the NMR chemical shifts of the methyl groups in viridifloric and trachelanthic esters, as exemplified by lycopsamine and intermedine (Culvenor & Smith, 1966). The methyls of the isopropyl group are of equal shift in intermedine but not in lycopsamine, and the methyl at C(13) is at lower field in lycopsamine than in intermedine. The first difference seems to be due to an effect of the hydroxyl substituent at C(12), which is symmetrically orientated relative to the isopropyl methyls in intermedine but not in lycopsamine, rather than to an influence of the carbonyl group, for which the opposite is true. The methyl at C(13), on the other hand, is closer to the carbonyl group in the conformation observed for lycopsamine, suggesting that this is the reason for the relative methyl chemical shifts.

Both molecules contain an intramolecular H bond in which the O of the hydroxyl group at C(7) on the pyrrolizidine nucleus donates to an hydroxyl O on the esterifying acid moiety. In lycopsamine the interaction involves O(19) and in intermedine it involves O(20). It is interesting that in heliotrine the hydroxyl substituent at C(7) is involved only in an intermolecular H bond. The comparable bond lengths and angles in the two structures are in good agreement and similar to values reported for other pyrrolizidine alkaloids.

The molecular packing in the crystals is illustrated in Fig. 2. In each structure there are two unique intermolecular H-bonding interactions which link the molecules into a three-dimensional network, each molecule being H-bonded to four others. For lycopsamine the hydroxyl substituent at C(12) is H-bonded to the N atom of an adjacent molecule related by the screw axis along **a**, and the hydroxyl group at C(13) is H-bonded to O(21) of a molecule related by the screw axis along **c**. For intermedine it is the hydroxyl substitutent at C(13) which is H-bonded to the N of an adjacent molecule (related by the screw axis along **c**) and the hydroxyl at C(12) is H-bonded to O(21) of a molecule related by the screw axis along **b**. All H-bond dimensions are normal.

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