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MINOR ALKALOIDS OF *HELIOTROPIUM CURASSAVICUM*

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Key Word Index—Pyrrolizidine alkaloids; heliocurassavine; heliocurassavinine; heliocurassavicine; heliocoromadaline; curassavinine; coromandalinine; heliovinine; curassanecine.

Abstract—Isolation and structure determination of the minor alkaloids of *Heliotropium curassavicum* are described. These include the new pyrrolizidine alkaloids, heliocurassavine [isoretronecanol (−) curassavine], heliocoromandaline [isoretronecanol (+) viridiflorate], heliocurassavicine [isoretronecanol (−) trachelanthate], heliocurassavinine [laburnine (−) trachelanthate], curassavinine [supinidine (−) curassavate], coromandalinine [supinidine (+) viridiflorate], heliovinine [supinidine (−) trachelanthate] and curassanecine [1-(α-hydroxymethyl)-8α pyrrolizidin-1β-ol]. Structures were established by high resolution ^{1}H NMR, mass spectrometry and paper electrophoresis of the alkaloids and their hydrolysis products.

INTRODUCTION

Heliotropium curassavicum is a glaucous fleshy herb found in the south-western desert of North America, on the Coromandel coast of India, in Australia and in Europe. It has been used by Indians of the American south-west as a curative for sores and wounds [1, 2]. The main alkaloids in collections of this plant from Madras, India, from Australia and from Pakistan have been identified [3, 4] as curassavine (**1**), coromandaline (**2**) and heliovicine (**3**), which are trachelanthamidine esters of (−) curassavic, (+) viridifloric and (−) trachelanthic acids, respectively. Trachelanthamidine itself (**4**) was also found. *H. curassavicum* from Mexico and the adjacent U.S.A. apparently contained curassavine, acetylcurassavine, possibly a mixture of acetylcoromandaline and acetylheliovicine, as well as minor saturated and unsaturated alkaloids which were not identified [5]. A collection of *H. curassavicum* from Delhi has been reported to contain esters of heliotridine [6]. We now describe the isolation and characterization of new minor alkaloids **5**, **7**, **8**, **9**, **11**, **12** and **13** from our previously studied Madras collection [3, 4] and revise the structure of the previously found base $C_8H_{15}O_2N$ [4] to **15**.

RESULTS AND DISCUSSION

Fractionation of the MeOH extract with Et_2O, $CHCl_3$, $CHCl_3$ (continuous) before and after reduction gave several fractions [4]. Fraction C (representing the material obtained by continuous extraction with $CHCl_3$ prior to reduction) gave *N*-oxides which after reduction with Zn–H_2SO_4 and chromatography over alkalized Si gel [7] afforded heliocurassavine (**7**) in addition to the alkaloids reported earlier [4]. Fraction D (representing the Et_2O extract after reduction) on chromatography over neutral Al_2O_3 followed by chromatography over alkalized Si gel gave heliocurassavinine (**5**), heliocurassavine (**7**), heliocurassavicine (**9**), heliocoromandaline (**8**), an alkaloid mixture *Z* and the main alkaloids reported earlier [4].

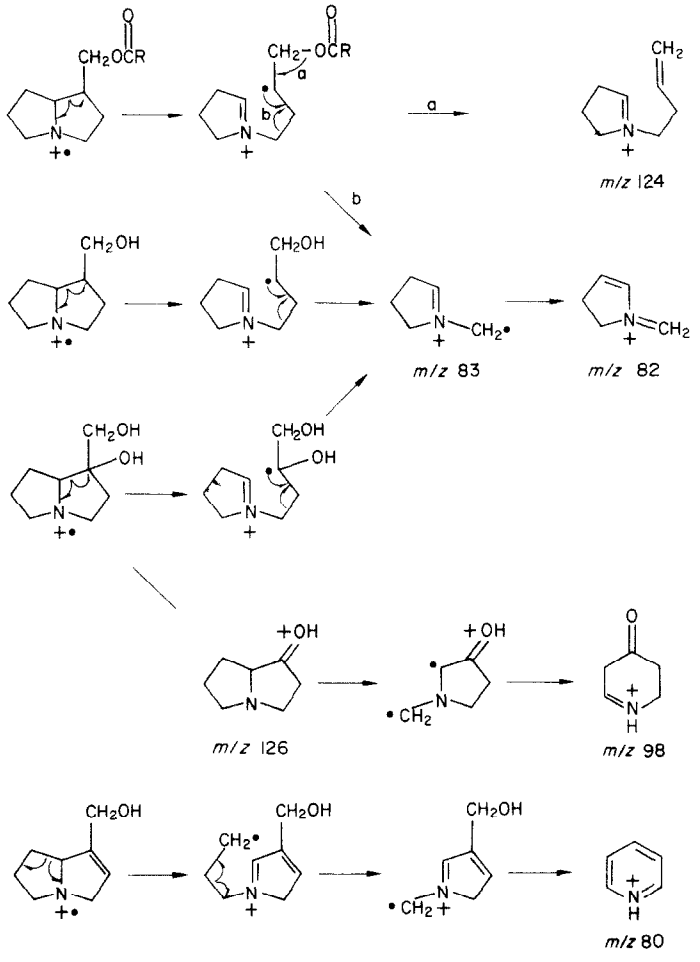
The mass spectrum of heliocurassavine, $C_{16}H_{29}O_4N$, showed the base peak at *m/z* 124 with a prominent peak at *m/z* 83 indicative of an ester of pyrrolizidin-1-yl methanol (Scheme 1) with a C-8 necic acid. The 270 MHz ^{1}H NMR spectrum (see Experimental) was similar to that of curassavine (**1**) [8]. Alkaline hydrolysis gave (−) isoretronecanol (**10**), identified by ^{1}H NMR, GC and mass spectrometry (the R_t time of 7.33 min was slightly longer than that of trachelanthamidine, 7.0 min, which was coinjected) and (−) curassavic acid (R_1H), identified by ^{1}H NMR, mass spectrometry optical rotation, GC, mp and mmp with an authentic sample.‡ Hence heliocurassavine is **7**.

The ^{1}H NMR spectra of heliocurassavicine, $C_{15}H_{27}O_4N$, and heliocurassavinine, $C_{15}H_{27}O_4N$, both similar to that of heliovicine (**3**) [8], and the mass spectra with base peaks at *m/z* 124 and prominent peaks at *m/z* 83, suggested that these compounds were trachelanthates of pyrrolizidin-1-yl methanols. Alkaline hydrolysis of heliocurassavicine gave (−) isoretronecanol (**10**) and (−) trachelanthic acid (R_3H) which was identified by comparison with an authentic sample. Heliocurassavicine is thus **9**. Alkaline hydrolysis of heliocurassavinine gave (−) trachelanthic acid and laburnine (**6**). The latter was identified by NMR, the spectrum being identical to that of **4**, by GC as it emerged as a single peak on admixture of **4**, and by rotation. Hence heliocurassavinine is **5**.

Heliocoromandaline, $C_{15}H_{27}O_4N$, with an ^{1}H NMR spectrum similar to that of coromandaline (**2**) [8] and a mass spectrum like that of the previous compounds was apparently a viridifloric acid ester of a pyrrolizidin-1-yl methanol. This was confirmed by hydrolysis to (−) isoretronecanol (**10**) and (+) viridifloric acid, the latter being identified by comparison with an authentic sample. Hence heliocoromandaline is **8**.

Alkaloid mixture *Z* consisted of ester alkaloids with molecular formulas $C_{16}H_{27}O_4N$ and $C_{15}H_{25}O_4N$. High-resolution NMR spectra in $CDCl_3$ and C_5D_5N in-

‡The sign and magnitude of rotation of curassavic acid from currassavine given in the preliminary report [3] are incorrect, but are correctly reproduced in the later publication giving experimental details [4].



Scheme 1.

dicated that the necine base was supinidine and the esterifying acids curassavic, trachelanthic and viridifloric acid in the ratio of *ca* 1:2:3. Separation of the mixture was not attempted due to paucity of material. Alkaline hydrolysis gave a single base, $C_8H_{13}ON$, identified as (−) supinidine (**14**) by NMR, mass spectrometry and rotation, and a mixture of acids, shown to contain mainly curassavic, trachelanthic and viridifloric acids as follows. GC of the Me esters of the acid mixture showed main peaks (R_t 10.0, 10.4, 13.3 min) and two minor peaks (R_t 12.1 and 14.9 min). Coinjection of authentic Me viridiflorate (R_t 10.0 min), Me trachelanthate (10.4 min) and Me curassavate (R_t 13.3) separately identified the three main constituents of the Me ester mixture as Me viridiflorate, Me trachelanthate and Me curassavate (47:33:17), a conclusion corroborated by GC/MS of the Me ester mixture (see Experimental) and by paper electrophoresis of the acids and the Me ester mixture (Table 1) in the absence and presence of added authentic acids and Me esters. The two very minor Me esters of R_t 12.1 (2%) and 14.9 min (1%) were esters of a C_8 and a C_9 acid, respectively, but they could not be identified further. While separation of the three major acids on a scale to permit measurement of their rotations was not attempted due to paucity of material, we assume that they are (−) curassavic, (+) viridifloric and (−) trachelanthic acids because the other major and minor ester alkaloids of *H. curassavicum* contain only these enantiomers. Thus, alkaloid mixture A is a mixture of three previously unreported alkaloids **11–13**, which were named curassavinine, coromandalinine and heliovinine, and two trace alkaloids which are (−) supinidine esters of a C_8 and a C_9 acid.

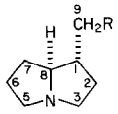
In our earlier paper [4] structure **16** was assigned to a necine base $C_8H_{15}O_2N$ from *H. curassavicum*. This must now be revised to **15** on the basis of the 270-MHz ^{1}H NMR spectrum which contains no frequency assignable to H-1, but a two-proton singlet at δ 3.98 (H-9), irradiation of which does not affect any of the signals at δ 2.30 and 2.22 *dt* (H-2), 3.35 and 3.30 *dt* (H-3), 3.86*t* (H-8) or those of the methylenes of unsubstituted ring A. A substance with this formula, 1α-hydroxymethyl-1β-hydroxy-8α-pyrrolizidine, has been prepared by catalytic hydrogenation of 1α-hydroxymethyl-1β,2β-epoxy-8α-pyrrolizidine [9], but except for the mass spectrum no properties were reported so that it is not possible to say whether our material is identical with it or not. The mass spectrum of our substance, with a weak ion at *m/z* 98, a much stronger ion at *m/z* 126 and a base peak at *m/z* 83 [4] (Scheme 1) tallies with the literature report. Since **15** has not been isolated previously as a natural product we have named it curassanecine.

Heliocurassavine, heliocoromandaline and helio-

Table 1. Relative rates of migration of acids and methyl esters derived from alkaloids*

Acids or methyl esters	M_H values†	
	Carbonate (pH 9.2)	Borate (pH 9.2)
Curassavic acid	−1.76	−1.53
Viridifloric acid	−1.86	−1.64
Trachelanthic acid	−1.95	−1.69
Acids in alkaloid mixture Z	−1.76, −1.86, −1.95	−1.53, −1.64, −1.69
Methyl curassavate	0	−1.03
Methyl viridiflorate	0	−1.07
Methyl trachelanthate	0	−0.43
Methyl esters of acids in alkaloid mixture Z	0	−0.43, −1.03, −1.07

*Paper electrophoresis was conducted at *ca* 20 V/cm and 20° for periods of 1–2 hr.
†Mobilities are relative to heliotridine; negative values represent anionic migration.



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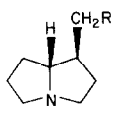
2 R = R_2
3 R = R_3
4 R = OH



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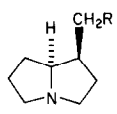
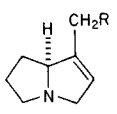
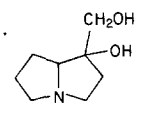
6 R = OH



7 R = R_1
8 R = R_2
9 R = R_3
10 R = OH



11 R = R_1
12 R = R_2
13 R = R_3
14 R = OH



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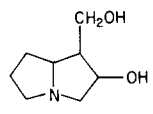

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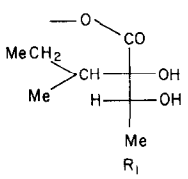
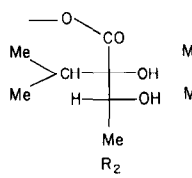
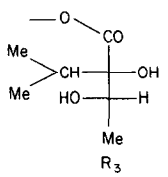


R_1



R_2



R_3

curassavicine are the first C_7 and C_8 esters of (−) isoretronecanol, the only other esters of this necine being the tiglate and the *trans*-3-methylthiopropanoate [10]. Heliocurassavinine is the first C_7 ester of laburnine, curassavine is the first C_8 ester of (−) supinidine, and curassanecine is the first naturally occurring necine with a 1-OH group. All alkaloids of *H. curassavicum*, major and minor, have the abnormal 2′*R* configuration at the α-carbon of the necic acid.

There is no record of *H. curassavicum* being poisonous to stock. All substances isolated by us are non-hepatotoxic [11] saturated pyrrolizidine alkaloids except for the trace amounts of curassavinine, coromandalinine and heliovinine which as esters of the unsaturated necine supinidine are of the hepatotoxic type. None of our compounds, including the very minor alkaloids, corresponds to the alkaloids, all hepatotoxic, isolated by Rajagopalan and Batra from *H. curassavicum* collected near Delhi [6].

EXPERIMENTAL

IR spectra were recorded on neat samples and NMR spectra were run at 270 MHz with TMS as int. standard. MS were obtained at 70 eV. GC/MS was obtained with a quadropole mass spectrometer and a data system. Samples were separated on a 1.5 m × 2 mm glass column packed with 3% OV 101 on Chromosorb W. The carrier gas flow was 15 ml N_2/min. R_ts are designated as follows: R_T^A programmed from 100 to 160° at 4°/min; R_T^B programmed from 60 to 150° at 4°/min. The procedure and conditions for thin layer (R_F data) and CC have been described previously [4] or are detailed elsewhere [7]. Apparatus and experimental procedure for paper electrophoresis of necic acids and their esters in carbonate and borate buffers were as described previously [4, 12]. Rotations (not corrected) were measured on an automatic polarimeter at the 589.3 nm Na-D line or 546.1 nm Hg line. To avoid fluctuations the Mg line (546.1 nm) was used for very small samples.

Extraction and fractionation of the alkaloids of *H. curassavicum* L. (1 kg dry wt) collected near Madras (India) in July 1975 were as described previously [4].

Isolation of new alkaloids. Alkaloid fraction D (Et_2O extract after reduction, 0.6 (g) [4] was chromatographed on neutral Al_2O_3 (120 g), with a $CHCl_3$–MeOH gradient as eluent. $CHCl_3$–MeOH (19:1) eluted gum, R_F 0.32, fraction I, 230 mg), followed by gum, R_F 0.21 (fraction II, 270 mg). Fraction 1 was rechromatographed on a column of alkalized Si gel (50 g) with $CHCl_3$–MeOH–25% MH_3 (17:3.8:0.25) as eluent, 0.5-ml fractions being collected. Fraction 1 (35 mg) on prep. TLC on alkalized Si gel with MeOH as developing solvent gave alkaloid mixture Z (10 mg) and **5** (15 mg); fractions 2–7 (25 mg), 7; fractions 10–13 (35 mg); fractions 2–7 (25 mg), fractions 10–13 (35 mg), **1**; fractions 15–16 (30 mg), **9**; fractions 18–19 (25 mg), **3** and fractions 21–22 (14 mg), **2**.

Fraction II (170 mg) was rechromatographed similarly to give **1** (fractions 1–5, 40 mg), **3** (fractions 8–10, 29 mg), **2** (fractions 12–13, 11 mg) and **6** (fraction 15, 7 mg).

Trituration of alkaloid fraction C [4] (obtained by continuous $CHCl_3$ extraction before reduction) gave a solid mixture of *N*-oxides (1 g) which was reduced with Zn dust (1.2 g) and 2 N H_2SO_4 (20 ml) for 24 hr at room temp. The recovered base was chromatographed [7] over alkalized Si gel (100 g) with $CHCl_3$–MeOH–25% MH_3 (17:3.8:0.25) to give **7** (fraction 1, 10 mg) followed by **1**, **3** and **2**.

Heliocurassavine **7** was obtained as a pale yellow gum, $[\alpha]_D^{25} - 14.9°$ (*c* 0.0037, $CHCl_3$), R_F^1 0.21, R_F^2 0.89, IR (neat) 3320, 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.17*m* (H-1), 2.04*m* and 1.93*m* (H-2), 3.39*dt* and 2.63*dt* (H-3), 3.17*dt* and 2.72*dt* (H-5), 1.9*m* (H-6), 2.06*m* and 1.65*m* (H-7), 3.57*qbr* (H-8), 4.24*d* (H-9), 3.99*q* (H-3'), 1.27*d* (H-4'), 1.84*m* (H-5'), 1.25*m* (H-6'), 0.90*t* (H-7'), and 0.93*d* (H-8'; NMR (C_6D_6) δ 1.65*m* (H-1), 1.56*m* (H-2), 3.14*dt* and 2.12*dt* (H-3), 2.94*dt* and 2.23*dt* (H-5), 1.49*m* (H-6), C.1.61*m* (H-7), 3.46*qbr* (H-8), 4.11*dd* and 3.98*dd* (H-9), 4.15*q* (H-3'), 1.41*d* (H-4'), 2.04*m* (H-5'), 1.12*m* (H-6'), 0.93*t* (H-7') and 1.02*d* (H-8'). [Calcd. for $C_{16}H_{29}O_4N$: MW 299.2095. Found: MW. (MS) 2.99.2058 (1%).] Other significant peaks in the HRMS were at *m/z* (composition, %), 284 ($C_{15}H_{26}O_4N$, 1) 281 ($C_{16}H_{27}O_3N$, 1), 255 ($C_{14}H_{25}O_3N$, 3), 254 ($C_{14}H_{24}O_3N$, 10), 252 ($C_{14}H_{22}O_3N$, 8), 243 ($C_{12}H_{21}O_4N$, 7), 226 ($C_{12}H_{20}O_3N$, 8), 142 ($C_8H_{16}ON$, 48), 124 ($C_8H_{14}N$, 100), ($C_5H_{10}N$, 51), 83 (C_5H_9N, 56), 82 (C_5H_8N, 40).

Heliocurassavicine (**9**), gum $[\alpha]_D^{25} + 0.3°$ (*c*, 0.0035, $CHCl_3$), R_F^1 0.21, R_F^2 0.87, IR (neat) 3310, 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.28*m* (H-1), 2.12*m* and 1.98*m* (H-2), 3.50*dt* and 2.65*dt* (H-3), 3.21*dt* and 2.79*dt* (H-5), 1.95*m* (H-6), 2.09*m* and 1.64*m* (H-7), 3.62*qbr* (H-8), 4.59*dd* and 4.06*dd* (H-9), 4.05*q* (H-3'), 1.19*d* (H-4'), 2.07*m* (H-5'), 0.94*d* and 0.93*d* (H-6' and H-7'); NMR (C_6D_6) δ 1.6*m* (H-1), C.1.50*m* (H-2), 3.17*dt* and 2.00*dt* (H-3), 2.87*dt* and 2.19*dt* (H-5), 1.37*m* (H-6), 1.54*m* (H-7), 3.38*q* (H-8), 4.25*dd* and 3.77*dd* (H-9), 4.27*q* (H-3'), 1.33*d* (H-4'), 2.24*m* (H-5'), 1.17*d* and 1.01*d* (H-7'). [Calcd. for $C_{15}H_{27}O_4N$: MW 285.1939. Found: MW (MS) 285.1895 (1%).] Other significant peaks in the HRMS were at *m/z* (composition, %), 267 ($C_{15}H_{25}O_3N$, 3), 252 ($C_{14}H_{22}O_3N$, 3), 240 ($C_{13}H_{22}O_3N$, 3), 142 ($C_8H_{16}ON$, 49), 125 ($C_8H_{15}N$, 22), 124 ($C_8H_{14}N$, 100), 84 ($C_5H_{10}N$, 63), 83 (C_5H_9N, 58), 82 (C_5H_8N, 41).

Heliocurassavinine (**5**), gum, $[\alpha]_D^{25} + 0.3°$ (*c*, 0.0035, $CHCl_3$), R_F^1 0.21, R_F^2 0.88, IR (neat) 3330, 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.28*m* (H-1), 2.13*m* and 1.89*m* (H-2), 3.41*dt* and 2.62*dt* (H-3), 3.14*dt* and 2.77*dt* (H-5), 1.91*m* (H-6), 2.1*m* and 1.6*m* (H-7), 3.51*q* (H-8), 4.60*dd* and 4.05*dd* (H-9), 4.04*q* (H-3'), 1.19*d* (H-4'), 2.09*m* (H-5'), 0.95*d* and 0.93*d* (H-7'); NMR (C_6D_6) δ 1.56*m* (H-1), C.1.49*m* (H-2), 3.12*dt* and 1.98*dt* (H-3), 2.83*dt* and 2.20*dt* (H-5), 1.36*m* (H-6), 1.54*m* (H-7), 3.30*q* (H-8), 4.26*dd* and 3.72*dd* (H-9), 4.23*q* (H-3'), 1.31*d* (H-4'), 2.25*m* (H-5'), 1.16*d* and 1.00*d* (H-6' and H-7')1. [Calcd. for $C_{15}H_{27}O_4N$: MW 285.1939. Found: MW (MS) 285.1899 (1%).] Other significant peaks in the high resolution MS were at *m/z* (composition, %), 267 ($C_{15}H_{25}O_3N$, 4), 252 ($C_{14}H_{22}O_3N$, 4), 240 ($C_{13}H_{22}O_3N$, 3), 142 ($C_8H_{16}ON$, 55), 125 ($C_8H_{15}N$, 24), 124 ($C_8H_{14}N$, 100), 84 ($C_5H_{10}N$, 22), 83 (C_5H_9N, 48), 82 (C_5H_9N, 48), 82 (C_5H_8N, 36).

Heliocoromandaline (**8**), gum, R_F^1 0.21, R_F^2 0.84, IR (neat) 3415, 1710 cm^{-1}; NMR ($CDCl_3$) δ 2.21*m* (H-1), 2.10*m* and 1.97*m* (H-2), 3.48*dt* and 2.66*dt* (H-3), 3.26*dt* and 2.74*dt* (H-5), 1.96), 1.17*m* and 1.67*m* (H-7), 3.74*qbr* (H-8), 4.31*dd* and 4.24*dd* (H-9), 3.99*q* (H-3'), 1.27*d* (H-4'), 2.16*m* (H-5'), 0.94*d* and 0.88*d* (H-6' and H-7'); NMR (C_6D_6) δ 1.66*m* (H-1), 1.36*m* (H-2), 3.04*dt* and 1.89*dt* (H-3), 2.84*dt* and 2.04*dt* (H-5), 1.29*m* (H-6), 1.43*m* (H-7), 3.47*qbr* (H-8), 4.09*dd* and 3.93*dd* (H-9), 4.08*q* (H-3'), 1.37*d* (H-4'), 2.27*m* (H-5'), 1.05*d* and 0.99*d* (H-6' and H-7'). [Calcd for $C_{15}H_{27}O_4N$: MW 285,1937, Found: MW (MS) 285.1916 (1%).] Other significant peaks in the MS were at *m/z* (composition, %), 267 ($C_{15}H_{25}O_3N$, 4), 252 ($C_{14}H_{22}O_3N$, 4), 240 ($C_{13}H_{22}O_3N$, 6), 142 ($C_8H_{16}ON$, 41), 125 ($C_8H_{16}ON$, 17), 124 ($C_8H_{14}N$, 100), 83 (C_5H_9N, 20), 82 (C_5H_8N, 15).

Alkaloid mixture Z, a 3:2:1 mixture of coromandalinine (**12**) heliovinine (**13**) and curassavinine (**11**): gum, R_F^1 0.32, R_F^2 0.90, IR ($CHCl_3$) 3320, 1710, 1640 cm^{-1}; NMR ($CDCl_3$) δ 5.70*br* (H-2), 3.94*brdd* and 3.38*brdd* ($J_{3\alpha,3\beta}$ = 14.0 Hz, $J_{2,3}$ = 3.5 Hz, H-3), 3.17*brm* and 2.52*brm* ($J_{5\alpha,5\beta}$ = 10.5 Hz, $J_{5\alpha,6}$ = 6.5 Hz, H-5), 1.8*m* ($J_{6,7}$ = 7 Hz, H-6), 2.01 *brm* and 1.56*brm* ($J_{7u,7d}$ = 12 Hz, $J_{7,8}$ = 6.5 Hz, H-7), 4.22*brm* ((H-8), 4.78*br* (H-9), 4.07, 4.0 and 4.02 (*q*, *J* = 6.5 Hz, H-3': **11**, **12**, **13**), 1.21*d* (*J* = 6.5 Hz, H-4': **11**), 1.25*d* (*J* = 6.5 Hz, H-4': **12**, **13**), 2.04, 2.17 and 2.14*m* (H-5': **11**, **12**, **13**), 1.14*m* (H-6': **11**), 0.89 and 0.93*d* (*J* = 7 Hz, H-6': **12**, **13**), 0.94*d* (*J* = 7 Hz, H-7': **12**, **13**), 0.94*d* (*J* = 7 Hz, H-7': **12**, **13**), 0.90*t* (*J* = 7 Hz, H-7': **11**), 0.96*d* (*J* = 7 Hz, H-8': **11**); NMR (C_6D_6) δ 5.31*br* (H-2), 3.83 and 3.08 (*brdd*, H-3), 3.05 and 3.01 (*m*, H-5), 1.49*m* (H-6), 2.21 and 1.72*m* (H-7), 4.19*brm* (H-8), 4.48, 4.55 and 4.53*br* (H-9: **11**, **12**, **13**), 4.13, 3.98 and 4.01*q* (*J* = 6.5 Hz, H-3': **11**, **12**, **13**), 1.16, 1.26 and 1.29*d*, *J* = 6.5 Hz, H-4': **11**, **12**, **13**), 2.03*m* (H-5': **11**), 2.18*m* (H-5': **12**, **13**), 1.38*m* (*H*-6': **11**), 0.93 and 0.91*d* (*J* = 7 Hz, H-6': **12**, **13**), 0.95 and 0.94*d* (*J* = 7 Hz, H-7': **12**, **13**), 0.86*t* (*J* = 7 Hz, H-7': **11**), 1.03*d* (*J* = 7 Hz, H-8': **11**) [Calcd for $C_{16}H_{27}O_4N$: MW 297.1940. Found: MW (MS) 297.1996 (**11**); Calcd. for $C_{15}H_{25}O_4N$: MW 283.1783. Found: MW (MS) 383.1749 (**12**, **13**); rel. proportion of *m/z* 297 to *m/z* 283 = 1:5.]

Curassanecine (**15**) (9 mg) was obtained as a pale brown gum from 1 kg of the dried plant material in the manner described previously [4], $[\alpha]_{Hg}^{25} - 6.3°$ (*c*, 0.0046, EtOH), R_F^3 0.17, NMR (C_5D_5N) 2.30 and 2.22*dt* (H-2), 3.35 and 3.00*dt* ($J_{2,3\alpha}$ = 2.5 Hz, $J_{2,3\beta}$ = 6 Hz, $J_{3\alpha,\beta}$ = 9 Hz, H-3), 3.11 and 2.78*dt* ($J_{\alpha,5\beta}$ = 9.5 Hz, $J_{5\alpha,6}$ = 5 Hz, $J_{5\beta,6}$ = 7 Hz, H-5), 1.79*m* (H-6), 2.39 and 2.03*m* (H-7), 3.86*t* ($J_{7u,8}$ = 6 Hz, H-8), 3.98 (H-9). [Calcd. for $C_8H_{15}O_2N$: MW 157.1102. Found: MW (MS) 157.1076 (15%).] Other significant peaks in the HRMS were at *m/z* (composition, %), 126 ($C_7H_{12}ON$, 14), 98 (C_5H_8ON, 10), 83 (C_5H_9N, 100), 82 (C_5H_8N, 23).

Hydrolysis of ester alkaloids. The ester alkaloids in 1 ml H_2O were refluxed with 1 ml of 10% NaOH at 95° for 1 hr. The reaction mixture was cooled and extracted with $CHCl_3$ to give the necine base. The aq. mother liquor was acidified with 2 N HCl and extracted with Et_2O to give the necic acid.

7 (23 mg) on hydrolysis gave: (a) (−) **10** [10] (6 mg), pale brown gum, $[\alpha]_{Hg}^{25} - 66.5°$ (*c*, 0.001, EtOH), R_F^3 0.46, R_T^A 7.33 min [(−) **4**, R_T^A 7.0 min], NMR ($CDCl_3$) δ 2.05*m* (H-1), 1.99 and 1.70*m* (H-2), 3.22 and 2.58*dt* (H-3), 3.04 and 2.64*dt* (H-5), 1.84*m* (H-6), 2.01 and 1.58*m* (H-7), 3.33*qbr* (H-8) and 3.63*dd* (H-9). [Calcd. for $C_8H_{15}ON$: MW 141.1153. Found: MW (MS) 141.1136 (18%).] Other significant peaks in the HRMS were at *m/z* (comp., %) 124 ($C_8H_{14}N$, 17), 110 ($C_7H_{12}N$, 12), 83 (C_5H_9N, 100), 82 (C_5H_8N, 47); (b) (−) curassavic acid (R_1H) (8 mg), colourless crystals from Et_2O–petrol, R_F^4 0.55, R_T^B (Me ester) 13.3 min, mp 101–103°, $[\alpha]_{Hg}^{25}$ −1.2° (*c*, 0.002, EtOH); NMR ($CDCl_3$) δ 4.06*m* (H-3'), 1.36*brd* (H-4'), 1.87*m* (H-5'), 1.39*m* (H-6'), 0.92*brt* (H-7') and 0.93*brd* (H-8'); NMR (C_5D_5N) 4.59*q* (*J* = 6.5 Hz, H-3'), 1.70*d* (*J* = 6.5 Hz, H-4'), 2.37*brm* (H-5'), 1.94*m* (H-6'), 0.97*t* (*J* = 7 Hz, H-7') and 1.21*d* (*J* = 7 Hz, H-8'). IR, NMR, MS and GC of the acid were identical with those of authentic acid [4].

9 (25 mg) on hydrolysis gave (a) (−) **10** (6 mg), pale brown gum, $[\alpha]_{Hg}^{25} - 68.2°$ (*c*, 0.001, EtOH), R_F^3 0.46, R_T^A 7.33 min. The NMR and MS of the base were identical with those of

(−) isoretronecanol (*vide supra*); (b) (−) trachelanthic acid (R_3H) (8 mg), colourless crystals from Et_2O–petrol, R_F^4 0.50, R_T^B (Me ester) 10.14 min, mp 90–91°, undepressed on admixture with authentic (−) trachelanthic acid [4], $[\alpha]_{Hg}^{25} - 2.0°$ (*c*, 0.002, EtOH), NMR ($CDCl_3$) 5.22*q* (H-3′), 1.26*d* (H-4′), 2.01*sp* (H-5′), 0.99 and 0.97*d* (H-6′ and H-7′); NMR (C_5D_5N) δ 4.57*q* (J = 6.5 Hz, Ha3′), 1.57*d* (J = 6.5 Hz, H-4′), 2.56*sp* (J = 7 Hz, Ha5′), 1.30 and 1.26*d* (J = 7 Hz, H-6′ and H-7′). IR, NMR, MS and GC of the acid were identical with those of authentic (−) acid [4].

5 (14 mg) on hydrolysis gave: (a) **6** [10] (4 mg), pale brown gum, $[\alpha]_{Hg}^{25} + 11.2°$ (*c*, 0.001, EtOH), R_F^3 0.46, R_T^A 7.0 min [(−) **4**, R_T^A 7.0 min], NMR ($CDCl_3$) δ 1.99*m*, (H-1), 1.97 and 1.63*m* (H-2), 3.14 and 2.52*dt* (H-3), 2.96 and 2.60*dt* (H-t), 1.79*m* (H-6), 1.96 and 1.53*m* (H-7), 3.21*q* (H-8) and 3.61*d* (H-9). [Calcd. for $C_8H_{15}ON$: MW 141.1153. Found: MW (MS) 141.1151 (16%).] Other significant peaks in the HRMS were at *m/z* (comp., %), 124 ($C_8H_{14}N$, 13), 110 ($C_7H_{12}N$, 9), 83 (C_5H_9N, 100), 82 (C_5H_8N, 55); (b) (−) trachelanthic acid (R_3H) (5 mg), colourless crystals from Et_2O–petrol), R_F^4 0.50, R_T^B (Me ester) 10.4 min, mp 90–91°, undepressed on admixture with authentic (−) acid, $[\alpha]_{Hg}^{25} - 1.8°$ (*c*, 0.001, EtOH). The IR, NMR, MS and GC of the acid were identical with those of authentic (−) acid (*vide supra*).

8 (7 mg) on hydrolysis gave: (a) (−) **10** (2 mg), pale brown gum, $[\alpha]_{Hg}^{25} - 62°$ (*c*, 0.0004, EtOH), R_F^3 0.46, R_T^A 7.33 min. The NMR and MS of the base were identical with those of (−) isoretronecanol (*vide supra*); (b) (+) viridifloric acid (R_2H) (2 mg), R_F^4 0.50, R_T^B (Me ester) 10.0 min, mp 117–119°, $[\alpha]_{Hg}^{25} + 2°$ (*c* 0.0004, EtOH), NMR ($CDCl_3$) δ 4.07*br* (H-3′), 1.33*brd* (H-4′), 2.17*m* (H-5′), 0.96 and 0.95*brd* (H-6′ and H-7′); NMR (C_2D_5N) δ 4.58*q* (J = 6.5 Hz, H-3′), 1.69*d* (J = 6.5 Hz, H-4′), 2.66*sp* (J = 7 Hz, H-5′), 1.34 and 1.23*d* (J = 7 Hz, H-6′ and H-7′). The NMR, MS and GC of the acid were identical with those of authentic (+) acid [4].

Alkaloid mixture Z on hydrolysis gave: (a) a single base, (−) **14** (4 mg), pale brown gum, $[\alpha]_{Hg}^{25} - 9.5°$ (*c*, 0.0008, EtOH), NMR ($CDCl_3$) 5.50*br* (H-2), 3.88 and 3.32*dd* (H-3), 3.09 and 2.53*dt* (H-5), 1.76*q* (H-6), 1.97 and 1.51*sx* (H-7), 4.19 (H-8), 4.24 and 4.15*dd* (J = 14, 2 Hz, H-9). [Calcd. for $C_8H_{13}ON$: MW 139.0997. Found: MW (MS) 139.1002 (37%).] Other significant peaks in the HRMS were at *m/z* (comp., %), 122 ($C_8H_{12}N$, 37), 121 ($C_8H_{11}N$, 29), 120 ($C_8H_{10}N$, 62), 108 ($C_7H_{10}N$, 30), 106 (C_7H_8N, 31), 80 (C_5H_6N, 100); (b) a mixture of acids (4 mg) mainly curassavic, viridifloric and trachelanthic acids, NMR (C_5D_5N) δ 4.59*q*, 1.70*d*, 2.38*m*, 1.94*m*, 0.97*t* and 1.21*d* (H-3′ to H-8′, curassavic acid), 4.58*q*, 1.69*d*, 2.66*m*, 1.34*d* and 1.22*d* (H-3′ to H-7′, viridifloric acid), 4.57*q*, 1.57*d*, 2.56*m*, 1.30*d* and 1.26d (H-3′ to H-7′, trachelanthic acid); GC/MS (Me esters) (1) R_T^B 10.0 min (Me viridiflorate, 47%) *m/z* (%) 132 ($M^+ - 44$, 65), 117 (100), 99 (14), 85 (27), 73 (20), 71 (38), 43 (36); (2) R_T^B 10.4 min (Me trachelanthate, 33%) *m/z* (%) 132 ($M^+ - 44$, 60), 117 (100), 99 (15), 85 (26), 73 (23), 71 (44), 43 (46); (3) R_T^B 12.1 min (ester P, 2%), *m/z* (%) 146 ($M^+ - 44$, 58), 131 (70), 114 (32), 113 (23), 99 (32), 87 (82), 86 (29), 85 (20), 75 (55), 71 (100), 59 (23), 55 (29) and 43 (38); (4) R_T^B 13.3 min (Me curassavate, 17%) *m/z* (%) 146 ($M^+ - 44$, 31), 131 (12), 117 (100), 90 (19), 87 (16), 85 (67), 69 (12), 57 (69), 56 (31); (5) R_T^B 14.9 min (ester Q, 1%), *m/z* (%) 160 ($M^+ - 55$, 55), 145 (36), 131 (91), 128 (36), 127 (90), 113 (45), 101 (100), 100 (36), 99 (100), 95 (64), 87 (36), 85 (55), 83 (45), 78 (36), 75 (55), 71 (36), 69 (45), 59 (64), 43 (36), 42 (36).

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