$CHCl_3$ and then $CHCl_3$ containing increasing amounts of MeOH to give, in order of elution, a mixture, skimmianine (major alkaloid), and edulinine, montrifoline, ribalinine and isoplatydesmine (all in trace amounts only). The mixture was subjected to further CC over Sephadex LH-20 eluting with $CHCl_3$–MeOH (1:1) to give **3** (30 mg) followed by **1** (16 mg).

Identification of alkaloids. Skimmianine, montrifoline, ribalinine, isoplatydesmine and edulinine were all characterised by direct comparison (co-TLC, HPLC, UV) with authentic materials obtained from *Teclea simplicifolia* [4].

Isohaplopine (**1**). Plates from Me_2CO–petrol, mp 121–123°. Found: 245.0690; $C_{13}H_{11}NO_4$ requires 245.0688. UV λ_{max} nm: 247, 325 (+NaOH) 263, 344; IR ν_{max} cm^{-1}: 3300, 1640, 1600, 1520, 1300. ^1H NMR (90 MHz, $CDCl_3$) δ: 7.74 (1H, *d*, *J* = 9 Hz, H-5), 7.56 (1H, *d*, *J* = 2 Hz, H-2), 7.40 (1H, *br s*, 8-OH), 7.22 (1H, *d*, *J* = 9 Hz, H-6), 7.06 (1H, *d*, *J* = 2 Hz, H-3), 4.43 (3H, *s*, 4-OMe), 4.04 (3H, *s*, 7-OMe). ^{13}C NMR (22.5 MHz, $CDCl_3$) ppm: 163.3 (C-8b), 157.7 (C-4), 145.0, 144.5 (C-8a, C-7), 142.8 (C-2), 138.4 (C-8), 114.0 (C-3a), 113.1, 112.8 (C-5, C-6), 105.3 (C-3), 102.4 (C-4a), 59.2 (4-OMe), 57.2 (7-OMe). EIMS *m/z* (rel. int.): 245 $[M]^+$ (100), 244 (22), 230 (38), 227 (83), 216 (19), 202 (33). NOE (360 MHz, $CDCl_3$): irradiation of δ 4.43 signal—enhancement of H-3 (10.6%) and H-5 (1.6%); irradiation of δ 4.04—enhancement of H-6 (11.5%).

Isohaplopine 3′,3′-dimethylallylether (**3**). Plates from MeOH–hexane, mp 118–119°. Found: 313.1301; $C_{18}H_{19}NO_4$ requires 313.1314. UV λ_{max} nm: 247, 323. IR ν_{max} cm^{-1}: 1630, 1600, 1500, 1300, 1250. ^1H NMR (90 MHz, $CDCl_3$) δ: 5.80 (1H, *t*, *J* = 7 Hz, H-2′), 4.80 (2H, *d*, *J* = 7 Hz, O–CH_2-1′), 4.40 (3H, *s*, 4-OMe), 4.00 (3H, *s*, 7-OMe), 1.73, 1.70 (2 × 3H, 2 × *s*, 3′-Me_2). EIMS *m/z* (rel. int.): 313 $[M]^+$ (7), 245 (100), 244 (14), 230 (30), 227 (82), 216 (24), 202 (18), 69 (10).

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PYRROLIZIDINE ALKALOIDS FROM *HELIOTROPIUM CURASSAVICUM*

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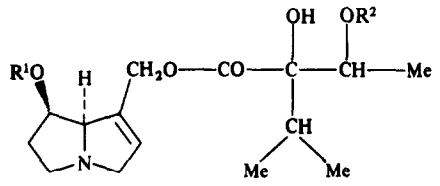
Key Word Index—*Heliotropium curassavicum* var. *argentinum*; *H. curassavicum* var. *curassavicum*; Boraginaceae; pyrrolizidine alkaloids; 9-(3′-isovaleryl)viridifloryl retronecine; 9-(3′-acetyl) viridifloryl retronecine.

Abstract—*Heliotropium curassavicum* var. *argentinum* and var. *curassavicum* have been investigated chemically and a new pyrrolizidine alkaloid has been isolated from both. The latter variety also yielded a related acetylated, 9-(3′-isovaleryl)viridifloryl retronecine alkaloid. The structures have been established by spectroscopic means. Trachelanthamidine was the dominant base found in previous studies of *H. curassavicum* whereas retronecine is the necine present in the alkaloids now reported.

INTRODUCTION

In the course of the systematic investigation of pyrrolizidine alkaloids carried out in our laboratory, we have reported the isolation of several from *Senecio* species [1–4]. The present paper deals with the results obtained from the chemical examination of pyrrolizidine alkaloids in *Heliotropium curassavicum* that grows in the Cuyo Region of Argentina. This species is a glaucous fleshy herb that grows in saline areas. The powdered roots have been used by the Indians of the American south-west to apply to sores and wounds [5]. It is sold in Argentina as a medicine recommended for the treatment of rheumatism, gout, arteriosclerosis and to improve blood circulation.

Although several collections of *H. curassavicum* have been made for chemical investigation in different parts of the world there are considerable differences in the results



1 R^1 = H R^2 = —CO—CH_2—CH(Me)$_2$
2 R^1 = Ac R^2 = —CO—CH_2—CH(Me)$_2$
3 R^1 = H R^2 = —CO—Me

reported. For instance, the main alkaloids isolated from plants obtained from India, Australia, Pakistan, Mexico and Texas have been identified as esters of the nonhepatotoxic saturated necine, trachelanthamidine [5–7]. Only the Indian collection showed trace amounts of esters of the hepatotoxic aminoalcohol, heliotridine [8, 9].

We now report on the isolation and characterization of a new pyrolizidine alkaloid (**1**) isolated from roots of *H. curassavicum* var. *curassavicum* and *H. curassavicum* var. *argentinum*, and of an alkaloid (**3**) related to acetyl indicine isolated from the former. Both alkaloids are C-9 esters of retronecine and exhibit 1,2-unsaturation and esterification at C-9 in the necine moiety. These are important structural requirements for physiological activities [10, 11].

RESULTS AND DISCUSSION

The molecular formula of **1** from the high resolution mass spectrum was deduced as $C_{20}H_{33}O_6N$. The presence of characteristic ions at *m/z* 120, 94 and 93 suggests that it is an ester of an unsaturated pyrrolizidine 7,9-diol [12]. However, the base peak at *m/z* 138, ascribed to the typical fragmentation at the allylic site by the monoester acyclic derivatives lycopsamine, intermedine, indicine and acetyl indicine [8, 9, 13] indicated that (**1**) was probably a C-9 monoester derivative.

The presence of the OH group at C-7 was confirmed for the broad singlet at 4.28 ppm in the ^{1}H NMR spectrum and for the D_2O exchangeable signal at 3.00 ppm. Furthermore, the ^{1}H NMR spectrum of the acetyl derivative of **1** showed that the signal ascribed to H-7, shifted to 5.4 ppm. The signal for an olefinic proton typical of a 1,2-dihydropyrrolizidine was also observed as a broad signlet at 5.86 ppm. Finally, the ^{13}C NMR signals at δ 132.4 and 129.7 ppm ascribed to the olefinic carbons C-1 and C-2, respectively, and the signals at 35.9, 78.2 and 70.2 ascribed to C-6, C-7 and C-8, with the typical shift upon acetylation at C-7 OH (see Table 1), allowed us to identify the necine moiety as retronecine in **1**. Although retronecine is the dominant aminoalcohol present in the *Heliotropium* genus, is has not been isolated before in the examined *curassavicum* species [5–7].

The ^{1}H NMR spectrum of the acidic portion of the alkaloid was consistent with the presence of an ester at C-3′ of the diasteroisomeric viridifloric or trachelanthic acids. In fact, the one proton quartet at δ 5.20, coupled only to a three proton doublet at 1.23 pm, as shown by double resonance experiments, showed that H-3′ was esterified, since the quartet for the corresponding methine of coromandaline, heliovinine and curassavinine which possess a free C-3′ hydroxy occurs at 4.02 ppm [5]. The nature of the esterifying group at C-3′ was deduced as isavaleroyl from the molecular formula, the prominent peak at *m/z* 85 (28%) which is assigned to the acyl group C_4H_9CO, and the signal of the two remaining methyl groups in the ^{1}H NMR spectrum (0.96, *m*, 12 H). The ^{13}C NMR data were consistent with the structure proposed.

Finally, the ^{13}C NMR signal (Table 2) assigned to C-3′ (71.5 ppm) and compared with those given in the litera-

Table 1. ^{1}H NMR data of alkaloids **1**–**3** from *Heliotropium*

H	1	2	3
2	5.86, 1H, *br s*	5.73, 1H, *m*	5.83, 1H, *br s*
3α	3.45, 1H, *m*	3.53, 1H, *m*	3.77, 1H, *m*
3β	4.01, 1H, *m*	3.90, 1H, *m*	4.10, 1H, *m*
5α	3.25, 1H, *m*	3.33, 1H, *m*	3.20, 1H, *m*
5β	2.76, 1H, *dd*, *J* = 18, 9	2.63, 1H, *dd*, *J* = 18, 9	2.57, 1H, *dd*, *J* = 18, 9
6	2.06, 2H, *m*	2.06, 2H, *m*	—
7	4.28, 1H, *m*	5.30, 1H, *m*	—
8	4.15, 1H, *br m*	4.33, 1H, *br m*	4.23, 1H, *br s*
9	4.80, 2H, *br s*	4.73, 2H, *d*, *J* = 6	4.78, 2H, *br s*
3′	5.20, 1H, *q*, *J* = 6	5.20, 1H, *q*, *J* = 6	5.15, 1H, *q*, *J* = 6
4′	1.18, 3H, *d*, *J* = 6	1.22, 3H, *d*, *J* = 6	1.21, 3H, *d*, *J* = 6
6′	0.93, 12H, *m*	0.92 *d*, *J* = 6	0.93, 3H, *d*, *J* = 6
7′		0.86 *d*, *J* = 6	0.86, 3H, *d*, *J* = 6
4″		12H	
5″		0.88 *d*, *J* = 6	
MeCO–		1.93, 3H, *s*	2.00, 3H, *s*

δ values in ppm; *J* in Hz.

Table 2. ^{13}C NMR data of alkaloids **1** and **2** from *Heliotropium*

	1	2
1	132.4	132.5
2	129.7	125.9
8	78.2	75.2
7	70.9	72.8
3–9	63.0, 62.5	61.6, 61.2
6	35.9	33.9
5	53.7	53.2
1′	174.2	173.8
2′	81.6	81.6
3′	71.5	71.7
4′	14.5	13.8
5′	32.3	32.7
6′–7′	17.5, 16.3	17.1, 16.6
1″	173.5	171.7
2″	43.3	43.4
3″	25.7	25.5
4″–5″	22.2	22.2
1‴	– –	169.5
2‴	– –	20.8

δ values in ppm.

ture [14] (70.9 ppm) and [15] (71.05 ppm), indicated that the esterifying group of the necine moiety in **1** would be a C-3′ ester of viridifloric acid. Alkaline hydrolysis of **1** carried out with the aim of confirming this hypothesis was difficult, and only the identification of the necine base was achieved.

The molecular formula of **3** from the mass spectrum was $C_{17}H_{27}O_6N$. Its spectral data (see Experimental) were nearly identical with those (**1**) except for the signal attributed to the esterifying group at C-3′ in the ^1H NMR spectrum. The signals attributed to the isovaleroyl group were replaced by those corresponding to an acetyl group. All this spectroscopic evidence was consistent with **3** being a diastereoisomer of acetylindicine [6].

EXPERIMENTAL

^{13}C NMR were recorded at 20 MHz in $CDCl_3$, ^1H NMR at 60 MHz in the same solvent. MS were measured at 70 eV and 0.7 mA.

Plant material. H. curassavicum L. var. *curassavicum* was collected by J. G. Davicino in Balde, Province of San Luis and identified by L. A. del Vitto (voucher: L. A. del Vitto N° 1100; Herbario de la Universidad Nacional de San Luis).

H. curassavicum L. var. *argentinum* Johnston was collected and identified by L. A. del Vitto in Maipú, Province of Mendoza (voucher: L. A. del Vitto Nos. 912; MERL).

Isolation and identification of alkaloids. Roots of *H. curassavicum* var. *argentinum* (1000 g) were cut into small pieces and extracted with hot MeOH (3 × 4 l). The ext was concd *in vacuo* and processed in the usual way as for alkaloid extraction [1], giving 2.51 g of an oily brown residue which contained the crude alkaloids. This extract was chromatographed on silica gel 60 H and eluted with $CHCl_3$–MeOH–NH_3 (85:14:1) and fractions 10–15 (0.065 g) were combined as well as fractions (25–26) (0.035 g). From the first group of fractions, **1** was isolated.

9-(3′-*Isovaleryl*)*viridifloryl retronecine* (**1**). IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3550, 2910, 1736, 1616. Calc. for $C_{20}H_{33}O_6N$ 383.2298 Found (MS) 383.2282. Other significant peaks in the MS were *m/z* (rel. int.) 383 $[M]^+$, (2.0) 255 (2.9), 240 (3.2), 223 (5.3), 201 (3.7), 138 (100), 120 (10.2), 93 (66.3), 85 (28), 80 (10.2), 57 (18.7), 43 (10.3). For ^1H and ^{13}C NMR data see Tables 1 and 2.

7-*Acetyl*-9-(3′-*isovaleryl*)*viridifloryl retronecine* (**2**). Compound **1** (50 mg) was acetylated (Ac_2O, pyridine) in the usual way so as to give 45 mg of **2**. Calc. for $C_{22}H_{35}O_7N$ 425.2403 Found (MS) 425.2409. Other significant peaks in the MS were *m/z* (rel. int.) 425 $[M]^+$, (1.7), 297 (6.7), 199 (6.7), 180 (100), 136 (18.5), 120 (44.5), 101 (13.4), 93 (45.3), 85 (37.8), 80 (8.4), 57 (25.2), 43 (38.6). For ^1H and ^{13}C NMR data see Tables 1 and 2. From the second group of fractions, **3** was isolated.

9-(3′-*Acetyl*)*viridifloryl retronecine* (**3**). Calc. for $C_{17}H_{27}O_6N$: 341.1830 Found (MS): 341.1827. Other significant peak in the MS were *m/z* (rel. int.) 341 $[M]^+$ (4.7), 255 (2.8), 182 (4.7), 157 (3.7), 138 (100), 120 (10.3), 93 (92.4), 85 (4.1), 83 (19.8), 80 (16.0), 43 (38.3). For ^1H NMR data see Table 1.

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