Full Papers

Pyrrolidinoöxazolidine Alkaloids from Two Species of Ladybird Beetles[1]

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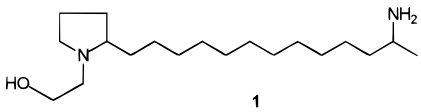
From the mixture of alkaloids obtained from adults of two species of ladybird beetles, *Epilachna varivestis* and *Epilachna borealis*, a novel bicyclic alkaloid, 5-(12′-aminotridecyl)pyrrolidinoöxazolidine [(5α,7a*β*)-hexahydro-α-methylpyrrolo[2,1-*b*]oxazole-5-dodecaneamine] (**2**) was characterized on the basis of spectrometric and synthetic investigations. This new alkaloid is related structurally to a monocyclic congener 1-(2-hydroxyethyl)-2-(12′-aminotridecyl)pyrrolidine (**1**), previously characterized from *E. varivestis*. Two additional alkaloids (lower homologs of **1** and **2**) from *E. borealis* were characterized as 5-(10′-aminoündecyl)pyrrolidinoöxazolidine [(5α,-7a*β*)-hexahydro-α-methylpyrrolo[2,1-*b*]oxazole-5-decaneamine] (**7**) and 1-(2-hydroxyethyl)-2-(10′-aminoündecyl)pyrrolidine (**8**), on the basis of their mass spectra.

A wide variety of alkaloids conferring protection against predators has been found in ladybird beetles (Coccinellidae).[2,3] In recent studies, for example, the hemolymph of the Mexican bean beetle, *Epilachna varivestis* Mulsant, was shown to contain a complex alkaloidal mixture.[4−7] We have recently reported the characterization of 1-(2-hydroxyethyl)-2-(12′-aminotridecyl)pyrrolidine (**1**) from adults of this beetle.[5] The EIMS of this compound (M^+ at *m*/*z* 312, and the base peak at *m*/*z* 114 due to the loss of the aminotridecyl side chain) was especially useful in its characterization. A related but incompletely characterized minor constituent of this mixture (M^+ at *m*/*z* 310, base peak at *m*/*z* 112) was also described.[5]



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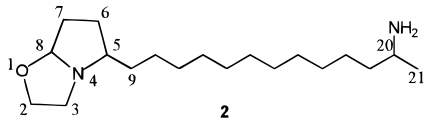
An independent investigation by Proksch *et al.*[7] also reported the presence of **1**, along with its *m*/*z* 310 congener, in eggs, larvae, pupae, and adults of *E. varivestis*. These investigators postulated the *m*/*z* 310 alkaloid to be a dehydro-**1**, with a double bond in the pyrrolidine ring. We now find this compound to be one of the major defensive constituents of the congeneric squash beetle, *Epilachna borealis* Fabricius. As a consequence of finding a better source of this alkaloid, it has been possible to characterize it as 5-(12′-aminotridecyl)pyrrolidinoöxazolidine (**2**).

Results and Discussion

Gas chromatograms obtained from the basic alkaloid extracts of *E. borealis* were similar to those of the previously examined *E. varivestis* alkaloids, and GC−MS analysis showed the previously uncharacterized component **2** to be present in both species. The addition of *m*-chloroperbenzoic acid to the *E. borealis* alkaloid mixture, and subsequent analysis of the reaction mixture by GC−MS, showed no intensity change in the gas chromatographic peak corresponding to this compound, making the presence of a double bond unlikely. The gas-phase IR spectrum of the unidentified alkaloid failed to indicate the presence of ═CH stretching absorptions, and the ^{1}H-NMR spectrum obtained from the total *E. borealis* alkaloid mixture showed no signals for olefinic hydrogens. Thus, neither the chemical nor the spectroscopic evidence supported the hypothesis that this alkaloid is unsaturated.



2

The mass spectrum of the new alkaloid (see to Experimental Section) showed many similarities to that of **1**.[5] Both spectra showed a significant peak at *m*/*z* 44, indicating the presence of a $-CH(NH_2)CH_3$ moiety, and both exhibited a loss of 15 mass units from the molecular ion due to the loss of a methyl group. In addition, both spectra showed a facile loss of 98 mass units from the parent ion to yield base peaks at *m*/*z* 114 and 112, respectively, indicating that an aminotridecyl side chain is common to both structures. The molecular ions of both **1** and the new compound had very weak molecular ions; however, HRMS established the composition of the base peak at *m*/*z* 112 as $C_6H_{10}NO$ (calcd mass 112.0762; found 112.0767). Because evidence for a carbon−carbon double bond was absent and because the gas-phase IR spectrum of the alkaloid showed neither carbonyl nor imine absorption, it was considered that an additional ring must be present.

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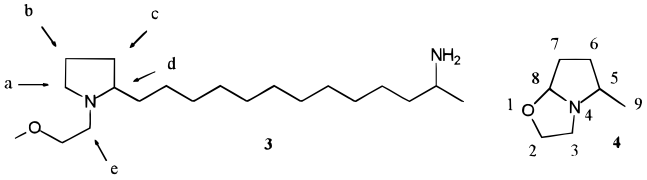
Table 1. ^{13}C- and ^{1}H-NMR Data of Natural **2**[a]

	^{13}C		^{1}H			
position[b]	δ (ppm)	DEPT	δ (ppm)	mult.	int.	J (Hz)
2	63.4	CH_2	3.81	br q	1H	9.5
			3.66	dt	1H	10.5, 5.5
3	51.3	CH_2	2.99−3.13	m	2H	*c*
5	64.4	CH	2.58	m	1H	*c*
6	30.9	CH_2	2.03	m	1H	*c*
			1.43	m	1H	*c*
7	29.9	CH_2	2.10	m	1H	*c*
			1.85	m	1H	*c*
8	98.7	CH	4.80	dd	1H	6.0, 2.0
9	36.4	CH_2	1.56	m	1H	*c*
			1.2	m	}	*c*
10−18	29.6	CH_2	1.25	m	21H	*c*
19	40.1	CH_2	1.2	m	}	*c*
20	46.7	CH	2.83	br q	1H	9.0
21	23.9	CH_3	1.02	d	3H	9.0

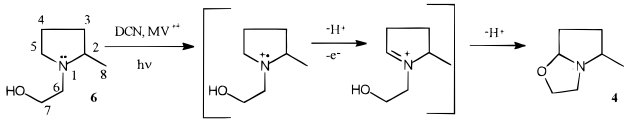
[a] ^{13}C (100 MHz) and ^{1}H (500 MHz) NMR data were obtained using $CDCl_3$ as the solvent. Chemical shifts are given in ppm relative to $CHCl_3$ peak at 77.0 and 7.24 ppm, respectively. [b] The ^{13}C- and ^{1}H-NMR peak assignments reported above are based on 1D and 2D methods (COSY, HMQC). [c] Due to the overlap and complexity of some peaks, *J* values could not be determined.

The similar mass and IR spectra of **1** and **2** suggested that the pyrrolidine ring is common to both molecules. Lack of IR evidence for a hydroxyl group in **2** indicated that the oxygen atom is involved in an ether linkage. The complete set of possible sites (**a**−**e**) at which the oxygen atom of **1** could be bonded to give an ether structure compatible with the above evidence is indicated by the arrows shown in partial structure **3**. Because the ^{1}H-NMR spectra of the alkaloid mixture suggested that the oxygen is connected to site **a** on the pyrrolidine ring to produce a pyrrolidinoöxazolidine ring system, NMR spectra of purified **2** and of a simple synthetic model system (**4**) were obtained for a more detailed study.

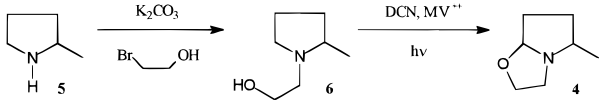


For the NMR studies of **2**, a sample (1.5 mg) of this alkaloid was isolated from teneral *E. borealis* adults. The ^{13}C-NMR data (Table 1) showed four downfield signals at δ 64.4, 63.4, 51.3, and 46.7, attributable to four mono−hetero-atom-attached carbons. The HMQC spectrum revealed that the carbon signal at δ 46.7 was coupled to a proton signal appearing at δ 2.83. Extensive decoupling experiments and a DEPT spectrum showed that this carbon atom is adjacent to a CH_3 group (δ 1.02, d). These data confirmed the presence of the $-CH(NH_2)CH_3$ fragment suggested by the mass spectrum. The HMQC spectrum also revealed that the carbon atoms whose signals appear at δ 63.4 and 51.3 are connected to proton pairs that appear at δ 3.81/3.66 and 3.07, respectively. The DEPT procedure showed that these signals represent two methylene groups, and the COSY spectrum established that the two CH_2 groups were coupled to each other, but isolated from all other protons. HMQC and DEPT spectra also indicated that the carbon atom corresponding to the signal at δ 64.4 bore a single proton (δ 2.58). Furthermore, the COSY spectrum showed that this single proton was

Scheme 1. Mechanism of Amine Oxidation



Scheme 2. Preparation of 5-Methylpyrrolidinoöxazolidine (**4**)



coupled to two pairs of protons that appeared at δ 1.20/1.56 and 1.43/2.03. The latter signals were correlated to the carbon resonance at δ 30.9 by the HMQC spectrum. The δ 1.43/2.03 protons showed a $^{1}H-^{1}H$ COSY relationship to those at δ 1.85/2.10. HMQC data showed that this new pair of protons is linked to the carbon atom appearing at δ 29.9. Finally, this CH_2 group was shown to be coupled to the δ 4.80 proton attached to the carbon atom appearing at δ 98.7. The chemical shift value of this downfield carbon resonance agreed well with that observed for the corresponding signal of similar pyrrolidinoöxazolidines in the literature.[8−10] All this evidence pointed unambiguously to structure **2** and encouraged us to prepare model compound **4** for NMR comparison.

Several methods have been described for the formation of bicyclic α-aminoethers from cyclic amines containing a free hydroxyl group via iminium ion intermediates. Iminium ions formed from chlorine dioxide oxidation of amines generally gives products with poor regioselectivity,[11] while mercuric acetate generates iminium ions specifically, but in the direction of the more substituted carbon atom.[12] The regiochemistry of another reagent, potassium hexacyanoferrate, has not been determined.[13] Recent work by Pandey *et al.*[14] however, has demonstrated that amines can be photooxidized to form iminium cations with the desired regiospecificity. The reaction is conducted by irradiating an MeCN solution of the amine with 1,4-dicyanonaphthalene (DCN)[15] and methyl viologen[16] in the presence of atmospheric water and oxygen.[17] In the proposed mechanism, the oxidation is initiated by transfer of an electron from the starting amine to photoexcited DCN. The resultant radical cation then loses a proton and an electron from the less substituted adjacent carbon atom, to form an iminium cation (Scheme 1). Finally, intramolecular addition of the hydroxyl group to the iminium group results in the formation of the desired α-aminoether.[14] We undertook the preparation of 5-methylpyrrolidinoöxazolidine (hexahydro-5-methyl-pyrrolo-[2,1-*b*]oxazole)(**4**) from 1-(2-hydroxyethyl)-2-methylpyrrolidine (**6**) based on this photooxidation procedure.

The desired model compound (**4**) was readily obtained in two steps from 2-methylpyrrolidine (**5**), which reacted with 2-bromoethanol and K_2CO_3 to give 1-(2-hydroxyethyl)-2-methylpyrrolidine (**6**). This product was then photo-oxidized to produce 5-methylpyrrolidinoöxazolidine (**4**) (Scheme 2).[14]

The HREIMS spectrum of **4** established its molecular formula to be $C_7H_{13}NO$ (calcd mass for M^+ $C_7H_{13}NO$: *m/z* 127.0997; found: 127.0994). Its mass spectrum showed a strong molecular ion at *m/z* 127, in addition to signals at *m/z* 126 $[M - 1]^+$ and 112 $[M - 15]^+$

Table 2. ^{13}C- and ^{1}H-NMR Data of **4**[a]

	^{13}C		^{1}H			
position[b]	δ (ppm)	DEPT	δ (ppm)	mult.	int.	J (Hz)
2	63.3	CH_2	3.79	br q	1H	8.0
			3.64	dt	1H	8.0,4.5
3	50.3	CH_2	2.97−3.07	m	2H	*c*
5	58.9	CH	2.78	ddq	1H	10.0, 6.0, 6.0
6	33.1	CH_2	1.96	m	1H	*c*
			1.42	ddt	1H	12.0, 10.0, 9.0
7	29.9	CH_2	2.10	m	1H	*c*
			1.80	m	1H	*c*
8	98.8	CH	4.85	dd	1H	6.0,1.5
9	20.4	CH_3	1.07	d	3H	6.0

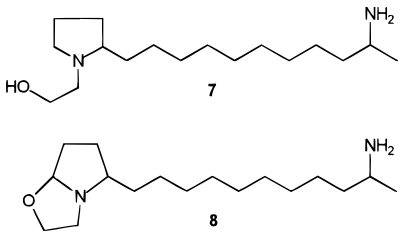
[a] ^{13}C (100 MHz) and ^{1}H (500 MHz) NMR data were obtained using $CDCl_3$ as the solvent. Chemical shifts are given in ppm relative to $CHCl_3$ peak at 77.0 and 7.24 ppm, respectively. [b] The ^{13}C- and ^{1}H-NMR peak assignments reported above are based on one- and two-dimensional methods (COSY, HMQC). [c] Due to the overlap and complexity of some peaks, J values could not be determined.

representing losses of a proton and a methyl group, respectively. Using HMQC data, we were able to link protons at δ 3.79/3.64, 3.02, 2.78, 1.96/1.42, 2.10/1.80, 4.85, and 1.07 ppm with their respective carbons at δ 63.3, 50.3, 58.9, 33.1, 29.9, 98.8, and 20.4 ppm (Table 2). Using COSY data we were then able to link carbons 2 and 3 together isolated from all the other carbons. Carbons 8, 7, 6, 5, and 9 (in that order) were then found to compose an unbroken chain. All this evidence unambiguously defined the photooxidation product as 5-methylpyrrolidinoöxazolidine (**4**).

The NMR spectra of **4** and **2** (Table 1 and 2) are closely analogous; corresponding chemical shift values are nearly identical. Also, the mass spectrum of **4** revealed a fragmentation pattern similar to that of the natural product **2**. These data provided further support for the assignment of structure **2** to the insect-derived alkaloid.

With an ample quantity of natural **1** in hand, it was possible to convert this alkaloid into **2** using the procedure we had developed for the synthesis of **4**, thus providing synthetic confirmation of the structural assignment. A small-scale transformation was performed in an NMR tube and monitored by ^{1}H-NMR spectroscopy. Although only a small yield of synthetic **2** was isolated, the amount of **2** obtained was ample for comparison of its ^{1}H-NMR and ^{13}C-NMR spectroscopic data with those of the natural product. In addition, GC−MS comparison of the photochemically synthesized product with the insect-produced alkaloid showed the two samples to be indistinguishable.

The pyrrolidinoöxazolidine ring system appears only rarely in the natural product literature.[18] Interestingly, GC−MS analysis of the *E. borealis* alkaloid mixture from 40-day-old adult males showed the presence of significant quantities of two lower homologs of **1** and **2** present only as minor constituents in the alkaloid mixture from teneral adults, to which we assign structures **7** and **8** (having a 10′-aminoündecyl side chain instead of a 12′-aminotridecyl side chain) on the basis of their mass spectra. Although both the qualitative and the quantitative changes in alkaloid content with age and developmental stage are striking in these beetles, the biological significance of this chemical variation remains to be elucidated.



Experimental Section

General Experimental Procedures. EIMS and gas-phase IR spectra were obtained using an HP 5890 gas chromatograph linked to an HP mass selective detector (MSD) or HP 5965A IR detector, respectively. High-resolution GC−MS was performed on a VG 70-VSE or a Finnigan 731 instrument. Gas chromatographic analysis was performed using a 25-m × 0.32-mm fused-silica column coated with DB-5. ^{1}H-NMR (500 MHz, 400 MHz, and 200 MHz) spectra were obtained using Varian XL-500, XL-400, and XL-200 spectrometers, respectively. ^{13}C-NMR (100 MHz) spectra were obtained using a Varian XL-400 spectrometer. Two-dimensional experiments were performed using a Varian XL-500 spectrometer (^{13}C NMR, 125 MHz). Chemical shifts are given in parts per million relative to the ^{1}H-NMR peak of $CHCl_3$ (residue in $CDCl_3$) at 7.24 ppm and the ^{13}C-NMR peak centered at 77.0 ppm (acidity of $CHCl_3$ was neutralized by keeping a drop of 10% NaOD in D_2O above the $CDCl_3$ layer).[19] Flash chromatography was carried out on EM Science Si gel (230−400 mesh ASTM). Reactions and isolates were monitored by TLC using Baker-flex Si gel IB2-F plates, which were visualized with ninhydrin and/or Dragendorff reagents. Methyl viologen dichloride was used as purchased (Aldrich).

Animal Material. Larvae of *E. borealis* were reared on a diet of zucchini squash plants (*Cucurbita pepo*, cultivar 'Milano') and allowed to pupate and emerge as adults.

Extraction and Isolation. Alkaloids were extracted from both teneral and mature adults of *E. borealis*. For the NMR study, 100 specimens of teneral beetles were crushed and extracted with 0.20% H_2SO_4 in MeOH (10 × 5 mL) over 4 h, and the extract was filtered and evaporated under reduced pressure. H_2O (2.0 mL) was added to the residue, and the mixture was extracted with Et_2O (8 × 2 mL). The aqueous layer was basified with solid KOH to a pH > 12. The mixture was extracted with CH_2Cl_2 (6 × 2 mL), and after the evaporation of the solvent, an oily mixture of alkaloids was obtained. Column chromatography on Si gel (CH_2Cl_2−MeOH−$NH_4OH_{(aq)}$, 30 mL:1 mL:3 drops) afforded a sufficiently pure sample of alkaloid **2** (1.5 mg) for structural work: GC−IR (gas phase) ν_{max} 2993, 2865, 1462, 1364, 1040 cm^{-1}; EIMS (70 eV) m/z [M]$^+$ 310 (1.2), [M − 1]$^+$ 309 (4), [M − 15]$^+$ 295 (15), 279 (15), 267 (16), 250 (3), 238 (5), 236 (13), 224 (5), 210 (3), 198 (8), 168 (3), 154 (4), 140 (7), 114 (6), 113 (17), 112 (100), 98 (8), 94 (8), 85 (11), 84 (11), 83 (10), 82 (9), 72 (13), 55 (12), 44 (98); HRMS m/z calcd for $C_6H_{10}NO$ 112.0762; found 112.0767.

Synthesis of 1-(2-Hydroxyethyl)-2-methylpyrrolidine (6) from 2-Methylpyrrolidine (5). To a mixture of 2-methylpyrrolidine (0.96 g, 1.3 mmol) and K_2CO_3 (1.42 g, 10.3 mmol) in MeCN (20 mL), 2-bromo-

ethanol (1.43 g, 11.4 mmol) was added dropwise, and the solution was refluxed overnight. The mixture was allowed to cool, and the solids were filtered off and washed with MeCN (2 × 2 mL). The combined filtrates were evaporated, and the residue was dissolved in Et_2O (10 mL) and extracted with HCl (1 M, 2 × 20 mL). The aqueous layers were separated, brought to pH > 12 with solid KOH, extracted with CH_2Cl_2 (2 × 20 mL), and the non-aqueous fractions were combined and dried with K_2CO_3. Evaporation of the solvent afforded 1-(2-hydroxyethyl)-2-methylpyrrolidine (1.13 g, 8.73 mmol, 77% yield) as a clear oil: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.06 (3H, d, J = 6.0 Hz, H-8), 1.38 (1H, m, H-3), 1.63−1.80 (2H, m, H-4), 1.91 (1H, m, H-3), 2.13 (1H, br q, J = 8.8 Hz, H-5), 2.25 (1H, dt, J = 12.4, 3.2 Hz, H-6), 2.43 (1H, dq, J = 6.0, 7.5 Hz, H-2), 2.95 (1H, ddd, J = 12.0, 10.0, 5.2 Hz, H-6), 3.13 (1H, ddd, J = 9.2, 8.0, 3.2 Hz, H-5), 3.56 (1H, m, H-7), 3.62 (1H, td, J = 10.4, 3.6 Hz, H-7), 3.73 (1H, br s, OH);^{13}C NMR ($CDCl_3$,100 MHz) δ 18.6 (C-8), 21.4 (C-4), 32.1 (C-3), 53.5 (C-5), 55.5 (C-6), 59.5 (C-7), 59.7 (C-2); EIMS (70 eV) m/z $[M + 1]^+$ 130 (0.6), $[M]^+$ 129 (4), $[M - 1]^+$ 128 (2), 115 (1), 114 (15), 99 (7), 98 (100), 84 (9), 70 (16), 69 (20), 57 (6), 56 (14), 55 (7), 54 (5), 45 (8), 44 (23), 43 (10), 42 (34), 41 (29).

Synthesis of 5-Methylpyrrolidinoöxazolidine (4) from 1-(2-Hydroxyethyl)-2-methylpyrrolidine (6). A 250-mL photoreactor was charged with 1-(2-hydroxyethyl)-2-methylpyrrolidine (1.13 g, 8.71 mmol), DCN[15] (107 mg, 0.599 mmol), methyl viologen dichloride (29.1 mg, 0.113 mmol), and MeCN (250 mL). The solution, exposed to atmospheric water and oxygen, was irradiated for 6 h using a 450 W Hanovia lamp with a Pyrex absorption filter (300−400 nm). After irradiation, the solution was poured over protonated Amberlyst ion-exchange resin and the resin, was then washed with sufficient Et_2O to remove the acetonitrile. The product was then eluted with Et_2O saturated with NH_3 (anhydrous). The Et_2O was evaporated, and the crude material was vacuum transferred to give 5-methylpyrrolidinoöxazolidine (400 mg, 3.14 mmol, 36% yield) as a clear oil: GC-IR (gas phase) ν_{max} 2968, 2889, 1651, 1459, 1366, 1196, 1153, 1100, 1044, 857 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) and ^{13}C NMR ($CDCl_3$, 100 MHz), see Table 2; EIMS (70 eV) m/z $[M + 1]^+$ 128 (4), $[M]^+$ 127 (46), $[M - 1]^+$ 126 (25), $[M - 15]^+$ 112 (29), 99 (34), 98 (23), 97 (38), 96 (23), 82 (38), 72 (34), 71 (43), 70 (23), 56 (60), 55 (100), 44 (24), 43 (38), 42 (58), 41 (55); HRMS m/z calcd for $C_7H_{13}NO$ 127.099714, found 127.099428.

Synthesis of 5-(12′-Aminotridecyl)pyrrolidinoöxazolidine (2) from 1-(2-Hydroxyethyl)-2-(12-aminotridecyl)pyrrolidine (1). A standard-sized NMR tube was charged with **1**, which had been isolated from crushed beetles (5.8 mg, 0.019 mmol), DCN[15] (0.1 mg, 0.6 μmol), methyl viologen dichloride (50 μg 0.2 μmol), and MeCN-d_3 (1.4 mL). The NMR tube was placed in the thermometer port of a photoreactor and irradiated for 3.5 h as described in the previous paragraph. The reaction was monitored by 200 MHz ^{1}H-NMR spectroscopy. After this period, an additional amount of DCN (0.1 mg) was added, and the mixture was irradiated for an additional 1 h. Evaporation under reduced pressure followed by column chromatography on Si gel (CH_2Cl_2−MeOH−$NH_4OH_{(aq)}$,10 mL:1 mL:1 drop) gave **2** (1.0 mg, 0.0032 mmol, 17% yield): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.12 (3H, d, J = 7.0 Hz), 1.25 (21H, br s), 1.43 (1H, m), 1.54 (1H, m), 1.85 (1H, m), 2.03 (1H, m), 2.10 (1H, m), 2.60 (1H, m), 2.84 (1H, m), 3.00−3.13 (2H, m), 3.66 (1H, m), 3.81 (1H, q, J = 7.6 Hz), 4.80 (1H, dd, J = 6.0, 1.3 Hz);^{13}C NMR ($CDCl_3$, 100 MHz) δ 98.7, 64.4, 63.4, 51.3, 46.7, 40.1, 36.4, 30.9, 29.9, 29.6, 23.9; EIMS (70 eV) m/z $[M]^+$ 310 (1.7), $[M - 1]^+$ 309 (3), 295 (13), 279 (14), 267 (18), 250 (2), 238 (6), 236 (15), 224 (5), 210 (3), 198 (7), 168 (3), 154 (4), 140 (8), 114 (7), 113 (27), 112 (100), 98 (10), 94 (8), 85 (12), 84 (10), 83 (10), 82 (9), 72 (14), 55 (14), 44 (95).

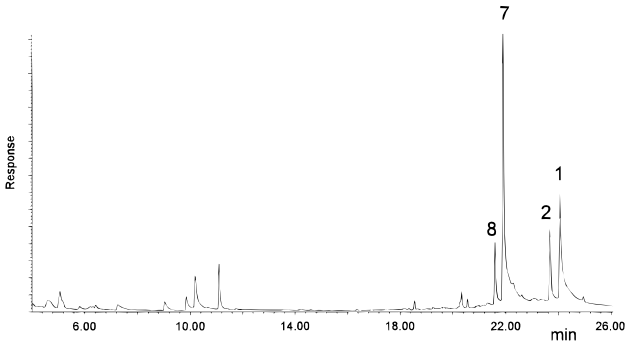


Figure 1. Reconstructed gas chromatogram of an alkaloidal extract from 40-day-old male *E. borealis*. Key: DB-5 coated 0.2 mm × 25 m capillary; oven temperature kept at 60 °C for 2 min, and programmed to 260 °C at 10 °C/min.

GC−MS Analysis of *E. borealis* Alkaloids from Older Adult Males. An alkaloid sample was prepared by extraction of four 40-day-old males, as described for the isolation of **2**. The MS data listed below served to characterize components **7** and **8** (see Figure 1).

1-(2-Hydroxyethyl)-2-(12′-aminotridecyl)-pyrrolidine (7): EIMS (70 eV) m/z $[M]^+$ 284 (0.1), $[M - 1]^+$ 283 (0.5), 269 (2), 266 (2), 254 (3), 253 (16), 211 (1), 210 (5), 198 (1), 196 (2),126 (1), 124 (2), 115 (7), 114 (100), 98 (6), 96 (5), 84 (22), 83 (4), 74 (5), 70 (17), 56 (5), 54 (7), 44 (35).

5-(10′-Aminotridecyl)pyrrolidinoöxazolidine (8): EIMS (70 eV) m/z $[M]^+$ 282 (0.4), $[M - 1]^+$ 281 (1), 267 (5), 251 (5), 239 (7), 210 (3), 208 (5), 198 (2), 196 (3), 170 (8), 140 (6), 126 (6), 113 (14), 112 (100), 98 (9), 94 (9), 85 (12), 84 (8), 83 (11), 82 (11), 72 (12), 56 (9), 55 (12), 44 (74).

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References and Notes

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(19) ^{1}H-NMR spectroscopic evidence showed that the protons in the C-7 position slowly exchange with D_2O/DO^- deuterons over a period of weeks; the δ 1.85 proton exchanging faster than that at δ 2.10. This process presumably results from reversible opening of the oxazolidine ring to give the *N*-hydroxyethyliminium ion, followed by loss of either C-7 proton to give the corresponding enamine. We observed the base peak at *m*/*z* 112 to decrease gradually and the peaks at *m*/*z* 113 and 114 to increase gradually as deuterium exchange took place.

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