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A NOVEL (5*E*,9*Z*)-DIALKYLINDOLIZIDINE FROM THE ANT *MONOMORIUM SMITHII*

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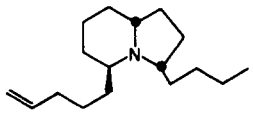
ABSTRACT.—The alkaloidal venom of *Monomorium smithii* was found to contain (5*E*,9*Z*)-3-butyl-5-(4-penten-1-yl)indolizidine [**1b**], a novel indolizidine, its monocyclic analogue *trans*-2-butyl-5-(8-nonen-1-yl)pyrrolidine [**2**], (5*E*,8*Z*)-3,5-di(5-hexen-1-yl)pyrrolizidine [**3**], and *trans*-2-(5-hexen-1-yl)-5-(8-nonen-1-yl)pyrrolidine [**4**]. The structure of **1b** was based on the results of two independent syntheses. Reductive amination of the appropriate triketone confirmed the carbon-nitrogen skeleton of **1b** and suggested its stereochemistry, which was verified by the results of a stereoselective synthesis based on pyrrole hydrogenation. The chemotaxonomic implications of this first report of the concomitance of a 3,5-dialkylindolizidine and a 3,5-dialkylpyrrolizidine in an ant venom are discussed.

A large variety of saturated nitrogen heterocycles have been identified in the venoms of several myrmicine ant genera (1–4). Perhaps the most noteworthy of these alkaloids are the 3,5-dialkylindolizidines, which have been reported from ants since 1973 (5), and, interestingly, from amphibians since 1978 (6). To date the 3,5-dialkylindolizidines found in ants have been shown to have the all-cis (5*Z*,9*Z*) configuration (1,2) and are present with monocyclic piperidine or pyrrolidine analogues. In this report, we describe the identification and synthesis of (5*E*,9*Z*)-3-butyl-5-(4-penten-1-yl)indolizidine [**1b**] from the venom of the New Zealand ant *Monomorium smithii* Forel. (Hymenoptera: Formicidae).

In New Zealand, two endemic species of ants in the genus *Monomorium* are now recognized (7,8), although the status of one of these, *M. smithii*, has been questioned (9). Previous research on the other species, *Monomorium antarcticum*, has established the probable presence of a complex of species, reflected in the distinctive sets of alkaloids produced by different populations of this species (4). In the present report, we establish that the unique mixture of alkaloids in the workers of *M. smithii*, marked by the novel indolizidine **1b**, clearly separates it from all populations of *M. antarcticum*.



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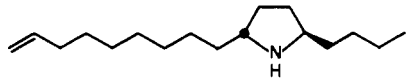

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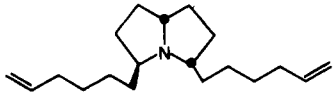

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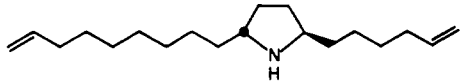

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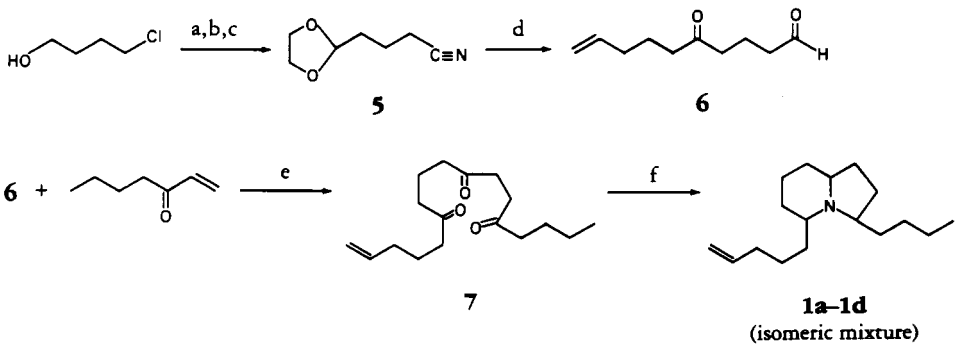
RESULTS AND DISCUSSION

Gc analysis of the CH_2Cl_2 extracts of *M. smithii* revealed the presence of three major volatile components. The mass spectrum of the first of these showed a molecular ion at *m/z* 249 and major fragments at *m/z* 192 and 180, corresponding to the loss of C_4H_9 and C_5H_9, respectively. The ms and glc retention times of the second and third major components were identical to those of authentic samples of *trans*-2-butyl-5-(8-nonen-1-yl)pyrrolidine [**2**] and (5*E*,8*Z*)-3,5-di(5-hexen-1-yl)pyrrolizidine [**3**] (4). Additionally, a small amount of *trans*-2-(5-hexen-1-yl)-5-(8-nonen-1-yl)pyrrolidine [**4**] was also detected (1). Upon hydrogenation, the first-eluting alkaloid took up one equivalent of hydrogen (*m/z* 251 $[M]^+$), and the mass spectrum of the reduction product had ions at *m/z* 194 and 180 indicating the loss of C_4H_9 and C_5H_{11}, respectively.

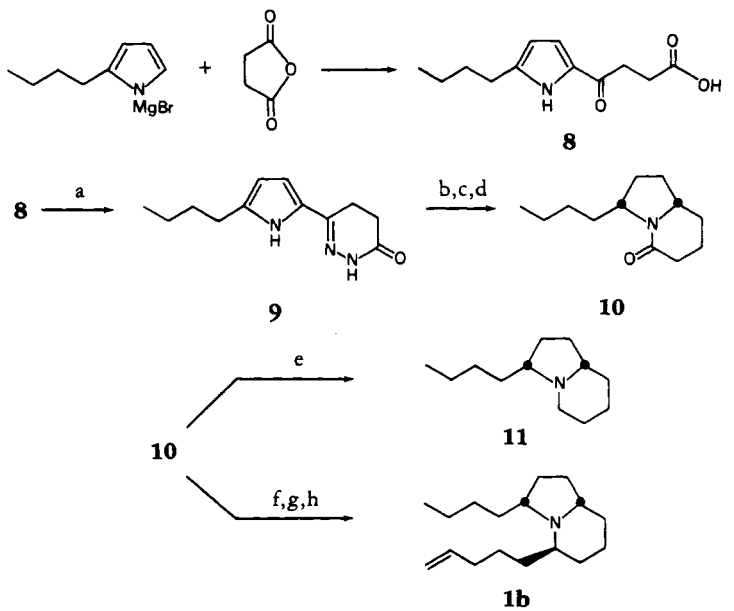
These data along with the concomitance of **2** suggested the structure of this component as 3-butyl-5-(4-penten-1-yl)indolizidine [**1**], which was confirmed by a synthesis based on the reductive amination (2) of the appropriate triketone (Scheme 1). This synthesis provided all four stereoisomers of **1** as a 3:1.2:1:2 mixture with essentially identical ms matching the ms of the first eluting compound from *M. smithii*. The gc retention time of the natural alkaloid was identical to that of the second eluting isomer **1b** of the mixture formed by reductive amination. Unfortunately, it was impossible to obtain pure samples of the synthetic isomers necessary for nmr studies from this mixture.

In previous studies of 3,5-dialkylindolizidine isomers, the second-eluting isomer was shown to have the (5*E*,9*Z*)-configuration (2,10) with a *cis*-substituted five-membered ring. Accordingly, a stereoselective synthesis based on pyrrole hydrogenation was undertaken (Scheme 2). The pyrrole ketoacid **8** was obtained in good yield from 2-butylpyrrole magnesium bromide (11,12) and succinic anhydride and was condensed with hydrazine to form the tetrahydropyridazine **9** (13). Although there is precedent for the Wolff-Kishner reduction of acylpyrroles such as **8** (11), isolation of **9** produced better results in this case. The preparation of indolizidone **10** was conducted without isolating intermediates. Crude 4-(5-butylpyrrol-2-yl)butanoic acid, obtained by heating **9** with KOH in ethylene glycol, was immediately hydrogenated over PtO_2 and then cyclized by warming in EtOH. Any delay in this sequence decreased the yield of **10** considerably.

The hydrogenation of 2,5-dialkylpyrroles is stereoselective but not stereospecific for the *cis*-pyrrolidine isomer (12,14). In order to confirm this stereochemical outcome, **10** was reduced to a 9:1 mixture of stereoisomers of 3-butylindolizidine [**11**] with $LiAlH_4$. The ^{13}C-nmr spectrum of this mixture (Table 1) showed that the chemical



SCHEME 1. (a) PCC; (b) $(HOCH_2)_2$, ptsa; (c) NaCN, DMSO; (d) (i) 4-pentenylmagnesium bromide, (ii) dilute HCl; (e) 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride, Et_3N; (f) NH_4OAc, $NaCNBH_3$.



SCHEME 2. (a) $(NH_2)_2$, C_6H_6, reflux; (b) KOH, $(HOCH_2)_2$, 170°; (c) H_2/PtO_2/HOAc; (d) EtOH, reflux; (e) $LiAlH_4$; (f) DIBAL, −78°, then $HClO_4$; (g) KCN; (h) 4-pentenylmagnesium bromide.

shifts of the C-3, C-5, and C-9 carbons of the major isomer occurred at 6.09, 4.65, and 5.51 ppm lower field than those of the minor isomer. This is consistent with the ca. 1 ppm downfield difference reported for the methine carbon signals of the *cis*-2,5-dialkyl-pyrrolidines from those of the *trans*-2,5-dialkyl-pyrrolidines (15). On the other hand, it is somewhat less pronounced than the differences of 5.5, 7.9, and 7.0 ppm reported for the C-3, C-5, and C-9 methine carbons of the all-cis (5*Z*,9*Z*)-3-butyl-5-methylindolizidine (monomorine I) from those of (5*E*,9*E*)-3-butyl-5-methylindolizidine, where the five-membered ring is trans disubstituted (Table 1). In these indolizidine isomers, the indolizidine nucleus is somewhat more distorted than in **11** by the additional C-5 methyl group (16).

The stereoselective preparation of **1b** from **10** was carried out using Stevens' cyanoamine methodology (17) inasmuch as difficulty has been reported in the direct reaction of Grignard reagents with iminium ions (18). The indolizidinium ion resulting from the partial reduction of **10** with diisobutylaluminum hydride (19) was trap-

TABLE 1. Selected ^{13}C-nmr Chemical Shifts for Indolizidine Isomers.

Compound	Assigned stereochemistry	C-3	C-5	C-9
11	9*Z*	65.81	51.75	65.89
11	9*E*	59.72	47.10	60.38
Monomorine I[a]	5*Z*,9*Z*	61.8	59.7	67.6
Monomorine I[a]	5*E*,9*E*	56.6	51.8	58.9
1b	5*E*,9*Z*	56.54	52.89	58.79
Indolizidine 223[b]	5*E*,9*Z*	56.4	52.7	58.4

[a]From Jones *et al.* (2) and Sonnet *et al.* (16).
[b]From Spande *et al.* (10).

ped with cyanide ion, and the resulting 5-cyanoindolizidine served as a latent iminium ion. Treatment of the crude cyanoindolizidine with excess 4-pentenylmagnesium bromide afforded **1b** in good yield along with a small amount of **11**. The **1b** prepared in this manner had glc retention times and ms identical to those of the first-eluting alkaloid from *M. smithii* and the second-eluting indolizidine isomer from the reductive amination of **7**.

Corroboration of the expected 5*E*,9*Z* stereochemistry of **1b** was obtained from the ^{13}C-nmr spectrum, wherein the chemical shifts of the methine carbons were very close to those reported for the 5*E*,9*Z* isomer of 2-butyl-5-propylindolizidine (indolizidine 223) (Table 1). It is noteworthy that small amounts of **1c** and **1d**, isomers in which the five-membered ring is trans-disubstituted, were also observed in the reaction mixture, while none of the all-cis **1a** was detected. Because **1c** and **1d** must have arisen from the small amount of (9*E*)-**10** present, these results suggest that the degree of stereoelectronic control previously reported (17) and observed here in indolizidinium ions where the five-membered ring is cis disubstituted is not present in indolizidinium ions where the five-membered ring is trans disubstituted.

This is the first report of a (5*E*,9*Z*)-3,5-dialkylindolizidine from an ant, only the all-cis (5*Z*,9*Z*)-3,5-dialkylindolizidines having been reported previously. The 3,5-dialkylindolizidines reported in amphibians have been predominantly the 5*E*,9*E* stereoisomer with the six-membered ring cis disubstituted, although recently mixtures of isomers, including the 5*Z*,9*Z* and the 5*E*,9*Z* stereoisomers of monomorine I and indolizidine 223AB, have been detected in the Argentine toad, *Melanophryniscus stelzneri stelzneri*[1].

This is further the first observation of indolizidine and pyrrolizidine alkaloids in the same ant species. In other species, each of these bicyclic compounds occurs together with its monocyclic analogues. For example, in *Solenopsis conjurata*, (5*Z*,9*Z*)-dialkylindolizidines are present with trans dialkylpiperidines, while in *M. antarcticum* populations (5*Z*,8*E*)-dialkylpyrrolizidines occur with trans dialkylpyrrolidines (2,4). Indeed, the concomitance of *trans*-**2** with **1b** and of *trans*-**4** with **3** in *M. smithii* supports the suggestion (2) that the bicyclic alkaloids may be produced in ants when the initially formed five- or six-membered membered ring is cis-disubstituted.

Finally, the unique venom chemistry of *M. smithii* is clearly distinguished from that of all other species of *Monomorium* studied to date, including the New Zealand species *M. antarcticum*. These results provide chemotaxonomic support for the classification of these two forms as separate species (7,8), which has been based on a combination of morphological and biological characters.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All bp's and mp's are uncorrected. Glc analyses were performed on a Shimadzu GC-12A equipped with a 30 m × 0.53 mm i.d. column with a bonded FFAP phase and a 30 m × 0.53 mm i.d. column with a bonded DB-17 phase. Preparative gc was performed on a Varian model 1400 instrument equipped with a 2 m × 5 mm i.d. column packed with 10% SP-1000 on 100–120 mesh Supelcoport. ^{1}H- and ^{13}C-nmr spectra were obtained with a Varian XL-200 spectrometer. Eims were obtrained using a LKB-9000 GC/MS fitted with a 30 m × 0.53 mm i.d. column with a bonded DB-17 phase. Hreims were obtained using a VG 7070F at an ionizing voltage of 70 eV. Combustion analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

ANIMAL MATERIALS, EXTRACTION, AND DETECTION OF ALKALOIDS.—*M. smithii* were collected at Faulkner's Bush, Wakefield, N.W. South Island, New Zealand, in January 1987. Specimens of these ants have been deposited in the collection of the Los Angeles County Museum of Natural History, Los Angeles, CA. Examination of the CH_2Cl_2 extracts of approximately eighty workers by gc-ms showed three

[1]Personal communication from the laboratory of J.W. Daly.

major alkaloid components in a 2:2:3 ratio. The first-eluting alkaloid **1** had the following ms: *m/z* (relative intensity) 249 (5) $[M]^+$, 248 (3), 193 (15), 192 (77), 181 (18), 180 (100), 124 (7), 123 (4), 122 (5), 96 (6), 95 (7), 94 (6), 82 (9), 81 (9), 69 (11), 67 (13), 55 (25), 41 (25). The second- and third-eluting alkaloids had ms and glc retention times identical to those of authentic samples of **2** and **3**, respectively. A minor component, eluting very late, was identified as **4** in the same way. In addition, a small amount (less than 5% of **1**) of an isomer of **1** was detected with a slightly longer retention time than **1** and an ms nearly identical to that of **1**. A steady stream of H_2 was passed through a few drops of the extract containing PtO_2. Examination by gc-ms revealed that the first eluting component had the following ms: *m/z* (%) 251 (3) $[M]^+$, 250 (4), 195 (15), 194 (100), 181 (10), 180 (70), 224 (6), 223 (5), 222 (5), 85 (5), 84 (3), 82 (5), 81 (6), 71 (6), 69 (7), 67 (7), 57 (12), 55 (15), 43 (13), 41 (15).

4-(1,3-Dioxolan-2-yl)-butanenitrile [**5**].—A mixture containg 17.2 g (0.12 mol) of 2-(3-chloropropyl)-1,3-dioxolane (20) and 6.4 g of NaCN in 30 ml of DMSO was heated to 90° for 2 h. The mixture was poured into 100 ml of H_2O and washed with 4 × 70 ml of Et_2O, and the combined Et_2O washings were dried over anhydrous $MgSO_4$. Distillation provided 13.5 g of pure **5** (80% yield): bp 125–128° (16 mm Hg); ^1H nmr δ 4.9 (1, t, J = 6 Hz, C*H*-CH_2), 3.9 (4, m, CH_2-O), 2.4 (2, m, CH_2CN), 1.8 (4, m, CH_2CH_2); ms *m/z* (rel. int.) $[M]^+$ 141 (1), 140 (10), 110 (2), 99 (3), 96 (7), 82 (5), 74 (10), 73 (100), 68 (9), 55 (17), 45 (59), 41 (25); hreims calcd for $C_7H_{10}NO_2$ $[M-1]^+$ 140.0712, found 140.0699. *Anal.* calcd for $C_7H_{11}NO_2$, C 59.55, H 7.85, N 9.92; found C 59.19, H 7.84, N 10.21.

5-Oxo-9-decenal [**6**].—A solution containing 3.3 g (23 mmol) of **5** in 10 ml of anhydrous Et_2O was added over 0.5 h to a solution of 4-pentenylmagnesium bromide (from 7.1 g of 5-bromo-1-pentene and 1.6 g of Mg) in 50 ml of anhydrous Et_2O. The mixture was stirred overnight and treated with 10% HCl, and the H_2O layer was removed. After the solvent was removed in vacuo, 5 ml of 50% HOAc was added and the mixture was heated over a steam bath for 0.5 h. The resulting solution was neutralized with solid $NaHCO_3$ and extracted with 4 × 50 ml of Et_2O. The Et_2O layer was dried and after Kugelrohr distillation provided 1.2 g (30% yield) of ketoaldehyde **6**: bp 150–160° (0.2 mm Hg); ^1H nmr δ 9.73 (1, t, J = 1.5 Hz, CHO), 5.75 (1, ddt, J = 6, 10, 18 Hz, =CH-), 5.0 (1, br d, J = 18 Hz, E-CH_2), 4.95 (1, br d, J = 10 Hz, Z-CH_2), 2.4–2.5 (6, m, CH_2CO), 2.05 (2, m, CH_2CH=), 1.88 (2, quintet, J = 7.5 Hz, CH_2), 1.65 (2, quintet, J = 7.5 Hz, CH_2); ms *m/z* (%) $[M]^+$ 168 (1), 140 (3), 114 (30), 112 (11), 99 (30), 97 (25), 86 (31), 71 (55), 69 (65), 58 (75), 55 (80), 45 (47), 43 (70), 41 (100).

16-Heptadecen-5,8,12-trione [**7**].—A mixture containing 1.2 g of **6** (7 mmol), 0.8 g of freshly prepared 1-hepten-3-one, and 0.2 g of 5-(2-hydroxyethyl)-4-methyl-3-benzylthiazolium chloride (21) in 3 ml of triethylamine was refluxed overnight under N_2 atmosphere. Upon cooling, the mixture was diluted with Et_2O, filtered through Florisil, and distilled. Kugelrohr distillation provided 1.2 g (64% yield) of the triketone **7**: ^1H nmr δ 5.71 (1, ddt, J = 6, 10, 18 Hz, CH_2=C*H*), 5.0 (1, br d, J = 18 Hz, E-CH_2=), 4.9 (1, br d, J = 10 Hz, Z-CH_2=), 2.6 (4, br s, $COCH_2CH_2CO$), 2.3–2.5 (8, m, CH_2CO), 1.98 (2, m, CH_2CH=), 1.78 (2, quint, J = 7.5 Hz, CH_2), 1.59 (2, quint, J = 7.5 Hz, CH_2), 1.47 (2, quint, J = 7.0 Hz, CH_2), 1.25 (2, sext, J = 7.5 Hz, CH_2CH_3), 0.85 (3, t, J = 7.5 Hz, CH_3); ^{13}C nmr δ 210.34 (CO), 209.54 (CO), 208.95 (CO), 137.87 (=CH-), 115.09 (CH_2=), 42.38, 41.78, 41.53, 41.45, 35.97, 35.88, 32.99, 25.85, 22.68, 22.20, 17.67, 13.73 (Me); ms *m/z* (rel. int.) $[M]^+$ 280 (8), 262 (2), 238 (3), 226 (3), 211 (35), 208 (20), 195 (15), 193 (5), 169 (55), 150 (20), 141 (80), 125 (30), 114 (10), 113 (20), 111 (30), 108 (40), 97 (40), 95 (17), 85 (55), 83 (23), 81 (14), 71 (23), 69 (42), 57 (65), 55 (100), 43 (25), 41 (90); hrms calcd for $C_{17}H_{28}O_3$, 280.2038, found 280.2065.

4-Oxo-4(5-butylpyrrol-2-yl)butanoic acid [**8**].—A solution containing 12.3 g (0.1 mol) of 2-butylpyrrole in 40 ml of THF was added to 35 ml of 3 M ethereal methylmagnesium bromide at 0° under an N_2 atmosphere. The resulting solution was added by cannula to a solution containing 10 g of succinic anhydride in THF cooled to −78° under an N_2 atmosphere. The mixture was allowed to warm to ambient temperature overnight, then treated with dilute HCl and Et_2O. The H_2O phase was separated and washed with 3 × 70 ml of Et_2O, and the combined Et_2O washings were washed with 2 × 50 ml of 10% NaOH, dried over anhydrous K_2CO_3, and distilled to give 4.1 g of 2-butylpyrrole. The alkaline phase was carefully acidified with dilute HCl to pH 4 to provide, after filtration, 12.5 g (84% yield based on unrecovered 2-butylpyrrole) of **8**: mp 125–127°; ms *m/z* (%) $[M]^+$ 223 (57), 206 (3), 181 (12), 180 (55), 163 (15), 162 (28), 151 (10), 150 (100), 134 (29), 108 (7), 107 (9), 80 (23), 79 (15), 55 (9), 44 (10), 43 (3), 41 (1); hrms calcd for $C_{12}H_{17}N_1O_3$, 223.1208, found 223.1201.

3-(5-Butylpyrrol-2-yl)-6-oxo-1,4,5,6-tetrahydropyridazine [**9**].—A solution containing 11.0 g (50 mmol) of ketoacid **8** in 13 ml of 95% hydrazine hydrate was taken up in 200 ml of C_6H_6 and heated to reflux with a Dean-Stark trap until the separation of H_2O ceased. The solvent was removed in vacuo, and the residue was recrystallized from EtOH/H_2O to give 10 g (92% yield) of **9**: mp 111–113°; ^1H nmr δ 10.9 (1, br s, NH), 10.6 (1, s, NH), 6.38 (1, t, J = 2 Hz, pyrrole 3H), 5.82 (1, t, J = 2 Hz, pyrrole

4 H), 2.76 (2, t, J = 7.5 Hz, CH_2C=N), 2.51 (2, m, CH_2-pyrrole), 2.3 (2, t, J = 7.5 Hz, CH_2CO), 1.50 (2, quint, J = 7.0 Hz, CH_2), 1.3 (2, sext, J = 7.0 Hz, CH_2CH_3), 0.9 (3, t, J = 7.0 Hz, Me); ^{13}C nmr δ 167.12 (CO), 144.35 (C=N), 137.24 (pyrrole 2C), 126.60 (pyrrole 5C), 111.16 (pyrrole 3C), 106.11 (pyrrole 4C), 31.49 (CH_2CO), 26.61, 26.42, 21.90, 21.73, 13.71 (Me); ms *m/z* (%) $[M]^+$ 219 (80), 177 (24), 176 (100), 148 (10), 146 (5), 134 (14), 119 (2), 118 (2), 105 (20); hrms calcd for $C_{12}H_{17}N_3O_1$, 219.1371, found 219.1372.

(9Z)-3-BUTYL-5-INDOLIZIDONE [**10**].—A well-stirred solution containing 10 g (46 mmol) of **9** and 10 g of KOH in 50 ml of ethylene glycol was heated under an N_2 atmosphere for 3 h (bath temperature 170°). Upon cooling, the mixture was diluted with 100 ml of H_2O, acidified to pH=3 with dilute HCl, and extracted with 3 × 75 ml of Et_2O, and the solvent was removed in vacuo from the combined Et_2O extracts. The unstable 4-(5-butylpyrrol-2-yl)butanoic acid had ms *m/z* (%) $[M]^+$ 209 (45), 167 (15), 166 (85), 149 (8), 148 (43), 137 (12), 136 (100), 120 (7), 106 (25), 94 (14), 93 (24), 80 (6), 55 (15). This product was immediately taken up in 30 ml of HOAc and stirred overnight under an H_2 pressure of 3.4 atm in the presence of 1.0 g of PtO_2. After filtration, the solvent was removed in vacuo, and the residue was taken up in 50 ml of EtOH and refluxed for 6 h. The solvent was removed in vacuo, and the residue was partitioned between Et_2O and saturated aqueous $NaHCO_3$ solution. The combined Et_2O extracts were dried over anhydrous $MgSO_4$ and distilled to give 4.0 g (45% yield) of **10**: bp 170–175° (0.3 mm Hg); ^{1}H nmr δ 3.94 (1H, m, H-9), 3.34 (1H, br m, H-3), 2.30 (2H, m, H_2-6), 2.1–1.4 (14H, m), 0.9 (3H, t, J = 7.0 Hz, Me); ^{13}C nmr δ 169.40 (C-5), 59.91 (C-9), 57.26 (C-3), 32.43, 31.41, 30.99, 29.30, 28.79, 27.55, 22.67, 21.14, 14.06 (Me); ms *m/z* (%) $[M]^+$ 195 (9), 166 (6), 152 (12), 139 (24), 138 (100), 126 (6), 110 (9), 82 (6), 70 (3), 69 (3), 68 (6), 67 (3), 55 (10), 45 (6), 41 (10); hrms calcd for $C_{12}H_{21}NO$, 195.1623, found 195.1613. *Anal.* calcd for $C_{12}H_{21}NO$, C 73.79, H 10.83, N 7.17; found C 73.12, H 11.07, N 7.61. Analysis of this product revealed approximately 10% of an isomer having a longer retention time and a mass spectrum identical to that of **10**.

(9Z)-3-BUTYLINDOLIZIDINE [**11**].—A solution containing 200 mg (1 mmol) of **10** in 20 ml of anhydrous Et_2O was treated with 10 ml (erxcess) of 1 M ethereal $LiAlH_4$ solution under an N_2 atmosphere and allowed to stir overnight. The mixture was treated with a few drops of H_2O and 10% NaOH, and after filtration of the resulting solids, removal of the solvent in vacuo gave 140 mg (76% yield) of **11** that was >95% pure by glc analysis as a 9:1 mixture of two isomers with identical ms: *m/z* (%) $[M]^+$ 181 (2), 180 (3), 125 (10), 124 (100), 55 (5), 41 (10); ^{1}H nmr δ 3.16 (2, m, H-3 and H-9), 2.02 (2, m, H_2-5), 1.5–1.9 (9, m), 1.1–1.45 (9, m), 0.9 (3, t, J = 7.5 Hz, Me); ^{13}C nmr δ 65.9 (C-9), 65.83 (C-3), 51.77 (C-5), 33.37, 31.47, 29.27, 29.16, 28.74, 25.71, 24.81, 23.30, 14.28 (Me). The ^{13}C-nmr spectrum of the isomeric mixture showed additional resonances at δ 60.38 (C-9), 59.72 (C-3), and 47.10 (C-5) ppm.

3-BUTYL-5-(4-PENTEN-1-YL)INDOLIZIDINE [**1**].—A. From triketone **7**. A solution containing 1.2 g of **7**, 0.33 g of NH_4OAc, 0.03 g of KOH, and 0.54 g of $NaCNBH_3$ in 15 ml of MeOH was stirred under an N_2 atmosphere overnight. The mixture was stirred an additional 15 min after the addition of 0.2 g of $NaBH_4$ and was carefully acidified with dilute HCl. After removal of the solvent, the residue was partitioned between 10% NaOH and Et_2O, and the Et_2O extracts were dried (anhydrous K_2CO_3) and evaporated to give 0.85 g (80% yield) of crude indolizidine **1**. Glc analysis (FFAP column programmed from 60° to 210° at 10°/min) showed four components, **1a**, **1b**, **1c**, and **1d** in the ratio 3:1.2:1:2; the components had retention times of 11.5, 11.7, 12, and 12.2 min, respectively. The four components had nearly identical ms: *m/z* (%) $[M]^+$ 249 (5), 248 (3), 193 (15), 192 (90), 181 (18), 180 (100), 124 (7), 123 (3), 122 (8), 96 (5), 95 (6), 94 (5), 93 (2), 82 (10), 81 (10), 69 (5), 67 (10), 55 (15), 41 (18); hrms calcd for $C_{17}H_{31}N$, 249.2457, found 249.2460. Glc analyses using the FFAP and the DB-17 column showed that the retention times of **1b** were identical to those of the first eluting component, **1**, in the extracts of *M. smithii*. *Anal.* calcd for $C_{17}H_{31}N$, C 81.85, H 12.53, N 5.62; found C 81.49, H 12.57, N 6.01.

B. From indolizidone **10**. A solution containing 100 mg (0.51 mmol) of **10** in 50 ml of anhydrous Et_2O was cooled to −78°, and 0.7 ml of a 1 M solution of DIBAL in hexane was added over 30 min. The mixture was stirred for 1.5 h and treated with 2 ml of 10% EtOH/$HClO_4$. After 1 h, the mixture was allowed to warm to room temperature and brought to pH 2 with a few drops of concentrated $HClO_4$. The mixture was stirred for 30 min, treated with 200 mg of solid KCN and 2 ml of H_2O, and stirred overnight. Gc-ms analysis of the Et_2O layer revealed a single major volatile component, ms *m/z* (%) $[M]^+$ 206 (1), 205 (2), 180 (2), 179 (7), 150 (13), 149 (100), 123 (7), 122 (69), 120 (3), 69 (2), 67 (6), 55 (7), 54 (6), 53 (3), 41 (10). The H_2O layer was removed, and the Et_2O layer was dried over anhydrous Na_2SO_4, filtered, and the solvent removed in vacuo. The residue was taken up in THF, cooled to 0°, treated with an excess of 4-pentenylmagnesium bromide in Et_2O, and stirred for 8 h. The mixture was treated with 10% NaOH and, after removal of the H_2O layer, was dried over anhydrous K_2CO_3. Gc-ms analysis revealed the presence of **11**, **1b**, and **10** in a 1:21:1.5 ratio. In addition, small peaks corresponding to **1c** (4% of **1b**) and **1d** (3% of **1b**) were observed. No peak corresponding to **1a** was detected. A sample of ca. 10 mg of **1b** was ob-

tained by preparative glc: ^{1}H nmr δ 5.8 (1, ddt, J = 6, 10, 18 Hz, =CH-), 5.0 (1, br d, J = 18 Hz, *E*-CH_2=), 4.9 (1, br d, J = 10 Hz, *Z*-CH_2=), 3.35 (1, br s, H-9), 2.75 (2, br s, H-3, H-5), 2.4–1.1 (12, m), 0.9 (3, t, J = 7 Hz, Me); ^{13}C nmr δ 139.10 (=CH-), 114.66 (=CH_2), 58.79 (C-9), 56.54 (C-3), 52.89 (C-5), 34.25, 32.78 32.63, 29.66, 28.94, 28.49, 27.93, 27.13, 23.30, 20.30, 19.53, 14.31 (Me).

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