Alkaloids of the Ant *Chelaner antarcticus*[1]

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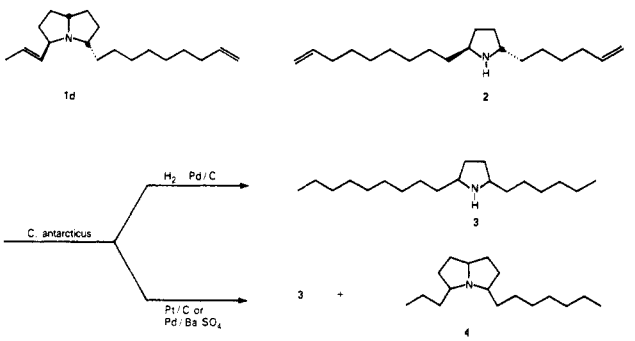
The major alkaloidal component from the ant *Chelaner antarcticus* (White) was found to be (5*E*,8*Z*)-3-(1-non-8-enyl)-5-((*E*)-1-prop-1-enyl)pyrrolizidine (**1**). The structure was suggested by spectral data and confirmed by a nonstereoselective synthesis, which also permitted the assignment of its stereochemistry. A minor component was the known compound *trans*-2-(1-hex-5-enyl)-5-(1-non-8-enyl)pyrrolidine (**2**), previously reported in *Monomorium* species.

The venoms of ants in the genera *Monomorium* and *Solenopsis* are well-known as sources of a variety of saturated nitrogen heterocycles.[2,3] In this note, we describe the occurrence and structure elucidation of (5*E*,8*Z*)-3-(1-non-8-enyl)-5-((*E*)-1-prop-1-enyl)pyrrolizidine (**1**) as the major alkaloid produced by a species of *Chelaner* (*C. antarcticus* (White)[4] a genus closely related to *Monomorium*.[5]

The ants were collected from three locations in Nelson Province, N.W., South Island, New Zealand, and immediately placed in methylene chloride. Analysis of the methylene chloride extracts by GC/MS showed the presence of two components in approximately 6:1 ratio. The minor component was readily identified as *trans*-2-(1-hex-5-enyl)-5-(1-non-8-enyl)pyrrolidine (**2**) by direct comparison with an authentic sample.[6]

The mass spectrum of the major component showed a molecular ion at m/z 275 and a single major fragment, the base peak, at m/z 150. Assuming one nitrogen atom, the compound must have four rings or units of unsaturation, a molecular formula of $C_{19}H_{33}N$, and must lose C_9H_{17} from a carbon adjacent to nitrogen. Hydrogenation of the extract over palladium on carbon catalyst converted both components to 2-hexyl-5-nonylpyrrolidine (**3**).[6] On the other hand, hydrogenation in the presence of platinum on carbon or palladium on barium sulfate, conditions less likely to produce hydrogenolysis, produced only a small amount of **3** along with a major component whose mass spectrum showed a molecular ion at m/z 279, indicating two units of unsaturation, and other significant peaks at m/z 236 and m/z 152. These fragments result from the loss of C_3H_7 and C_9H_{19}, respectively, from carbons adjacent to nitrogen, and leave a bicyclic nucleus containing seven carbons and one nitrogen. This fragmentation is analogous to that of 3-heptyl-5-methylpyrrolizidine[7] and suggests that the carbon–nitrogen skeleton of **1** is 3-nonyl-5-propylpyrrolizidine (**4**).



Nearly 1 mg of natural **1** was obtained by preparative GC. The 360-MHz ^1H NMR spectrum of **1** showed the presence of five olefinic protons, three as a terminal olefin (d of d of t at 5.81 ppm, J = 18, 10, and 6 Hz; d at 4.97 ppm, J = 18 Hz; and d at 4.93 ppm, J = 10 Hz) and two as an *E* double bond attached to a methyl group (d of quartets at 5.59 ppm, J = 17, 6.5 Hz; and a d of d of quartets at 5.45 ppm, J = 17, 8.7, and 1.5 Hz) along with a resonance at 1.71 ppm (d of d, J = 6.5 and 1.5 Hz) for the attached methyl group. In addition, three methine protons on carbons adjacent to nitrogen appeared: a two-proton multiplet at 3.6 ppm and the third methine proton at 2.95 ppm. These data, the absence of three-carbon loss in the mass spectrum of **1**, and the ready hydrogenolysis of the allylic C–N bond support the presence of the pyrrolizidine system and establish the double-bond positions and geometry in **1**.

To demonstrate the presence of the pyrrolizidine ring system beyond question and determine the stereochemistry of **1**, a nonstereoselective synthesis was carried out. The reductive amination of the corresponding triketone **10** was expected to provide all four possible stereoisomers for comparison to the natural product.

(1) Presented in part at the 36th S.E. Regional Meeting of the American Chemical Society, Raleigh N.C., Oct. 24–26, 1984. Abst. 377.
(2) Jones, T. H.; Blum, M. S.; Fales, H. M. *Tetrahedron* **1982**, *38*, 194.
(3) Jones, T. H.; Highet, R. J.; Blum, M. S.; Fales, H. M. *J. Chem. Ecol.* **1984**, *10*, 1233.
(4) G. Ettershank, in a generic revision of the world Myrmicinae related to *Solenopsis* and *Pheidologeton*, raises the subgenus *Chelaner* Emery to generic status. *Aust. J. Zool.* **1966**, *14*, 93. *Chelaner* encompasses the Australasian ants formerly assigned to the subgenus *Notomyrmex* Emery (Type *Monomorium* (*Notomyrmex*) *antarcticum* = *Formica antarctica* White). *Chelaner* occurs throughout Australia and extends into New Guinea, New Caledonia, Lord Howe Island, and New Zealand. *C. antarcticus* (formerly *Monomorium antarcticum*) in New Zealand varies in size and color and may represent a complex of several species. Brown, W. L. *Acta Hymenopt.* **1958**, *1*, 29. A wide variety of ecological conditions is tolerated, included pastures, household gardens, *Nothoagus* forest and mountain tussock grassland. Biological information is scanty.
(5) Emery, C. *Genera Insectoram* **1922**, *174*, 166.
(6) Jones, T. H., Blum, M. S.; Howard, R. W.; McDaniel, C. R.; Fales, H. M.; DuBois, M. D.; Torees, J. *J. Chem. Ecol.* **1982**, *8*, 285.
(7) Jones, T. H.; Blum, M. D.; Fales, H. M.; Thompson, C. R. *J. Org. Chem.* **1980**, *45*, 4778.

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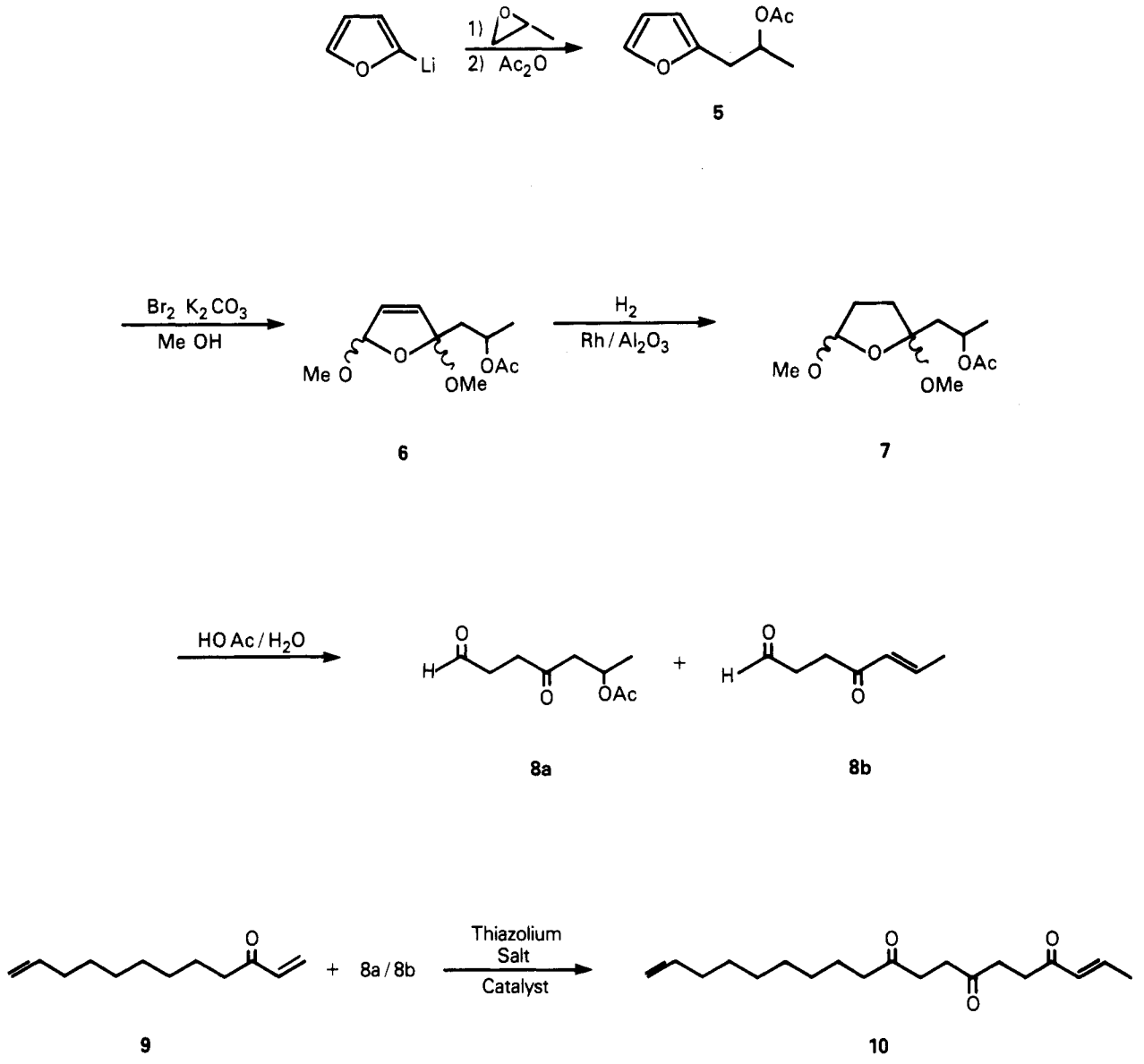
Scheme I. Synthesis of 10



Furan provided a 1,4-dicarbonyl precursor for the synthesis of **10** (Scheme I). Treating 2-furyllithium[8] sequentially with propylene oxide and acetic anhydride converted it to 2-(2-acetoxy-1-propyl)furan (**5**). Oxidative methoxylation of **5** with bromine in methanol provided a mixture of isomers of the unstable dimethoxy compound **6**.[9] Unfortunately, attempts to reduce the double bond of **6** by the usual platinum and palladium catalysts effected hydrogenolysis of the methoxy groups as well as hydrogenation. However, selective hydrogenation of the ring double bond was achieved by the use of rhodium on alumina catalyst and the resulting dimethoxytetrahydrofuran **7** could be hydrolyzed with 50% acetic acid to the keto aldehyde mixture **8a** and **8b**. The keto aldehyde **8a** was quite unstable, gradually decomposing to the unsaturated keto aldehyde, **8b** which subsequently polymerized.

When freshly prepared **8** was condensed with freshly prepared vinyl ketone **9**[5] in the presence of a thiazolium salt catalyst,[10] the 19-carbon triketone **10** could be obtained in ca. 50% yield from **5**. When the direct reductive amination[7] of **10** was attempted, only 3-(1-non-8-enyl)-5-propylpyrrolizidine (**11**) was formed as a mixture of isomers (m/z 277, M^+; 234, $M - C_3H_7$; 152, $M - C_9H_{17}$) as a result of the concomitant reduction of the conjugated double bond. When the conjugated double bond of **10** was epoxidized, subsequent reductive amination provided the unstable epoxypyrrolizidine **12**, a mixture of isomers, as the only nitrogenous product (m/z 291, M^+; 234, $M - C_3H_5O$; and 166, $M - C_9H_{17}$) (Scheme II).

Removal of the epoxide to reform the olefin on the three-carbon side chain of **1** was attempted with zinc and sodium iodide in acetic acid[11] and with sodium iodide in trifluoroacetic anhydride,[12] and in both cases, mixtures of double bond isomers of **1** were formed. However, reaction of **12** with potassium selenocyanate[13] afforded **1** as a mixture of isomers whose ^1H NMR spectra had olefinic signals identical with those of natural **1**. It could be hydrogenated to provide **4** under mild conditions.

As was the case for 3-heptyl-5-methylpyrrolizidine,[7] the stereochemistry of **1** could be assigned from its ^1H NMR

(8) Thomas, A. F.; Dubini, R. *Helv. Chim. Acta* **1974**, *57*, 2066.
(9) Floyd, M. B. *J. Org. Chem.* **1978**, *43*, 1641.
(10) Stetter, H.; Kuhlmann, H. *Tetrahedron Lett.* **1974**, 450.
(11) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.
(12) Sonnet, P. E. *J. Org. Chem.* **1978**, *43*, 1841.
(13) Behan, J. M., Johnston, R. A. W.; Wright, M. J. *J. Chem. Soc. Perkin Trans. 1* **1975**, 1216.

Scheme II. Conversion of 10 to 12

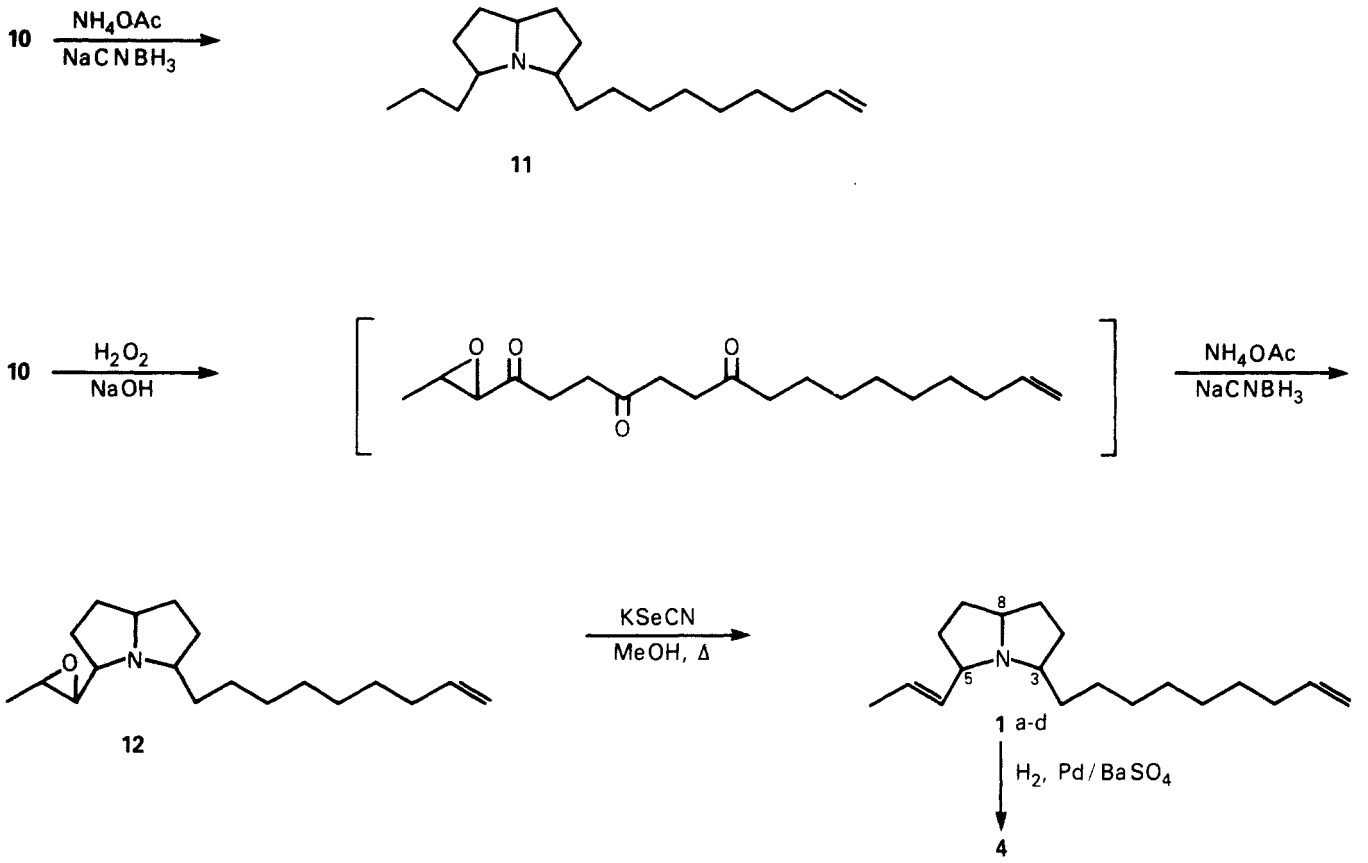
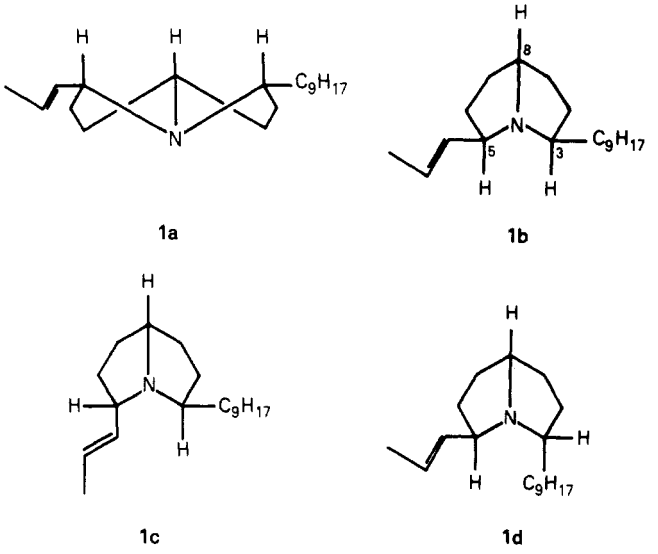


Chart I. Isomers 1a-d



spectrum once spectra were available from each of the four isomers. Only isomer **1a** has no signals further downfield than 2.5 ppm for its methine hydrogens, indicating that it is the trans-fused (5*Z*,8*Z*) isomer (Figure 1 and Chart I).[14] Each of the other three isomers shows at least one resonance at 3.6 ppm for the C-8 hydrogen, characteristic of a cis-fused pyrrolizidine system. The stereochemistry of the C-3 and C-5 substituents in **1b–d** is also revealed

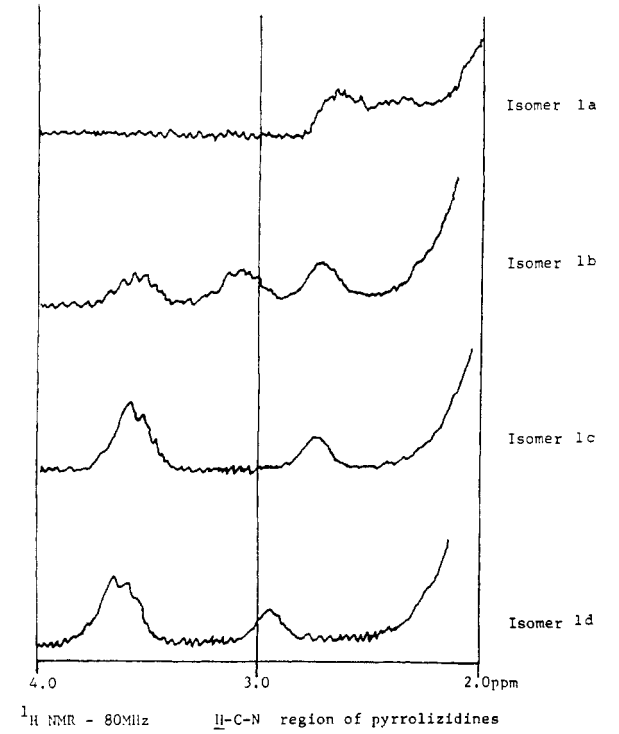


Figure 1. ^{1}H NMR spectra (80 MHZ) of the four isomers of 1.

by their nuclear magnetic resonance data. The 5*Z*,8*E* isomer **1b** has the furthest upfield signals for the other two methine hydrogens, which are on the opposite side of the ring system from the nitrogen lone pair.[15] In **1c** and **1d** there are signals for two protons at 3.6 ppm, indicating that either the C-3 or the C-5 methine hydrogen is cis to the

(14) Sonnet, P. E.; Netzel, D. A.; Mendoza, R. *Heterocycl. Chem.* This nomenclature system is that used to describe the configurational isomers of 3-butyl-5-methylindolizidine from the Pharaoh ant, *Monomorium pharaonis*. *J. Heterocycl. Chem.*, **1979**, *16*, 1041. In this system the methine hydrogens are described relative to the lowest numbered methine hydrogen, regardless of the conformation of the pyrrolizidine ring nucleus.

(15) Skvortsov, I. M.; Elvidge, V. A. *J. Chem. Soc. B* **1968**, 1589.

C-8 hydrogen, shifted downfield by the nitrogen lone pair.

Isomer **1c** is distinguished by its relatively shielded third methine hydrogen at 2.6 ppm. It is therfore assigned the 5*E*,8*E* configuration in which H-5 can experience anisotropic shielding from the propenyl group,[16] which is also in the cavity between the rings of the cis-fused pyrrolizidine system. An examination of Dreiding models reveals that the C-5 hydrogen is 2 Å from the propenyl double bond.

The models further suggested that in **1c** (and only in **1c**) the H-1 proton of the propenyl group is quite close to H-3 of the indolizidine, a situation which should give rise to an observable nuclear Overhauser effect. Sufficient quantities of **1b** and **1c** were available from this study to allow such experiments. NOE difference spectra of **1c**, in which the propenyl proton at 5.8 ppm was irradiated showed a clear positive effect in the aliphatic portions of the spectrum, absent from the corresponding spectra of **1b**. It is apparent from the models that the propenyl group of **1b** is preferentially oriented away from the nitrogen lone pair and the rest of the pyrrolizidine nucleus and the nonenyl side chain. On the other hand, in **1c** the propenyl protons are quite near two or three of the ring protons and the nonenyl side chain lies along the side of the propenyl group. The assignments of **1b** and **1c** thus secured further support the assignments of **1a** and **1d**.

Assignment of **1c** as the 5*E*,8*E* isomer and **1d** as the 5*E*,8*Z* isomer is also supported by the relative amounts of each in the isomeric mixture obtained by reductive amination of a triketone. The 5*E*,8*E* isomer **1c** predominates over the 5*E*,8*Z* isomer **1d**, since, in the latter, the larger 8-nonenyl chain would be forced into the cavity of the cis-fused pyrrolizidine rings. In addition, the 5*E*,8*Z* isomer **1d** has a much longer retention time than does **1c**, even greater than the retention time difference between **1b** and **1c** on a polar (SP-1000) GC column. This might be expected from the exposed, polar grouping of the propenyl double bond and the nitrogen lone pair, which is only possible in isomer **1d**. The naturally occurring pyrrolizidine has a gas chromatographic retention time and ^{1}H NMR spectrum identical with those of this last eluting isomer **1d**.

A 3,5-dialkylpyrrolizidine has been reported earlier from ants of the genus *Solenopsis*, but, in that case, the natural product was the "expected" least strained and hindered stereoisomer, having alkyl groups "exo" to the cis-fused pyrrolizidine ring system.[7] In the case of *Chelaner antarcticus*, the 3,5-disubstituted pyrrolizidine (**1d**), produced as the major venom component, is the stereoisomer in which the largest group is oriented into the cavity of the cis-fused pyrrolizidine ring system. In addition, the terminal double bonds and nonadecyl carbon skeleton of **1d** and **2** are more characteristic of the venom alkaloids of New World *Monomorium* species than of *Solenopsis* alkaloids. This is the first report of saturated nitrogen heterocycles from the venoms of ants other than those in the genera *Monomorium* and *Solenopsis*.

Experimental Section

All boiling points are uncorrected. ^{1}H NMR spectra were obtained at 80 MHz on a Varian FT-80 spectrometer and at 360 MHz on a Nicolet 360 MHz spectrometer. Mass spectra were obtained on either a Hewlett-Packard Model 5992 GC/MS equipped with a 2 m × 2 mm glass column packed with 1% OV-1 or on a LKB 9000 GC/MS equipped with 2 m × 2 mm glass column packed with 1% SP-1000 on Supelcoport. Gas chromatographic analyses were performed on a Gow-Mac Model 750 equipped with 2 m × 2 mm glass columns packed with 5% SP-1000 on Supelcoport or 5% OV-25 on Gaschrom Q. Preparative gas chromatography was performed on a modified Gow-Mac Model 150 fitted with 2 m × 5 mm alumina columns packed with 10% SE-30 on Chromosorb W or 10% SP-1000 on Supelcoport. Combustion analyses were performed by Galbraith Laboratories, Knoxville, TN.

Chelaner antarcticus. Three collections of *Chelaner antarcticus* from Nelson Province, N.W. South Island, New Zealand, were examined. The first contained 350 workers in approximately 4 mL of CH_2Cl_2, from Aorere Valley, the second contained 269 workers in approximately 4 mL of CH_2Cl_2, from near Motupipi, and the third contained 160 workers in approximately 4 mL of CH_2Cl_2 from Teal River Valley. GC/MS analysis (SP-1000) revealed the presence of two major alkaloidal components in a 6:1 ratio in all these collections. The second, minor, component had the following mass spectrum: MS, *m/z* (rel intensity) 277 (3, M^+), 276 (2), 195 (13), 194 (81), 153 (12), 152 (100), 110 (3), 109 (4), 98 (2), 96 (4), 95 (7), 84 (3), 82 (16), 81 (8), 79 (3), 70 (9), 69 (16), 68 (18), 67 (30), and 56 (19). The mass spectrum and retention time of this component were identical with those of authentic sample of *trans*-2-(1-hex-5-enyl)-5-(non-8-enyl)-pyrrolidine (**2**).[6] The first eluting, major component had the following mass spectrum: MS, *m/z* (rel intensity) 275 (M^+, 1), 274 (1), 260 (1), 246 (1), 244 (1), 23 (1), 151 (12), 150 (100), 122 (5), 108 (2), 107 (4), 106 (2), 105 (2), 95 (2), 94 (4), 91 (4), 82 (5), 81 (5), 80 (6), 79 (9), 70 (3), 69 (5), 68 (10), 67 (8), 56 (5), and 55 (12). Preparative gas chromatography (SP-1000) of the concentrated CH_2Cl_2 extracts of the sample from Aorere Valley provided nearly 1 mg of this component which had the following ^{1}H NMR spectrum: (360 MHz) δ 5.81 (1 H, d of d of t, J = 18, 10, and 6 Hz), 5.59 (1 H, dq, J = 17, 6.2 Hz), 5.45 (1 H, ddq, J = 17, 8.7, and 1.5 Hz), 4.97 (1 H, br d, J = 18 Hz), 4.93 (1 H, br d, J = 10 Hz), 3.6 (2 H, br s), 2.95 (1 H, br s), 2.1–1.7 (2 H, m) 1.71 (3 H, dd, J = 6.2, 1.5 Hz), 1.5–1.2 (20 H, broad signal).

Hydrogenation of the Extract. Approximately 5 mg of 5% Pd/C was added to a small portion of the CH_2Cl_2 extract, and a gentle stream of hydrogen was bubbled through the mixture for ca. 5 min. GC/MS analysis revealed the presence of only one alkaloidal product: MS, *m/z* (rel intensity) 281 (1, M^+), 280 (3), 197 (14), 196 (88), 155 (11), 154 (100), 82 (12), 69 (22), 68 (16), 56 (12), and 55 (19), which was identical with that of 2-hexyl-5-nonylpyrrolidine.[6] When small portions of the extract were hydrogenated in the same manner in the presence of 5% Pd/$BaSO_4$, GC/MS analysis showed the presence of two components in the same ratio as the original alkaloids. The first eluting, major component (**4**) had MS, *m/z* (rel intensity) 279 (4, M^+), 278 (4), 237 (12), 236 (68), 180 (3), 153 (12), 152 (100), 110 (5), 96 (3), 82 (6), 70 (6), 69 (8), 67 (12), 55 (5), and 54 (4). In this case the minor component had a mass spectrum identical with that obtained by hydrogenation over 5% Pd/C.

2-(2-Acetoxy-1-propyl)furan (5). A well-stirred solution containing 13 g (0.2 mol) of furan in 200 mL of anhydrous ether at 10 °C was treated with 150 mL of a 1.5 M solution of *n*-butyllithium in hexane under a nitrogen atmosphere. After 1 h, the solution was allowed to warm to room temperature for an additional 3 h. The solution was cooled to 5 °C, 11.6 g of propylene oxide was added dropwise, and the mixture was allowed to stir at room temperature for an additional 3 h. This mixture was cooled once again in an ice bath and carefully treated with 30 mL of acetic anhydride and then allowed to stir overnight at room temperature. Following the addition of 100 mL of water, the mixture was extracted with 3 × 50 mL portions of ether. The combined organic extracts were washed with saturated $NaHCO_3$ and brine and dried over anhydrous Na_2SO_4. After filtration, distillation gave 19.8 g of a colorless liquid (59% yield): bp 39–43 °C (0.2 mmHg); ^{1}H NMR (80 MHz) δ 7.31 (1 H, t, J = 1.6 Hz), 6.27 (1 H, m), 6.05 (1 H, d, J = 1.6 Hz), 5.14 (1 H, sextet, J = 6.5 Hz), 2.86 (2 H, d, J = 6.5 Hz), 2.00 (3 H, s), 1.24 (3 H, d, J = 6.5 Hz); MS, *m/z* (rel intensity) 125 (1), 109 (5), 108 (36), 82 (4), 81 (20), 79 (11), 77 (3), 53 (14), and 43 (100). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 63.94; H, 7.10.

Nonadeca-2,18-diene-4,7,10-trione (10). A solution containing 0.33 mL of bromine in 5 mL of methanol was added dropwise to a well-stirred mixture containing 1.0 g of furan **5** (6 mmol) and

(16) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: New York, 1969 pp 83–86.

1.25 g of anhydrous Na_2CO_3 in 20 mL of methanol at 0 °C. The mixture was poured into brine and extracted with three 25-mL portions of ether. The combined ether extracts were washed with 5% $Na_2S_2O_3$, saturated $NaHCO_3$, and brine and dried over anhydrous $MgSO_4$. Filtration and subsequent removal of the solvent yielded 1.2 g of an oil which consisted of a mixture of isomers of 2-(2-acetoxy-1-propyl)-2,5-dimethoxy-2,5-dihydrofuran (**6**), which were not completely separable by gas chromatography: NMR (80 MHz) δ 5.90 (2 H, m, CH–CH), 5.70 and 5.45 (1 H, br s, OCH-)), 5.05 (1 H, m, CHOAc), 3.49, 3.45, 3.15, and 3.05 (6 H, methoxy singlets), 2.05 and 1.95 (3 H, acetoxy singlets), 2.1 (2 H, d, J = 7.6 Hz, CH_2CH). Both components had identical mass spectra: MS, m/z (rel intensity) 230 (0.5, M^+), 199 (2), 170 (2), 169 (5), 140 (9), 139 (75), 130 (9), 129 (99), 113 (5), 112 (10), 111 (97), 102 (3), 101 (54), 81 (20), 79 (27), 69 (11), 55 (23), 53 (12), and 43 (100). A solution containing 1.0 g of the crude **6** and 0.2 g of 5% Rh on Al_2O_3 in 20 mL of methanol was shaken at 50 psi under an atmosphere of hydrogen for 10 min. Filtration followed by removal of the solvent in vacuo gave 0.9 g of crude **2-(2-acetoxy-1-propyl)-2,5-dimethoxytetrahydrofuran (7)**: NMR (80 MHz) δ 4.99 (2 H, br), 3.4 and 3.3 (3 H, a pair of methoxy singlets), 3.22 and 3.18 (3 H, a pair of methoxy singlets), 2.0 (3 H, s, OAc), 1.75–2.05 (6 H, m), and 1.25 (3 H, d, J = 7.6 Hz); MS, m/z (rel intensity) 140 (M – (60 + 32)), 109 (17), 109 (9), 97 (10), 85 (3), 84 (6), 83 (13), 81 (22), 80 (20), 79 (40), 77 (13), 71 (28), 69 (100), 55 (17), 53 (17), 43 (21), 41 (80). A solution containing 1.0 g of the crude **7** in 6 mL of 50% acetic acid was heated to 80 °C for 0.5 h. After careful treatment with excess $NaHCO_3$, followed by extraction with ether, the combined ether extracts were washed with brine and dried over anhydrous $MgSO_4$. Removal of the solvent provided an oil consisting of one major component by gas chromatographic analysis, ca. 0.8 g of crude **5-acetoxy-4-oxoheptanal (8a)**: NMR (80 MHz) δ 9.78 (1 H, m, CHO), 5.29 (1 H, sextet, J = 7.4 Hz, CHOAc), 2.74 (4 H, s, $COCH_2CH_2CO$), 2.01 (3 H, s, OAc), 1.92 (2 H, d, J = 7.6 Hz, -CH_2CH), and 1.26 (3 H, d, J = 7.6 Hz, $CHCH_3$). A pair of quartets at δ 6.85 (J = 16, 7.3 Hz) and a broad doublet at δ 6.10 (J = 16 Hz) were also present, indicative of a conjugated E double bond. GC/MS analysis revealed the presence of an early eluting component, which became predominant with time: MS, m/z (rel intensity) 126 (1, M^+), 98 (3), 97 (1), 84 (11), 83 (24), 70 (4), 69 (100), 57 (3), 55 (6), 43 (4), and 41 (80). The long retention time component corresponding to the acetoxy keto aldehyde had MS, m/z (rel intensity) 158 (M – 28), 129 (2), 127 (1), 126 (1), 125 (1), 98 (11), 85 (25), 83 (7), 69 (37), 57 (7), 56 (10), 55 (6), 43 (100). A solution containing 1.5 g of the crude acetoxy keto aldehyde **8a**, 1.4 g of 1,11-dodecadien-3-one (**9**), and 0.2 g of 5-(2-hydroxyethyl)-4-methyl-3-benzylthiazolium chloride in 3 mL of triethylamine was heated to reflux overnight under a nitrogen atmosphere. After the usual workup, 3.0 g of crude solid was obtained from which 1.5 g of a waxy yellow solid could be obtained by trituration of an ether solution with petroleum ether. Sublimation under reduced pressure gave a pure sample of trione **10** as a white solid: mp 56–58 °C; NMR (80 MHz) δ 6.85 (1 H, dq, J = 16, 7.3 Hz), 6.10 (1 H, br d, J = 16 Hz), 5.75 (1 H, ddt, J = 18, 10, and 6 Hz), 5.0 (1 H, br d, J = 18 Hz), 4.9 (1 H, br d, J = 10 Hz), 2.80 (4 H, s), 2.71 (4 H, s), 2.43 (2 H, t, J = 7.5 Hz), 1.89 (3 H, d, J = 7.3 Hz), 2.0 (2 H, m), and 1.3 (10 H, br s); MS (direct probe), m/z (rel intensity) 306 (11, M^+), 288 (19), 237 (8), 229 (10), 209 (23), 197 (11), 196 (100), 181 (44), 178 (49), 155 (13), 154 (97), 135 (19), 127 (35), 125 (90), 121 (14), 112 (18), 111 (20), 99 (10), 98 (15), 97 (32), 95 (16), 85 (12), 84 (14), 83 (15), 69 (79), and 55 (8).

Reductive Amination of Trione 10. A solution containing 0.25 g of trione **10** (0.8 mmol), 0.1 g of $NaCNBH_3$, 0.1 g of NH_4OAc, and 0.0 1 g of KOH in 20 mL of methanol was stirred overnight under a nitrogen atmosphere. After the usual workup, GC/MS analysis of the resulting oil (0.2 g) revealed the presence of four isomeric nitrogenous products: MS, m/z (rel intensity) 277 (1, M^+), 235 (7), 234 (43), 153 (14), 152 (100), 124 (5), 122 (4), 112 (3), 109 (4), 108 (4), 82 (4), 81 (3), 70 (6), 68 (5), 67 (9), 55 (10), and 41 (16).

3-(1-Non-8-enyl)-5-((*E*)-1-prop-1-enyl)pyrrolizidine (1). A solution containing 1.0 g (3.2 mmol) of trione **10** in 10 mL of 2:1 methanol–tetrahydrofuran was cooled to 5 °C and treated with 1.5 mL of 30% H_2O_2. Subsequently, 1.5 mL of 1 M NaOH was added dropwise and the mixture was stirred for 2 h at 0 °C and allowed to warm to room temperature for 1 h. Following the addition of brine, the mixture was extracted with ether, and the ether extracts were dried over anhydrous $MgSO_4$. After filtration, the solvent was removed in vacuo, and the residue was taken up in 20 mL of methanol, treated with 0.3 g of NH_4OAc and 0.25 g of $NaCNBH_3$, and allowed to stir overnight under a nitrogen atmosphere. After the usual workup, CG/MS analysis of the residual oil (0.7 g) revealed only the presence of inseparable isomeric products (greater than 90% of the residue), all having the same mass spectrum: MS m/z (rel intensity) 291 (1, M^+), 290 (0.5), 276 (2), 235 (4), 234 (22), 167 (12), 166 (100), 124 (3), 122 (7), 122 (7), 110 (3), 108 (3), 94 (2), 82 (2), 68 (3), 67 (3), 55 (7), and 41 (12). The olefinic region of the NMR (80 MHz) spectrum of this unpurified product had only the following signals: δ 5.9 (ddt, J = 18, 10, and 6 Hz), 5.0 (br d, J = 18 Hz), and 4.9 (br d, J = 10 Hz). This residue was taken up in 10 mL of methanol, treated with 1.0 g of KSeCN, and heated to reflux for 72 h. Following removal of the solvent in vacuo, the mixture was chromatographed over 10 g of alumina by using a 1:1 mixture of cyclohexane/toluene to give 0.5 g of pyrrolizidine **1**. GLC analysis (5% SP-1000 column) showed four components **1a**, **1b** **1c**, and **1d** in the ratio 3:7:10:1, which had retention times of 5.6, 7.8, 8.8, and 10.5 min, respectively, at an oven temperature of 175 °C (N_2 carrier gas, flow rate 60 mL/min). The four components had almost identical mass spectra: MS, m/z (rel intensity) 275 (M^+, 2), 274 (1), 260 (1), 246 (1), 244 (1), 234 (1), 151 (11), 150 (100), 122 (6), 110 (1), 109 (2), 108 (3), 107 (3), 106 (1), 105 (1), 95 (1), 94 (1), 91 (1), 82 (5), 81 (4), 80 (4), 79 (8), 70 (2), 69 (3), 68 (9), 67 (7), 56 (3), and 55 (12).

Anal. Calcd for $C_{19}H_{33}N$: C, 82.84; H, 12.08. Found: C, 82.49; H, 12.13.

The four isomers were separated by preparative GLC (10% SP-1000 column), and ^1H NMR spectra were obtained for each. All four isomers had the following resonances in common: (360 MHz) δ 5.81 (1 H, ddt, J = 18, 10, and 6 Hz), 5.59 (1 H, dq, J = 17, 6.5 Hz), 5.45 (1 H, ddq, J = 17, 8.7, and 1.5 Hz), 4.97 (1 H, br d, J = 18 Hz), 4.93 (1 H, br d, J = 10 Hz), 1.7 (3 H, dd, J = 6.5, 1.5 Hz), 2.1–1.7 (2 H, m), and 1.5–1.2 (20 H, broad complex signal). As shown in Figure 1, the chemical shifts of the methine protons were quite different for each isomer. **1a**: δ 2.5 (2 H, m), and 2.3 (1 H, m). **1b**: δ 3.6 (1 H, m), 3.1 (1 H, m), and 2.7 (1 H, m). **1c**: δ 3.61 (2 H, m), and 2.69 (1 H, m). **1d**: δ 3.6 (2 H, m), and 2.95 (1 H, m). A small portion of the synthetic mixture was carefully hydrogenated in the presence of $Pd/BaSO_4$ to give an inseparable mixture of isomers having mass spectra identical with that recorded for 3-nonyl-5-propylpyrrolizidine (**4**) as described above. Isomer **1d** had identical GC retention times by direct comparison under isothermal conditions with the major component of the methylene chloride extract from *C. antarcticus*.

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Registry No. **1a**, 102422-82-2; **1b**, 102492-03-5; **1c**, 102492-04-6; **1d**, 102492-05-7; **2**, 81943-70-6; **4**, 102422-84-4; **5**, 102422-76-4; **6**, 102422-77-5; **7**, 102422-78-6; **8a**, 102422-79-7; **8b**, 102422-85-5; **9**, 51284-51-6; **10**, 102422-80-0; **11** (isomer1), 102422-81-1; **11** (isomer 2), 102492-00-2; **11** (isomer 3), 102492-01-3; **11** (isomer 4), 102492-02-4; **12**, 102422-83-3; furan, 110-00-9; propylene oxide, 75-56-9.