NaOH, and heated at reflux (105 °C) for 21 h. The cooled reaction mixture was acidified to pH 1 with 3 M HCl. The precipitated solids were collected by filtration and dried at 125 °C to give 32.1 g (100%) of 2-chloro-4-(methylsulfonyl)benzoic acid (**5b**) as a white solid: mp 194–6 °C (H_2O, lit.[5] mp 198–9 °C).

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Registry No. **1a**, 10130-89-9; **1b**, 61953-04-6; **1d**, 98-59-9; **1e**, 51904-91-7; **1f**, 2494-79-3; **1g**, 134178-04-4; **1h**, 10130-89-9; **1n**, 54090-40-3; **5a**, 4052-30-6; **5b**, 53250-83-2; **5c**, 118939-05-2; **5d**, 3185-99-7; **5e**, 50390-76-6; **5f**, 51522-07-7; **5g**, 134178-05-5; **5h**, 32910-75-1; **51**, 98948-26-6; **5j**, 99186-88-6; **5k**, 101349-84-2; **5l**, 21571-66-4; **5m**, 100059-51-6; **5n**, 110964-79-9; Na_2SO_3, 7757-83-7; $ClCH_2CO_2H$, 79-11-8; $BrCH_2CO_2H$, 79-08-3; $H_3CCHClCO_2H$, 598-78-7; $H_3C(CH_2)_3CHBrCO_2H$, 616-05-7; $HO_2CCH_2CHBrCO_2H$, 923-06-8; $H_3CCH_2CHBrCO_2H$, 80-58-0; Cl_2CHCO_2H, 79-43-6; $H_3C(CH_2)_2CHBrCO_2H$, 584-93-0; 2-chloro-4-(chlorosulfonyl)-benzoyl chloride, 130264-17-4.

Short Synthesis of (±)-5-(3-Furyl)octahydro-8-methylindolizines, Alkaloids Related to a Component of Castoreum. Use of Radical Cyclization

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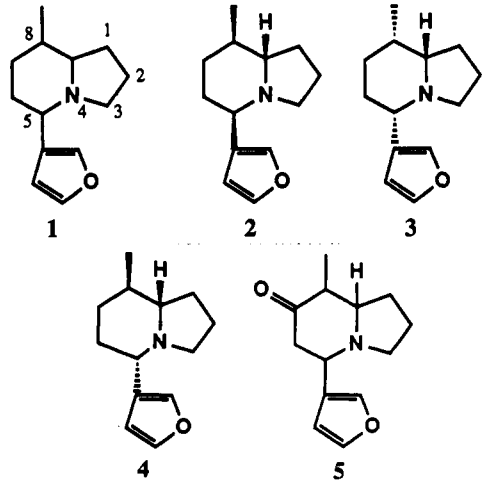
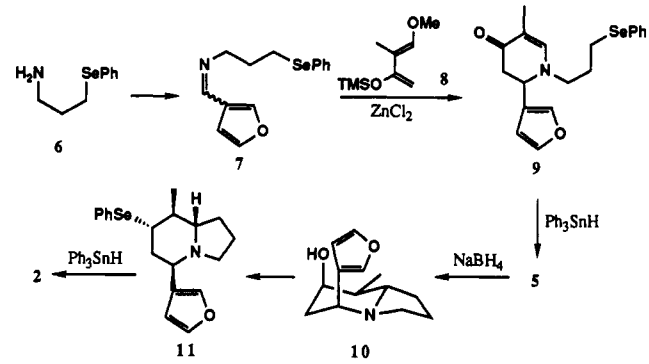
Castoreum, an extract from the scent glands of the Canadian beaver (*Castor fiber* L.), is a commercial product used in perfumery.[1] The material contains a minute amount of a substance believed to be 5-(3-furyl)octahydro-8-methylindolizine (**1**),[2] which is a simple member of the Nuphar alkaloid[3] class. The structural assignment is based on mass spectral considerations, as there was insufficient material for further characterization.[2]



1 **2** **3** **4** **5**

Of the possible isomers corresponding to the proposed structure, three have been synthesized in racemic form,

Scheme I



and these have the relative stereochemistries shown in **2**,[4] **3**,[4] and **4**.[5] The latter was made from the bicyclic ketone **5** (obtained as a mixture of stereoisomers) by base-catalyzed equilibration and removal of the carbonyl (C=O → CH_2). We report here an alternative and very short route to a ketone of gross structure **5** and its conversion into **2**. Our bicyclic ketone **5** was identical (^1H NMR) with the major isomer obtained previously,[5a] and so the present work also represents a formal synthesis of **4**. The approach we have used is based on Diels–Alder cycloaddition followed by radical closure[6] (Scheme I).

The required imine **7** was assembled by mixing the readily available amine **6**[7] with commercial 3-furaldehyde. The crude imine was then treated with an excess of diene **8**[8] in the presence of 2 equivalents of anhydrous zinc chloride.[9] It was then possible to isolate the adduct **9** in 72% yield. This material underwent efficient ring closure (83%) upon treatment with triphenyltin hydride to give a single ketone **5**. Reduction ($NaBH_4$) afforded alcohol **10**, and the structure of this compound was determined by X-ray analysis. Treatment of **10** with phenyl selenocyanate in the presence of tributylphosphine[10] produced the corresponding selenide **11**, and stannane reduction[11] then gave **2**. The stereochemistry assigned to **2** follows from that established for the alcohol **10**.

Experimental Section

General. The same experimental techniques were used as reported previously.[12]

***N*-(3-Furylmethylene)-3-(phenylseleno)propylamine (7).** A mixture of amine **6**[7] (58 mg, 0.271 mmol), 3-furaldehyde (26 mg, 0.271 mmol), and $MgSO_4$ (ca. 100 mg) in ether (2 mL) was stirred at room temperature for 1 h. Filtration, followed by evaporation of the solvent, gave the crude imine in near quantitative yield (^1H NMR, 200 MHz), and the material was used directly without purification: ^1H NMR ($CDCl_3$, 200 MHz) δ

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0.85–2.20 (m, 2 H), 3.00 (t, J = 7.2 Hz, 2 H), 3.61 (t, J = 6.6 Hz, 2 H), 6.78 (s, 1 H), 7.18–7.78 (m, 7 H), 8.15–8.20 (m, 1 H).

(3*E*)-4-Methoxy-3-methyl-2-[(trimethylsilyl)oxy]-1,3-butadiene (8). (a) (3*E*)-4-Methoxy-3-methyl-3-buten-2-one. A modification of the literature procedure[8b] was used. Methyl ethyl ketone (8.5 mL, 94.9 mmol) was added dropwise over 30 min to a refluxing mixture of NaH (60% w/w dispersion in oil, 3.50 g, 91.3 mmol) and methyl formate (4.2 mL) in THF (500 mL). After 1 h, Me_2SO_4 (12.667 g, 100.4 mmol) was injected, and refluxing was continued for 30 min. Water (15 mL) was then added, and heating was continued for a further 30 min. The mixture was cooled and diluted with ether (500 mL). The organic phase was washed with aqueous ammonia (2 M, 300 mL), water (300 mL), and brine (300 mL) and dried ($MgSO_4$). Evaporation of the solvent and flash chromatography of the residue over silica gel (5 × 15 cm) with 1:3 EtOAc–hexane gave (3*E*)-4-methoxy-3-methyl-3-buten-2-one (3.5 g, 34%) as a homogeneous (^{1}H NMR) oil: ^{1}H NMR ($CDCl_3$, 80 MHz) δ 1.65 (s, 3 H), 2.25 (s, 3 H), 3.85 (s, 3 H), 7.25 (s, 1 H).

(b) (3*E*)-3-Methyl-4-methoxy-2-[(trimethylsilyl)oxy]-1,3-butadiene (8). A different procedure from that reported[8] in the literature was followed. The above butenone (2.21 g, 19.36 mmol) was added dropwise to a stirred and cooled (−78 °C) solution of LDA [21.39 mmol, from *n*-butyllithium (1.55 M, 13.8 mL, 21.39 mmol) and *i*-Pr_2NH (2.17 g, 21.40 mmol)] in THF (30 mL). After 30 min, Me_3SiCl (75% v/v in Et_3N, 5 mL) was added dropwise. After a further 10 min, the cooling bath was removed. After about 1 h, the mixture was quenched with ether (50 mL), filtered through Florisil, evaporated, and distilled to give diene 8[8] (2.50 g, 70%): bp 65–70 °C (14 mmHg); ^{1}H NMR ($CDCl_3$, 80 MHz) δ 0.22 (s, 9 H), 1.68 (s, 3 H), 3.65 (s, 3 H), 4.14 (s, 1 H), 4.25 (s, 1 H) 6.50 (s, 1 H).

(±)-2-(3-Furyl)-2,3-dihydro-5-methyl-1-[3-(phenylseleno)propyl]-4-pyridinone (9). The crude imine 7 (79 mg, 0.271 mmol) in THF (1 mL) was added to a stirred solution of diene 8 (250 mg, 1.340 mmol) and anhydrous $ZnCl_2$ (60 mg, 0.440 mmol) in THF (2 mL) at room temperature. After 40 h, the resulting mixture was diluted with EtOAc (10 mL), washed with water (2 × 5 mL) and brine (5 mL), dried ($MgSO_4$), and evaporated. Flash chromatography of the residue over silica gel (1 × 15 cm) with 1:1 EtOAc–hexane gave 9 (73 mg, 72%) as an oil containing 8% of an isomer (^{1}H NMR, 400 MHz): FT-IR ($CHCl_3$ cast) 1602, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.68 (s, 3 H), 1.89 (quintet, J = 7.0 Hz, 2 H), 2.58 (AB q, J = 16.5, 7.5 Hz, 1 H), 2.72 (AB q, J = 16.5, 6.5 Hz, 1 H), 2.77–2.93 (m, 2 H), 3.19 (t, J = 7.0 Hz, 2 H), 4.42 (dd, J = 7.5, 6.5 Hz, 1 H), 6.34, (s, 1 H), 6.85 (s, 1 H), 7.25–7.30 (m, 4 H), 7.37 (s, 1 H), 7.45–7.51 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 12.57, 24.26, 29.00, 42.69, 52.30, 52.96, 105.49, 109.03, 123.01, 127.24, 129.15, 132.95, 140.09, 143.71, 151.50, 190.03; exact mass m/z calcd for $C_{19}H_{21}NO_3Se$ 375.0738, found 375.0738.

(±)-5-(3-Furyl)hexahydro-8-methyl-7(1*H*)-indolizinone (5). The general procedure for radical cyclization[6] was followed by using the above selenide 9 (93 mg, 0.248 mmol) in benzene (20 mL), Ph_3SnH (105 μL, 144 mg, 0.411 mmol) in benzene (10 mL), and AIBN (8 mg, 0.048 mmol) in benzene (10 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm) with 3:2 EtOAc–hexane gave 5 (45 mg, 83%) as a homogeneous (^{1}H NMR, 400 MHz) oil: FT-IR ($CHCl_3$ cast) 1709 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.04 (d, J = 6.3 Hz, 3 H), 1.54–1.64 (m, 1 H), 1.65–1.75 (m, 1 H), 1.88–2.03 (m, 2 H), 2.34–2.39 (m, 2 H), 2.46 (q, J = 8.3 Hz, 1 H), 2.57 (dd, J = 6.5, 2.8 Hz, 2 H), 2.91–3.02 (m, 2 H), 4.45 (dd, J = 6.5, 2.3 Hz, 1 H), 6.70 (s, 1 H), 7.22 (s, 1 H), 7.38 (s, 1 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 10.52, 21.96, 30.68, 45.35, 49.50, 50.50, 52.01, 61.83, 111.08, 121.53, 140.66, 142.59, 211.33; exact mass m/z calcd for $C_{13}H_{17}NO_2$ 219.1259, found 219.1258. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.15; H, 7.72; N, 6.53.

(5α,7α,8α,8aα)-(±)-5-(3-Furyl)octahydro-8-methyl-7-indolizinol (10). $NaBH_4$ (ca. 50 mg, 1.32 mmol) was added to a cooled (0 °C) solution of ketone 5 (200 mg, 0.904 mmol) in EtOH (2 mL). After 10 min the mixture was filtered through a pad of silica gel. Evaporation of the solvent followed by crystallization of the crude product from 1:19 EtOAc–hexane gave 10 (175 mg, 86%): FT-IR ($CHCl_3$ cast) 3500 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.03 (d, J = 7.0 Hz, 3 H), 1.35–1.51 (m, 1 H), 1.51–2.10 (m, 7 H), 2.18–2.28 (m, 1 H), 2.49 (br q, J ~ 8.3 Hz, 1 H), 2.70 (br q, J ~ 8.2 Hz, 1 H), 2.80 (td, J = 6.0, 3.6 Hz, 1 H), 3.90–3.96 (m, 1 H), 4.06 (dd, J = 5.9, 3.6 Hz, 1 H), 6.49 (s, 1 H), 7.36 (s, 1 H), 7.50 (s, 1 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.33, 20.96, 29.35, 37.82, 40.56, 50.24, 50.60, 57.27, 69.35, 111.96, 124.90, 140.70, 142.38; exact mass m/z calcd for $C_{13}H_{19}NO_2$ 221.1416, found 221.1411.

(5α,7β,8α,8aα)-(±)-5-(3-Furyl)octahydro-8-methyl-7-(phenylseleno)indolizine (11). A modification of a general literature procedure[10] was used. A solution of PhSeCN (66 mg, 0.360 mmol) in THF (1.5 mL) was added over 15 min to a refluxing solution of 10 (40 mg, 0.181 mmol) and Bu_3P (73 mg, 0.360 mmol) in THF (2 mL), and refluxing was continued for a further 1.5 h. The solvent was then evaporated, and flash chromatography of the residue over silica gel (1 × 15 cm) with 2:5 EtOAc–hexane gave 11 (41 mg, 63%) as a homogeneous (^{1}H NMR, 400 MHz) oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18 (d, J = 7.0 Hz, 3 H), 1.35–1.55 (m, 3 H), 1.70–1.810 (m, 1 H), 1.89–1.98 (m, 1 H), 2.17–2.33 (m, 3 H), 2.36 (q, J = 8.3 Hz, 1 H), 2.78 (td, J = 6.0, 3.6 Hz, 1 H), 3.12 (td, J = 8.2, 5.0 Hz, 1 H), 4.12 (dd, J = 8.3, 3.6 Hz, 1 H), 6.27 (s, 1 H), 7.20–7.30 (m, 4 H), 7.36 (s, 1 H), 7.50–7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.10, 20.96, 30.14, 39.33, 42.62, 46.05, 49.89, 52.83, 62.20, 111.94, 122.59, 127.63, 128.96, 129.20, 135.57, 140.05, 142.33; exact mass m/z calcd for $C_{19}H_{23}NOSe$ 361.0944, found 361.0953.

(5α,8α,8aα)-(±)-5-(3-Furyl)octahydro-8-methylindolizine (2). A solution of selenide 11 (32 mg, 0.089 mmol), Ph_3SnH (134 μL, 47 mg, 0.133 mmol), and AIBN (4 mg, 0.024 mmol) in benzene (10 mL) was refluxed for 2 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (1 × 15 cm) with 1:1 EtOAc–hexane gave 2 (18 mg, 99%) as a homogeneous (^{1}H NMR, 400 MHz) oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93 (d, J = 6.4 Hz, 3 H), 1.22–1.42 (m, 3 H), 1.48–1.69 (m, 1 H), 1.62–1.93 (m, 4 H), 2.00–2.10 (m, 2 H), 2.29 (q, J = 8.7 Hz, 1 H), 2.82 (td, J = 8.7, 2.8 Hz, 1 H), 4.16 (m, 1 H), 6.34 (s, 1 H), 7.35–7.37 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 19.07, 20.36, 29.44, 29.55, 30.67, 37.40, 50.03, 51.85, 62.09, 112.42, 123.00, 140.13, 141.99; exact mass m/z calcd for $C_{13}H_{19}NO$ 205.1466, found 205.1461.

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Supplementary Material Available: Crystal structure data for 9 and ^{1}H NMR spectra of 2, 6, 9, and 11 (13 pages). Ordering information is given an any current masthead page.

Photocyclization in an Alcohol Solution Containing Dissolved Base. A New Development in Enamide Photochemistry

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Introduction

To organic chemists, the photocyclization of 1,3,5-hexatrienic systems undoubtedly represents one of the most synthetically useful photochemical processes. Indeed, the photoinduced electrocyclic ring closure of 6π electron conjugated hydrocarbon systems has been extensively exploited. For example, it has been known for over 40 years that stilbene and related compounds undergo pho-

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