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Synthesis of Pyrrolizidine Oximes 222 and 236: Novel Alkaloids of a Dendrobatid Poison Frog

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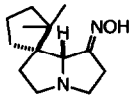
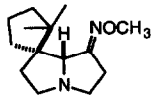
Abstract: The structures of two novel spiropentanopyrrolizidine oxime alkaloids, namely 2',3',5',6',7',7a'-hexahydro-2,2-dimethylspiro[cyclopentane-1,1'-[1H]-pyrrolizine]-7'-oxime (**1**) and 2',3',5',6',7',7a'-hexahydro-2,2-dimethylspiro-[cyclopentane-1,1'-[1H]pyrrolizine]-7'-oxime-O-methyl ether (**2**) have been confirmed by synthesis. The route involved synthesis of nitropolyzonamine (**4**), a known millipede alkaloid, from 2,2-dimethylcyclopentanone in 6 steps. After conversion of **4** to the ketone **6**, the oxime **1** and O-methyl oxime **2** were obtained. The relative stereochemistry of synthetic nitropolyzonamine was confirmed by x-ray crystallography.

Three unique minor alkaloids were isolated in the eighties from skin extracts of the Panamanian poison-frog *Dendrobates pumilio*.[1] The simplest (alkaloid **222**), has been characterized as a spiropentano-pyrrolizidine oxime, **1**, while the second(alkaloid **236**), as the corresponding *O*-methyl oxime, **2**, and the third (alkaloid **252H**) as a hydroxy *O*-methyl oxime, **3**. These oxime alkaloids are remarkably similar to nitropolyzonamine, **4**, an alkaloid isolated from the defense secretions of the North American millipede *Polyzonium rosalbum*.[2] In 1987, tentative tricyclic amidine structures were proposed for these compounds[1]; however, subsequent studies demonstrated that these tentative structures were incorrect and new structures, based upon more extensive ^{1}H- and ^{13}C-NMR spectroscopy were proposed.[3] The synthesis of oximes **1** and **2** now has been completed and serves to secure the structural assignments of these compounds and to allow for pharmacological investigation.



1



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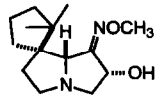

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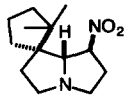

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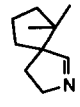

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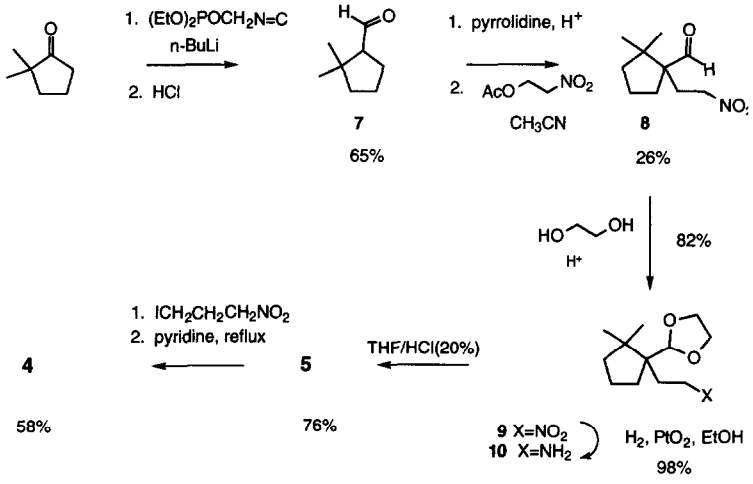
The strategy for the synthesis of oximes **1-3** is based on the route developed by Meinwald *et al.*[2] for the synthesis of both nitropolyzonamine (**4**) and polyzonimine (**5**). The pyrrolizidine oximes **1** and **2** would then be obtained from nitropolyzonamine by conversion of the nitro group to the ketone, **6** (Scheme 3), followed by formation of the corresponding oxime and oxime ether. Pyrrolizidine oxime **3** could also be obtained from the same ketone, but would require additional manipulation to incorporate the C-3 hydroxyl group.

Meinwald reports an overall yield of 22% for the synthesis of polyzonimine from the epoxide of 3,3-dimethylcyclohexene.[2] Addition of 3-iodonitropropane[4] to polyzonimine led to formation of a quaternary iminium salt which underwent cyclization to nitropolyzonamine (**4**) in refluxing pyridine. They reported that the formation of nitropolyzonamine, a crystalline solid, was highly selective, resulting in the formation of only one diastereomer. The relative and absolute stereochemistry of a perchlorate salt of nitropolyzonamine isolated from millipedes has been established by x-ray crystallography.[2]

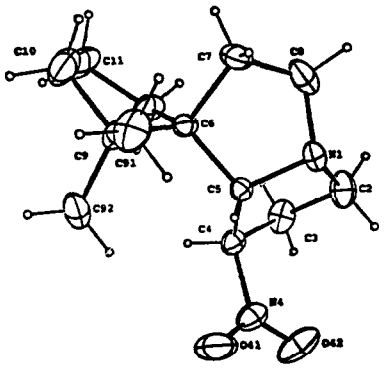
Scheme 1



Our synthetic route (Scheme 1) departed from Meinwald's in that we prepared aldehyde **7** from 2,2-dimethylcyclopentanone in 65% yield utilizing the Wittig-Horner reagent diethyl isocyanomethylphosphonate.[5] 2,2-Dimethylcyclopentanone is commercially available whereas 3,3-dimethylcyclohexene is not and requires several synthetic steps. The pyrrolidine enamine of aldehyde **7** underwent the desired Michael reaction (26% for two steps) with nitroethylene, generated in situ from 2-nitroethyl acetate[6], forming the two contiguous quaternary centers found in all of the natural products. Aldehyde **8** was protected as the ethylene acetal and then reduced as reported by Takano *et al.*[2] to give **10** in 80% yield (two steps). This intermediate (**10**) was converted with acid treatment to the volatile compound polyzonimine (**5**) which was converted to the quaternary iminium salt with 3-iodonitropropane and then to nitropolyzonamine (**4**) by heating the crude salt at 100 °C in pyridine for several hours. The overall yield for this 3-step conversion is 44% (76% for each of

three steps). Nitropolyzonamine, prepared by the above synthetic route, has a mass spectrum identical to that reported by Meinwald[2] and the ^1H (300 MHz, $CDCl_3$) and ^{13}C (75 MHz, $CDCl_3$) NMR spectra are consistent with the proposed structure. Unfortunately, spectral data for natural or Meinwald's synthetic nitropolyzonamine is not available for comparison. We confirmed the relative stereochemistry of synthetic nitropolyzonamine by x-ray crystallography[7] and it was identical to that reported for nitropolyzonamine isolated from millipedes.[2]

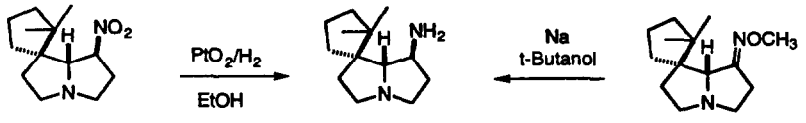
ORTEP Representation of Nitropolyzonamine



Nitropolyzonamine, prepared by our synthetic route was correlated with pyrrolizidine oxime **2** by reduction (PtO_2/H_2/EtOH) to give the same amine (**11**) as obtained when natural pyrrolizidine oxime **2** was reduced[3] (Na, t-butanol) (Scheme 2). This result served as preliminary evidence that the chemical structure assignments for **1** and **2** are correct.

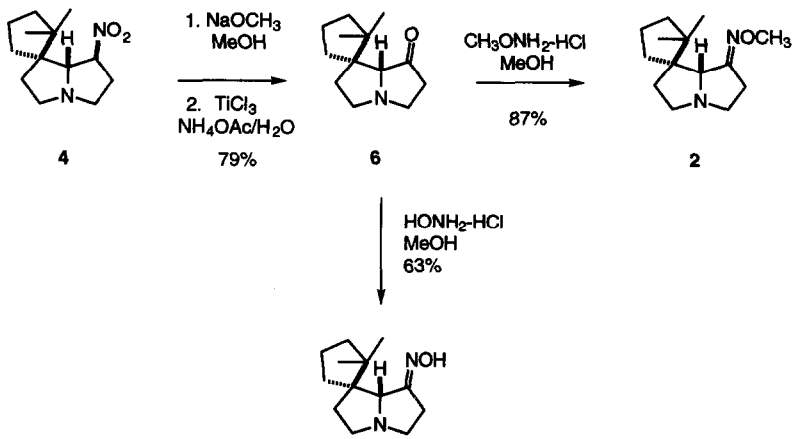
Nitropolyzonamine could be converted to the ketone **6** with sodium methoxide and buffered, aqueous $TiCl_3$[8] in 79% yield (Scheme 3). This ketone could be subsequently converted into the oximes **1** and **2** with hydroxylamine hydrochloride or methoxylamine hydrochloride, respectively, in refluxing methanol.

Scheme 2



4 Synthetic **11** **2** Natural

Scheme 3



The ^1H NMR (C_6D_6, 300 MHz) spectra of the synthetic pyrrolizidine oximes **1** and **2** were virtually identical to that reported for the natural compound. Both the ^{13}C NMR and ^1H NMR in deuterochloroform of synthetic **2** was similar to, but not identical to that reported for the natural compound, possibly due to traces of DCl in the solvent of the isolated compound. The ^{13}C NMR (300 MHz, C_6D_6) of synthetic **1** was very similar to that reported for the natural compound except that we did not observe any signals for the quaternary carbons due to a small sample size. The mass spectral data, GC-MS (ion trap), and GC-FTIR data for the natural and synthetic compound are identical. Co-injection of the synthetic pyrrolizidine oximes with the corresponding natural compound resulted in one peak on the GC trace.

Experimental

General Experimental Details: Tetrahydrofuran (THF) was distilled from sodium and benzophenone. Anhydrous ether (Et_2O) and hexanes were purchased from Mallinkrodt and used without further purification. Toluene, pyridine and acetonitrile (CH_3CN) were distilled from CaH_2 at atmospheric pressure. Butyllithium was titrated using 2,5-dimethoxybenzyl alcohol as an indicator.[9] Diethyl isocyanomethylphosphonate was purchased from Fluka. Anhydrous methanol (MeOH) and ethanol (EtOH) were purchased from Midwest Grain Products and Mallinkrodt, respectively, and used without further purification. All other reagents were used without further purification unless otherwise specified. All low-temperature reactions were run with an internal monitor. ^1H NMR and ^{13}C NMR spectra were obtained at 300 and 75 MHz, respectively, with a Varian Gemini spectrometer. ^1H NMR chemical shifts are reported as δ values in ppm relative to TMS. ^1H NMR coupling constants are reported in Hz and refer to apparent multiplicities and not true coupling constants. Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet); dd (doublet of doublets); etc. All mass spectra were measured on a JEOL SX102 spectrometer. Intensities are

reported in parentheses relative to the base peak set equal to 100. GC-Mass spectra were measured with a Finnigan Model 800 ion trap mass detector interfaced with a Varian model 3400 gas chromatograph equipped with a bonded fused silica (25 m x 0.32 mm) HP-5 column. Infrared spectra were vapor phase as obtained with a Hewlett Packard 5890 GC/IR also with a bonded fused silica (25 m x 0.32 mm) HP-5 column. Hydrogenations were performed using a Packard Model 7525 Hydrogen Generator. Column chromatography was performed with Fluka HF_{254} silica gel. All reactions were run under nitrogen and concentrations were done under water aspirator pressure with a Buchi rotary evaporator unless otherwise specified.

2,2-Dimethylcyclopentanecarboxaldehyde (7): A solution of n-BuLi (18.6 mL of a 1.5 M solution in hexane, 28 mmol) was added dropwise to a solution of diethylisocyanomethyl phosphonate (4.6 mL, 29 mmol) and ether (40 mL) at -70 °C, keeping the temperature of the reaction below -55 °C during the addition. The reaction was maintained at -70 °C for 1 h, then a solution of 2,2-dimethylcyclopentanone (3.2 g, 29 mmol) and ether (40 mL) was added dropwise. The reaction was allowed to warm and maintained at room temperature for 5 h, then conc. HCl (40 mL) was added dropwise. The reaction was maintained at room temperature for 12 h, diluted with H_2O (100 mL) and the aqueous and organic layers were separated and the aqueous layer was extracted with ether (3 x 50 mL). The combined organic extracts were passed through a plug of alumina, concentrated and distilled at reduced pressure (27 mm, 65-70 °C) to give 2.3 g (65%) of **7** as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.71(d, J=3.2 Hz, CHO), 2.33(ddd, J=3.1, 8.0, 8.0 Hz, H-1), 2.00-2.13(m, 1H), 1.67-1.89(m, 3H), 1.48-1.57(m, 2H), 1.12(s, CH_3), 0.98(s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 205.2, 61.3, 43.6, 42.5, 29.2, 24.5, 23.4, 22.6; FTIR 2588, 1735 cm^{-1}; MS (EI) m/z 126 (5), 108 (14), 96 (60), 81 (63), 70 (100).

1-(2-Nitroethyl)-2,2-dimethyl-cyclopentanecarboxaldehyde (8): A solution of **7** (2.5 g, 20 mmol), pyrrolidine (1.7 g, 20 mmol), p-toluenesulfonic acid (15 mg) and toluene (50 mL) was refluxed utilizing a Dean-Stark apparatus. After 5 h the reaction was allowed to cool to room temperature, concentrated and used without purification in the next step. A solution of 2-nitroethyl acetate[6] (3.4 g, 28 mmol), and CH_3CN (22 mL) was added to a crude solution of the enamine of **7** and CH_3CN (68 mL). The reaction was maintained at room temperature for 2 h, then HCl (5% aqueous solution, 80 mL) was added and the resulting mixture was extracted with EtOAc (3 x 50 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution and then brine, dried ($MgSO_4$), concentrated and purified by column chromatography (4:1 hexane-EtOAc) to give 1.0 g (26% for two steps) of **8** as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.62(s, CHO), 4.37(ddd, J=5.6, 10.4, 12.9 Hz, 1H, C*H*HNO_2), 4.19(ddd, J=5.6, 10.4, 12.9 Hz, 1H, C*H*HNO_2), 2.51(ddd, J=5.7, 10.3, 13.7 Hz, 1H, C*H*HCH_2NO_2), 1.98-2.17(m, 2H), 1.81-1.92(m, 2H), 1.60-1.70(m, 3H), 1.03(s, 3H, CH_3), 1.01(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 205.2, 72.8, 60.1, 46.4, 40.4, 29.2, 27.8, 24.9, 23.9, 20.7; FTIR 2970, 2887, 1731, 1570, 1378 cm^{-1}; MS (EI) m/z 199(3), 198(75) 151(100), 110(85), 91(53), 69(68), (CI-NH_3) m/z 200.1274 (MH^+ 200.1287 calcd for $C_{10}H_{17}NO_3$).

2-(2,2-Dimethyl-1-(2-nitroethyl)cyclopentyl)-1,3-dioxolane (9): A solution of **8** (110 mg, 0.55 mmol), ethylene glycol (0.32 mL, 5.5 mmol), toluene (4.5 mL) and p-toluenesulfonic acid (10 mg) was heated to reflux for 3 h. The reaction was allowed to cool to room temperature and diluted with EtOAc (15 mL). The

solution was washed with H_2O (15 mL) and then brine, dried ($MgSO_4$), and concentrated to an oil, which was purified by column chromatography (9:1 hexane-EtOAc) to give 110 mg (82%) of **9** as an oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.58-4.68(m, 2H, OCHO, C*H*HNO_2), 4.42(ddd, J=5.0, 11.0, 12.9 Hz, C*H*HNO_2), 3.95-4.05(m, 1H), 3.80-3.91(m, 2H), 3.70-3.80(m, 1H), 2.38(ddd, J=5.9, 11.9, 13.7 Hz, 1H), 1.86-1.97(m, 2H), 1.54-1.74(m, 5H), 1.01(s, CH_3), 1.00(s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 107.5, 74.5, 65.2, 63.6, 50.3, 44.9, 40.5, 31.1, 28.2, 25.2, 24.9, 20.3; FTIR 2988, 2891, 1566, 1475, 1380, 1102 cm^{-1}; MS (CI-NH_3) m/z 244.1537 (MH^+ 244.1549 calcd for $C_{12}H_{22}NO_4$).

2-(2,2-Dimethyl-1-(2-aminoethyl)cyclopentyl)-1,3-dioxolane (10): A suspension of PtO_2 (16 mg) in a solution of **9** (0.25 g, 1.0 mmol) and EtOH (5.0 mL) was maintained at room temperature for 10 h under a hydrogen atmosphere (30 psi). The reaction was filtered through a plug of Celite and washed with EtOH. The filtrate was concentrated to give 0.21 g (98%) of **10**, which was not further purified. ^1H NMR (300 MHz, $CDCl_3$) δ 4.72 (s, OCHO), 3.68-4.02(m, 6H), 2.84(dt, J=5.2, 11.6, 11.6 Hz, 1H, C*H*HNH_2), 2.72(dt, J=5.2, 11.5, 11.5 Hz, 1H, CH*H*NH_2), 1.35-1.92(m, 6H), 0.994(s, 3H, CH_3), 0.987(s, 3H, CH_3);.^{13}C NMR (75 MHz, $CDCl_3$), 108.1, 65.0, 64.0, 50.5, 44.4, 41.1, 39.3, 36.1, 31.5, 25.1(double intensity), 20.6; FTIR 2988, 2891, 1566, 1475, 1380, 1102 cm^{-1}; MS (CI-NH_3) m/z 214.1807 (MH^+ 214.1807 calcd for $C_{12}H_{24}NO_2$).

Polyzonamine (6,6-dimethyl-2-azaspiro[4.4]non-1-ene), (5) and nitropolyzonamine, (hexahydro-2,2-dimethyl-7'-nitro-spiro[cyclopentane-1,1'-[1H]pyrrolizine]), (4): A solution of **10** (80 mg, 0.38 mmol), THF (1.5 mL) and HCl (1.5 mL of a 20% aqueous solution), was maintained at room temperature overnight. The reaction was diluted to 10 mL with EtOAc and neutralized with excess $NaHCO_3$ saturated solution (10 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and the solvent removed under a stream of nitrogen. The crude oil contained the rather volatile polyzonimine (**5**), which was converted to nitropolyzonamine (**4**) without purification. Neat iodonitropropane[4] (0.65 g, 3.0 mmol) was added to the crude oil and the reaction was heated to 60 °C for 20 min. The flask was cooled and concentrated to an oily solid under vacuum. The oily solid was washed with ether (10 mL) and the ether was decanted from the solid and saved. Pyridine (4 mL) was added to the solid material and the resulting solution was heated to reflux for 3h. The reaction was allowed to cool, concentrated by rotary evaporation, diluted with EtOAc and washed with H_2O (10 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$), concentrated and purified by column chromatography (EtOAc) to give 36 mg (40%) of **4**. The ether extracts were cooled to 0 °C for 2 days and more salt was collected which was heated in pyridine (1 mL) and gave an additional 4 mg (4%) of **4** upon workup. Total yield 44% from **10**. Polyzonimine (**5**): ^1H NMR (300 MHz, $CDCl_3$) δ 7.4 (br s, 1H), 3.80(m, 2H), 1.48-1.94(m, 8H), 0.91(s, 3H, CH_3), 0.88(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 172.8, 60.7, 43.5, 40.1, 35.5, 30.7, 24.7, 23.9, 20.5; FTIR 2982, 2881, 1622, 1468, 1379, 1321, 1078, 963 cm^{-1}; MS (EI) m/z 151(15), 136(34), 108(22), 95(57), 82(100), 67(20), 55(20); (FAB) m/z 152.1438 (MH^+ 152.1439 calcd for $C_{10}H_{18}N$). Nitropolyzonamine (**4**): mp 50-55 °C (Literature[2] 65.5-66.5 °C). ^1H NMR (300 MHz, $CDCl_3$) δ 4.82(td, J=3.8, 3.8, 7.6 Hz, H-4), 3.78(d, J=3.9 Hz, H-5), 3.28(ddd, J=6.6, 8.8, 11.5 Hz, H-2), 3.09(ddd, J=2.2, 9.0, 11.0 Hz, H-8), 2.87(ddd, J=4.0, 7.3, 11.5 Hz, H-2), 2.39-2.52(m, 2H, H-3, H-8), 2.15-2.28(m, H-3), 2.00(ddd,

J=6.9, 11.4, 11.4 Hz, H-7), 1.64-1.80(m, 3H), 1.38-1.53(m, 4H), 0.99 (s, 3H, CH_3), 0.89(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 88.2, 73.6, 56.6, 53.3, 52.4, 42.8, 39.2, 35.3, 32.4, 32.0, 24.9, 23.5, 19.6; FTIR 2988, 2889, 1561, 1472, 1369 cm^{-1}; MS (EI) m/z 238(6), 192(21), 179(10), 165(18), 150(10), 136(26), 122(41), 108(50), 95(67), 82(100), 67(59), (CI-NH_3) m/z 256($M+NH_3$)$^+$, 239 (MH^+); (FAB) m/z 238.1671 (M^+ 238.1681 calcd for $C_{13}H_{22}N_2O_2$).

Hexahydro-2,2-dimethyl-7'-oxo-spiro[cyclopentane-1,1'-[1H]pyrrolizine] (6): A solution of nitropolyzonamine **4** (16 mg, 0.067 mmol) and sodium methoxide (1.6 mL of a 0.1 M solution in methanol) was added to a solution of $TiCl_3$ (105 mg, 0.67 mmol), H_2O (420 μL) and NH_4OAc (1 mL of a 4.0 M solution). After 45 min the reaction was diluted with H_2O, and neutralized with saturated $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3x8 mL), and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The crude material was purified by column chromatography (EtOAc) to give 11 mg (79%) of **6** as an oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.25-3.34(m, 2H), 3.08(ddd, J=4.8, 6.7, 10.4 Hz, 1H), 2.99(ddd, J=6.3, 9.1, 11.5 Hz, 1H), 2.86(ddd, J=6.1, 8.2, 9.9 Hz, 1H), 2.50(td, J=8.5, 8.5, 17 Hz, 1H), 2.30(ddd, J=6.0, 7.4, 17.8 Hz, 1H), 1.81-2.02(m, 2H), 1.39-1.71(m, 5H), 1.25(ddd, J=3.6, 8.5, 15.6 Hz, 1H), 0.958(s, CH_3), 0.950(s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 218.1, 70.7, 58.8, 53.4, 48.0, 43.4, 38.6, 37.2, 35.6, 33.5, 26.0, 23.3, 19.8; FTIR 2985, 1758, 1471, 1132 cm^{-1}; MS (EI) m/z 179(80), 149(27), 136(38), 122(29), 109(95), 95(64), 82(100), 67(36); (CI-NH_3) m/z 208 (MH^+).

Hexahydro-2,2-dimethyl-7'-amino-spiro[cyclopentane-1,1'-[1H]pyrrolizine] (11): PtO_2 (5 mg) was suspended in a solution of **4** (6.5 mg, 0.027 mmol) and EtOH(0.5 mL) under a hydrogen atmosphere (25 psi) for 10 h. The reaction mixture was filtered through Celite and concentrated to give 6 mg (100%) of **11,** which was not further purified. ^1H NMR (300 MHz, $CDCl_3$) δ 3.00-3.30(m, 4H), 2.58-2.66(m, 1H), 2.41-2.51(m, 1H), 1.34-2.11(m, 12H), 0.92(s, CH_3), 1.01(s, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 75.9, 55.7, 53.8, 53.4, 52.6, 42.7, 39.7, 36.7, 35.7, 32.0, 25.5, 23.8, 19.8; FTIR 2901, 2885, 2796, 1618, 1470, 1123 cm^{-1}; MS (FAB) 209.2014 (MH^+ 209.2018 calcd for $C_{13}H_{25}N_2$).

2',3',5',6',7',7a'-Hexahydro-2,2-dimethylspiro[cyclopentane-1,1'-[1H]pyrrolizine]-7'-oxime (1): A solution of **6** (4.6 mg, 0.022 mmol), MeOH(1.0 mL) and hydroxylamine hydrochloride (15 mg, 0.22 mmol) was heated to 70-75 °C for 12 h in a sealed tube. The solution was concentrated to an oily solid, which was dissolved in saturated $NaHCO_3$ solution (3 mL) and extracted with EtOAc (3 x 3 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated to give 3.1 mg (63%) of **1** as an oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.79(s, 1H), 2.92-3.14(m, 2H), 2.70-2.88(m, 3H), 2.50-2.63(m, 1H), 1.91-2.07(m, 2H), 1.39-1.68(m, 5H), 1.17-1.28(m, 2H), 0.90(s, CH_3), 0.905(s, CH_3); ^1H NMR (300 MHz, C_6D_6), δ 3.90(s, 1H), 2.72-2.90(m, 3H), 2.36-2.48(m, 3H), 2.03-2.13(m, 1H), 1.34-1.82(m, 4H), 1.16-1.24(m, 1H), 1.10(s, 3H), 1.01-1.07(m, 1H), 0.89(s, 3H); ^{13}C NMR (75 MHz, C_6D_6) 68.3, 52.9, 50.7, 39.6, 35.9, 34.6, 26.9, 26.0, 24.0, 20.3; FTIR 3641, 2984, 2885, 2829, 1470, 1345,1218,1104, 922; MS (FAB) 223.1817 (MH^+ 223.1810 calcd for $C_{13}H_{23}N_2O$).

2',3',5',6',7',7a'-Hexahydro-2,2-dimethylspiro[cyclopentane-1,1'-[1H]pyrrolizine]-7'-oxime-O-methyl ether (2): A solution of **6** (8.0 mg, 0.039 mmol), MeOH (1.5 mL) and methoxylamine hydrochloride (16 mg, 0.20 mmol) was heated to 65-70 °C for 12 h. The solution was concentrated to an oily solid, which was

dissolved in saturated $NaHCO_3$ solution (3 mL) and extracted with EtOAc (3 x 3 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated to an oil which was passed through a short plug of silica gel, eluting with EtOAc to yield 8.0 mg (87%) of **2**. ^1H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H, $NOCH_3$), 3.74(s, 1H, H-5), 2.92-3.08(m, 3H), 2.63-2.86(m, 3H), 2.43-2.54(m, 1H), 1.90-2.01(m, 2H), 1.42-1.66(m, 4H), 1.16-1.28(m, 1H), 0.96(s, 3H, CH_3), 0.98(s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 164.4, 68.0, 61.7, 58.5, 52.9, 50.5, 43.5, 39.1, 35.6, 34.3, 27.0, 25.8, 23.9, 20.0; FTIR 2982, 2886, 2825, 1470, 1390, 1321, 1243, 1054, 863 cm^{-1}; MS (FAB) 237.1960 (MH^+ 237.1967 calcd for $C_{14}H_{25}N_2O$).

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