Microanalytical Laboratories, Urbana, Ill. Mass spectra were determined by Dr. Roger Upham and his assistants at the University of Minnesota on an AEI-MS-30 instrument. Optical rotations were determined on a Perkin-Elmer 241 instrument. Radioactivity measurements were carried out on a Nuclear Chicago liquid scintillation Mark II counter, using as solvent dioxane–ethanol with the usual scintillators.[17]

(17) A. R. Friedman and E. Leete, *J. Am. Chem. Soc.*, **85**, 2141 (1963).
(18) The Fourier transform ^{13}C NMR spectra were determined by Dr. Robert M. Riddle at the University of Minnesota on a Varian XL-100 spectrometer (25.2 MHz). Assignments were made by comparison with the ^{13}C NMR spectrum of nicotine[19] and by continuous wave off-resonance decoupling.
(19) E. Leete, *Bioorg. Chem.*, **6**, 273 (1977).
(20) Obtained by the acid hydrolysis of 2-ethoxy-4-methyl-2,3-dihydropyran (Aldrich Chemical Co.) and distilled (bp 80 °C, 100 mm) immediately before use. Its IR (neat) had absorptions at 2740 (CH stretch of CHO) and 1730 cm^{-1} (C=O): K. Adler, H. Betzing, R. Kuth, and H. A. Dortmann, *Justus Liebigs Ann. Chem.*, **620**, 73 (1959).

Synthesis of a "Bridged Nicotine": 1,2,3,5,6,10b-Hexahydropyrido[2,3-*g*]indolizine[1]

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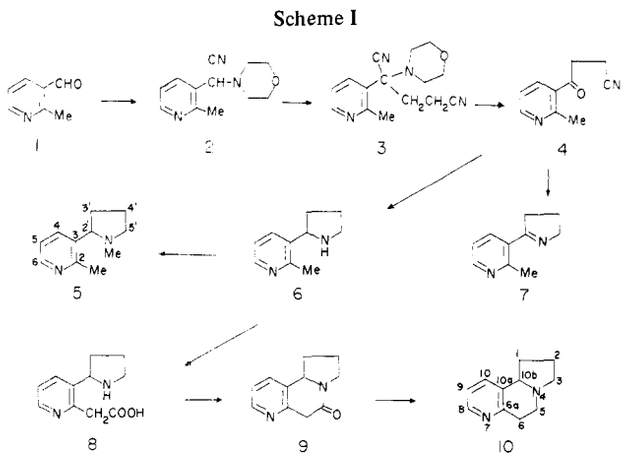
The bridged nicotine **10**, a pyridoindolizidine, has been prepared by reduction of the tricyclic lactam **9**, which was obtained by cyclization of the amino acid **8**. This compound was produced by carboxylation of the dilithium derivative of 2-methylnornicotine, which was synthesized by recently developed methods.

Many analogues of nicotine have been prepared, and their pharmacology has been studied in an effort to obtain structure–activity relationships.[3] Haglid has reviewed[4] this work and stated that it would be of great interest to examine the pharmacology of bridged nicotines, such as the pyridoindolizidine **10**, in which the configuration of the pyrrolidine ring would be fixed relative to the pyridine ring. This article describes the synthesis of compound **10** and also 2-methylnicotine (**5**) by the route illustrated in Scheme I.[5]

2-Methylpyridine-3-aldehyde (**1**) was converted to 2-methylnornicotine (**6**) by the procedure recently developed for the synthesis of myosmine and nornicotine.[7] Reaction of **1** with morpholine and sodium cyanide in the presence of perchloric acid yielded **2**. The anion generated by reaction of **2** with potassium *tert*-butoxide was added to acrylonitrile to yield the Michael addition product **3**. Acid hydrolysis of this compound afforded the keto nitrile **4**.[8] Hydrogenation of this compound in the presence of Raney nickel yielded a mixture of 2-methylmyosmine (**7**) and 2-methylnornicotine (**6**). The yield of the latter increased with the duration of the hydrogenation. Reaction of 2-methylnornicotine with 2 equiv[9] of butyllithium, followed by treatment with carbon dioxide, afforded the carboxylic acid **8**, which was cyclized to the lactam **9**. This reaction was achieved with the aid of 1-ethyl-3(3-dimethylaminopropyl)carbodiimide.[10] However, a better yield of the lactam was obtained by prolonged chloroform extraction of a solution of the amino acid **8** in dilute aqueous hydrochloric acid. Reduction of the lactam with borane in tetrahydrofuran produced the desired bridged nicotine **10** in excellent yield. Reduction of the lactam with lithium aluminum hydride gave only a 30% yield.

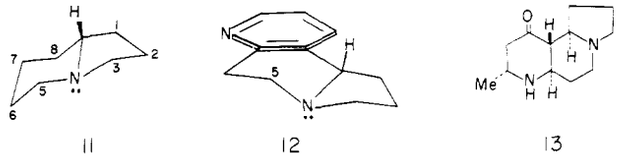
Scheme I



The indolizidine ring system can exist in two configurations, a conversion of the cis to the trans fused ring junction occurring by inversion of the lone electron pair. It is generally agreed that the trans configuration (**11**) is thermodynamically more stable.[11] The infrared spectrum of **10** has Bohlmann bands[12] at 2730, 2675, and 2630 cm^{-1} characteristic of an axial C–H group trans to the lone electron pair on nitrogen. We thus assign the trans configuration to the indolizidine ring system in the bridged nicotine **10**. The (*S*) enantiomer of **10** is illustrated in formula **12**. In nicotine an analogous configuration has been found,[13] i.e., the *N*-methyl group (equivalent to C-5 in the bridged nicotine) is trans to the pyridine ring.

No Bohlmann bands were found in the IR spectrum of the lactam **9**. It is, therefore, suggested that this compound has a *cis*-indolizidine ring junction. Indeed, inspection of a Dreiding model of the lactam indicates a preference for the cis isomer.

The heterocyclic system found in compounds **9** and **10** exists in elaeokanidine A (**13**), one of the alkaloids of *Elaeocarpus*



11 12 13

kaniensis.[14] The pharmacology of 2-methylnicotine and the bridged nicotine **10** is being examined and will be reported elsewhere.

Experimental Section[15]

α-(2-Methyl-3-pyridyl)-α-morpholinoacetonitrile (2). 2-Methylpyridine-3-aldehyde[16] (3.31 g, 27 mmol) was added to a solution of morpholine perchlorate (5.64 g, 30 mmol) in morpholine (35 mL), and the mixture was heated at 76 °C for 1 h under N_2. Sodium cyanide (1.32 g, 27 mmol) in water (2 mL) was added and the mixture was heated at 100 °C for 45 min. The cooled solution was poured into 10% sodium carbonate (100 mL) and extracted with chloroform. The residue obtained on evaporation of the dried (K_2CO_3) extract was triturated with ether to yield **2** (4.82 g, 82%). Crystallization from ether afforded colorless prisms: mp 112.5–113.5 °C; IR (Nujol) ν_{max} 1590, 1580, 1105 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.58 (t, 4 H, NCH_2), 2.65 (s, 3 H, $PyCH_3$), 3.69 (t, 4 H, OCH_2), 4.90 (s, 1 H, α-H), 7.17 (dd, 1 H, 5-PyH), 7.80 (dd, 1 H, 4-PyH), 8.54 (dd, 1 H, 6-PyH); *m/e* 217 (M^+). Anal.

0022-3263/78/1943-2125$01.00/0

Calcd for $C_{12}H_{15}N_3O$: C, 66.34; H, 6.96; N, 19.34. Found: C, 66.60; H, 7.19; N, 19.53.

γ-Cyano-γ-(2-methyl-3-pyridyl)-γ-morpholinobutyronitrile (3). Methanolic potassium hydroxide (30%, 0.75 mL) was added dropwise during 5 min to a stirred solution of **2** (2.64 g, 12.2 mmol) in *tert*-butyl alcohol (60 mL) under N_2 at room temperature. After 30 min acrylonitrile (0.78 g, 14.6 mmol) in *tert*-butyl alcohol (30 mL) was added during 2.5 h. The mixture was stirred an additional 1.5 h and then water (90 mL) was added. A dried (K_2CO_3) chloroform extract, on evaporation, afforded a pale pink oil (3.3 g, 100%) which crystallized on standing. An analytical sample was obtained as colorless plates from ether: mp 99.5–100.5 °C; IR (KBr pellet) ν_{max} 2240 (C≡N), 1685, 1560 cm^{-1}; H^1 NMR ($CDCl_3$) δ 2.31 (m, 8 H), 2.82 (s, 3 H, $PyCH_3$), 3.78 (t, 4 H, OCH_2), 7.22 (dd, 1 H, 5-PyH), 7.94 (dd, 1 H, 4-PyH), 8.59 (dd, 1 H, 6-PyH); *m/e* no M^+, 243 (M − HCN), 228, 203, 118, 117, 86. Anal. Calcd for $C_{15}H_{18}N_4O$: C, 66.64; H, 6.71; N, 20.72. Found: C, 66.47 H, 6.84; N, 20.66.

3-Cyano-1-(2-methyl-3-pyridyl)propan-1-one (4). Compound **3** (1.81 g) was heated in 50% aqueous acetic acid (25 mL) at 60 °C for 18 h. The solution was then made basic with K_2CO_3 and extracted with chloroform. The residue obtained on evaporation of the dried (K_2CO_3) extract was crystallized from a mixture of ether and chloroform to afford colorless plates of the keto nitrile **4** (0.99 g, 85%): mp 81.5–83.5 °C; IR (Nujol) ν_{max} 2250 (C≡N), 1675 (C=O), 1565 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.74 (s, 3 H, $PyCH_3$), 2.75 (t, 2 H, CH_2CN), 3.30 (t, 2 H, $COCH_2$), 7.23 (dd, 1 H, 5-PyH), 7.93 (dd, 1 H, 4-PyH), 8.52 (dd, 1 H, 6-PyH); *m/e* 174 (M^+). Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 69.13; H, 5.72; N, 16.31.

2-Methylnornicotine (6) and 2-Methylmyosmine (7). The keto nitrile (**4**) (1.07 g) dissolved in 95% ethanol (200 mL), previously saturated with ammonia, was hydrogenated in the presence of Raney nickel (about 5 g) for 6 h at 3 atm of pressure. Evaporation of the filtered reaction mixture afforded a pale yellow oil which was subjected to preparative TLC on silica gel PF-254 (Merck), developing with a mixture of chloroform, methanol, and concentrated ammonia (90:10:1). Extraction (methanol–chloroform) of the lower zone (R_f 0.25) followed by distillation (110 °C, 4×10^{-3} mm) of the residue obtained on evaporation afforded (*R,S*)-2-methylnornicotine (0.39 g, 39%) as a colorless oil: IR (neat) ν_{max} 3310 (NH), 1590 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32–2.39 (m, 5 H, NH, 3′,4′-H), 2.54 (s, 3 H, $PyCH_3$), 2.58–3.29 (m, 2 H, 5′-H), 4.30 (t, 1 H, 2′-H), 7.03 (dd, 1 H, 5-PyH), 7.78 (dd, 1 H, 4-PyH), 8.27 (dd, 1 H, 6-PyH); *m/e* 162 (M^+), 161, 133, 119, 70. It yielded a dipicrate, mp 186.5–187 °C dec, from ethanol. Anal. Calcd for $C_{22}H_{20}N_8O_{14}$: C, 42.59; H, 3.25; N, 18.06. Found: C, 42.59; H, 3.25; N, 17.95. **6** has been prepared independently.[8]

The upper zone (R_f 0.66) on extraction yielded 2-methylmyosmine (0.61 g, 61%) as a colorless oil: IR (neat) ν_{max} 1620 (C=N), 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.01 (m, 2 H, 4′-H), 2.73 (s, 3 H, $PyCH_3$), 2.92 (t, 2 H, 5′-H), 4.11 (t, 2 H, 3′-H), 7.11 (dd, 1 H, 5-PyH), 7.70 (dd, 1 H, 4-PyH), 8.51 (dd, 1 H, 6-PyH); *m/e* 160 (M^+), 159, 132, 131. Its dipicrate had mp 185.5–186 °C. Anal. Calcd for $C_{22}H_{18}N_8O_{14}$: C, 42.74; H, 2.93; N, 18.12. Found: C, 42.61; H, 3.05; N, 17.88.

By extending the hydrogenation time the amount of 2-methylnornicotine was increased at the expense of the 2-methylmyosmine. Thus hydrogenation of the keto nitrile **4** (4.5 g) for 17 h afforded 2-methylnornicotine (3.49 g, 83%). Reduction of 2-methylmyosmine with sodium borohydride in ethanol also yielded 2-methylnornicotine.

2-Methylnicotine (5). 2-Methylnornicotine (106 mg), 40% formaldehyde (3 mL), and 90% formic acid (3 mL) were heated at 100 °C for 24 h. The residue obtained on evaporation of the reaction mixture was made basic with K_2CO_3, extracted with chloroform, dried (K_2CO_3), and evaporated. The residue was subjected to preparative TLC on silica gel PF-254, developing with a mixture of chloroform, ethanol, and concentrated ammonia (100:20:1). The lower zone (R_f 0.31) afforded unreacted 2-methylnornicotine (11 mg, 11%). The upper zone (R_f 0.56) yielded (*R,S*)-2-methylnicotine, obtained as a colorless oil (81 mg, 70%) after distillation (110 °C, 4×10^{-3} mm): IR (neat) ν_{max} 1580, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.18 (s, 3 H, NCH_3), 2.55 (s, 3 H, $PyCH_3$), 7.30 (dd, 1 H, 5-PyH), 7.78 (dd, 1 H, 4-PyH), 8.29 (dd, 1 H, 6-PyH); *m/e* 176 (M^+), 175, 84. Its dipicrate was obtained as yellow prisms from ethanol, mp 224.5–225 °C. Anal. Calcd for $C_{23}H_{22}N_8O_{14}$: C, 43.54; H, 3.50; N, 17.66. Found: C, 43.29; H, 3.42; N, 17.87. **5** has been prepared independently.[8]

Its diperchlorate was obtained as colorless needles from a mixture of methanol and ether, mp 264–270 °C dec. Anal. Calcd for $C_{11}H_{16}N_2 \cdot 2HClO_4$: C, 35.03; H, 4.81; N, 7.43; Cl, 18.80. Found: C, 35.10; H, 4.90; N, 7.58; Cl, 18.93.

5-Oxo-1,2,3,5,6,10b-hexahydropyrido[2,3-*g*]indolizine (9). 2-Methylnornicotine (0.84 g, 5.2 mmol) dissolved in tetrahydrofuran (15 mL) was added to a solution of butyllithium (5.2 mL of a 2.2 M solution in hexane, 11.4 mmol) in tetrahydrofuran at −78 °C in a N_2 atmosphere. After stirring at this temperature for 2 h, carbon dioxide (liberated from $BaCO_3$ (2.06 g, 10.5 mmol) with concentrated sulfuric acid) was passed into the reaction mixture, which was then allowed to slowly warm to room temperature during 4 h. 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (3.72 g, 20.9 mmol) in water (20 mL) was added and the solution was stirred at room temperature for 6 h. The reaction mixture was made basic with ammonia and evaporated; the residue was extracted with methylene chloride. The dried (K_2CO_3) extract was evaporated and the residue was subjected to preparative TLC on silica gel PF-254, developing with a mixture of chloroform, ethanol, and concentrated ammonia (90:10:1). The main zone (R_f 0.45) was extracted with a mixture of chloroform and methanol (85:15) and evaporated; the residue was distilled (110 °C, 4×10^{-3} mm) to yield a pale yellow oil (0.4 g, 41%) which crystallized on standing: mp 91.5–92.5 °C; UV (95% ethanol) λ_{max} (log ε) 254 (sh, 3.66), 260 (3.75), 264 nm (sh, 3.70); IR (neat liquid) ν_{max} 1640 cm^{-1}; ^1H NMR ($CDCl_3$) complex overlapping signals including δ 3.70 (s, 2 H, CH_2CO), 7.20 (dd, 1 H, 9-PyH), 7.51 (d, 1 H, 10-PyH), 8.48 (d, 1 H, 8-PyH). Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.18; H, 6.43; N, 14.88. Found: C, 70.37; H, 6.20; N, 15.11.

A higher yield (78%) of the lactam **9** was obtained by the following procedure. The reaction mixture after carboxylation was added to 1 N HCl (25 mL) which was then extracted with ether (2 × 20 mL). The residual aqueous solution was then extracted in a continuous extractor with chloroform for 60 h. The aqueous solution was then adjusted to pH 9.5 with ammonia and extracted for an additional 18 h with chloroform. The combined, dried (K_2CO_3) chloroform extracts were evaporated to yield the lactam, purified by sublimation as before.

1,2,3,5,6,10b-Hexahydropyrido[2,3-*g*]indolizine (10). Borane in tetrahydrofuran (1 M, 10 mL, 12 mmol) was added rapidly at 0 °C to a solution of the lactam **9** (256 mg, 1.36 mmol) in tetrahydrofuran (12 mL) in a N_2 atmosphere. The solution was then refluxed for 1.5 h and cooled and water (5 mL) was carefully added. The residue obtained on evaporation was refluxed with 2 N HCl (25 mL) for 1.5 h. Evaporation and refluxing with HCl was repeated. The final residue was made basic with 20% KOH (20 mL) and extracted with chloroform. Evaporation of the dried (K_2CO_3) extract yielded a pale yellow oil which was distilled (100 °C, 10^{-3} mm) to afford **10** as a colorless oil (186 mg, 79%): UV (95% ethanol) λ_{max} (log ε) 255 (sh, 3.44), 263 (3.56), 268 (sh, 3.52), 276 nm (sh, 3.40); IR (neat) ν_{max} 2795, 1568, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56–3.50 (complex multiplet, 11 H), 7.04 (dd, 1 H, 9-PyH), 7.34 (d, 1 H, 10-PyH), 8.36 (d, 1 H, 8-PyH); *m/e* 174 (M^+), 173, 118, 146. The dipicrate was obtained as yellow needles from ethanol, mp 224–224.5 °C. Anal. Calcd for $C_{23}H_{20}N_8O_{14}$: C, 43.68; H, 3.19; N, 17.72. Found: C, 43.96; H, 3.15; N, 17.46.

Registry No.—**1**, 60032-57-7; **2**, 65718-98-1; **3**, 65718-99-2; **4**, 60032-59-9; **5**, 64114-31-4; **5** dipicrate, 65719-00-8; **5** diperchlorate, 65719-01-9; **6**, 64114-19-8; **6** dipicrate, 65719-02-0; **7**, 65719-03-1; **7** dipicrate, 65719-04-2; **8**, 65719-05-3; **9**, 65719-06-4; **10**, 65719-07-5; **10** dipicrate, 65719-08-6; morphorine perchlorate, 35175-75-8; acrylonitrile, 107-13-1; methyl 2-methylnicotinate, 65719-09-7; 3-hydroxymethyl-2-methylpyridine, 56826-61-0; propynal, 74-99-7; methyl 3-aminocrotonate, 14205-39-1.

Supplementary Material Available: Proton noise decoupled ^{13}C-NMR spectra of compounds **5, 6, 7, 9,** and **10** (1 page). Ordering information is given on any current masthead page.

References and Notes

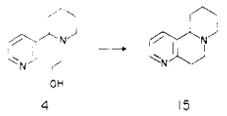
(1) This investigation was supported by Research Grant GM-13246 from the National Institutes of Health, U.S. Public Health Service, and also Grant 929 from the Council for Tobacco Research—U.S.A., Inc.

(2) Contribution No. 154 from this Laboratory.

(3) (a) J. H. Burckhalter and J. H. Short, *J. Org. Chem.*, **23,** 1281 (1958); (b) H. Erdtman, F. Haglid, I. Wellings, and U. S. von Euler, *Acta Chem. Scand.*, **17,** 1717 (1963); (c) F. Haglid and I. Wellings, *ibid.*, **17,** 1727, 1735, 1743 (1963); (d) I. Yamamoto, H. Kamimura, and R. Yamamoto, *Mem. Tokyo Univ. Agric.*, **7,** 67 (1963); (e) F. Haglid, *Acta Chem. Scand.*, **21,** 329 (1967); (f) F. Haglid and J. O. Norén, *Acta Chem. Scand.*, **21,** 335 (1967); (g) F. Haglid, *Ark. Kemi*, **26,** 489 (1967); (h) N. Castagnoli, A. P. Melikian, and V. Rosnati, *J. Pharm. Sci.*, **58,** 860 (1969); (i) W. Hawkins and A. Burger, *ibid.*, **59,** 342 (1970); (j) M. Cushman and N. Castagnoli, *J. Org. Chem.*, **37,** 1268 (1972).

(4) F. Haglid, *Acta Pharm. Suec.* **4,** 117 (1967).

(5) It was claimed (A. Sadykov and O. Otroshchenko, *Dokl. Akad Nauk SSSR*, **84,** 77 (1952)) that the alcohol (**14**) could be converted to the pyridoquinolizidine (**15**), a "bridged anabasine", by the action of P_2O_5. However, when this reaction was reexamined by Haglid,[6] only intractable tars and recovered starting material were obtained.



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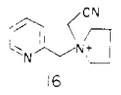
(6) F. Haglid, *Acta Chem. Scand.*, **21**, 580 (1967).
(7) E. Leete, M. R. Chedekel, and G. B. Bodem, *J. Org. Chem.*, **37**, 4465 (1972).
(8) This keto nitrile has been obtained independently by E. B. Sanders, H. V. Secor, and J. I, Seeman, *J. Org. Chem.*, **41**, 2658 (1976), **43** 324 (1978), via the Sommelet–Hauser rearrangement product of compound **16.**



16

(9) Two equivalents of butyllithium are required since one is consumed by reaction with the NH group of the pyrrolidine ring.
(10) J. C. Sheehan, P. A. Cruickshank, and G. L. Boshart, *J. Org. Chem.*, **26**, 2525 (1961).
(11) (a) S. V. Kessar, *Experientia*, **18**, 56 (1962); (b) H. S. Aaron, *Chem. Ind. (London)*, 1338 (1965); (c) A. E. Theobald and R. G. Lingard, *Spectrochim. Acta, Part A*, **24a**, 1245 (1968); (d) H. S. Aaron and C. P. Ferguson, *Tetrahedron Lett.*, 6191 (1968); (e) R. Cahill, T. A. Crabb, and R. F. Newton, *Org. Magn. Reson.*, **3**, 263 (1971).
(12) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).
(13) J. F. Whidby and J. I. Seeman, *J. Org. Chem.*, **41**, 1585 (1976).
(14) N. K. Hart, S. R. Johns, and J. A. Lamberton *J. Chem. Soc., Chem. Commun.*, 460 (1971).
(15) Melting points are uncorrected. Elemental analyses were determined by MHW Laboratories, Garden City, Mich. Mass Spectra were determined by Dr. Roger Upham and his assistants at the University of Minnesota on an AEI-MS-30 instrument. The Fourier transform ^{13}C-NMR spectra were determined by Dr. Robert M. Riddle at the University of Minnesota on a Varian XL-100 spectrometer (25.2 MHz). ^1H-NMR spectra were determined on a Varian HFT-80 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Model 257 spectrometer. Ultraviolet spectra were determined on a Cary 11 spectrometer.
(16) The 2-methylpyridine-3-aldehyde was obtained from methyl 2-methylnicotinate[17] via 3-hydroxymethyl-2-methylpyridine, using the method whereby J. M. Bobbit and D. A. Scola, *J. Org. Chem.*, **25**, 560 (1960), obtained 4-methylpyridine-3-aldehyde from methyl 4-methylnicotinate.
(17) Prepared in 66% yield from propynal and methyl 3-aminocrotonate according to the method used by F. Bohlmann and D. Rahtz, *Chem. Ber.*, **90**, 2265 (1957), for the synthesis of the corresponding ethyl ester.

Cembranoid Diterpenes from a South Pacific Soft Coral

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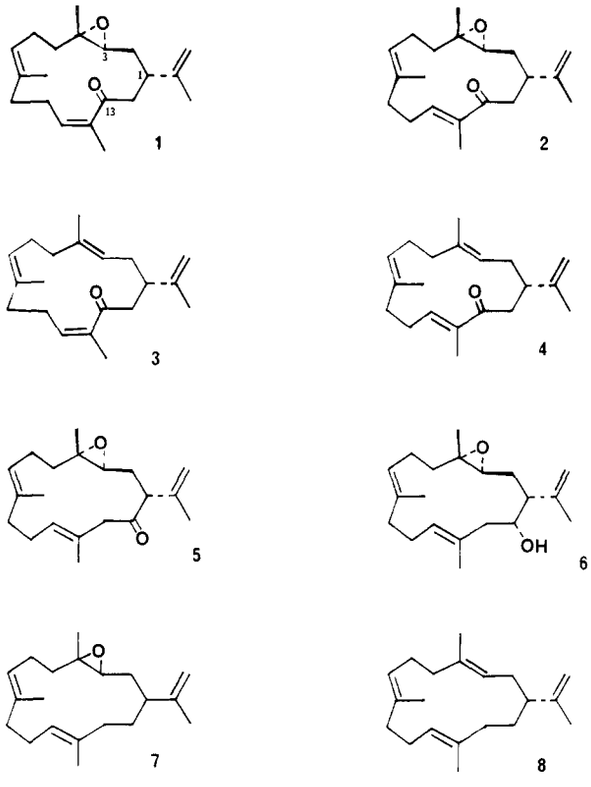
Eight cembranoid diterpenes have been isolated from an unidentified soft coral. The structures were elucidated from spectral data and chemical degradation sequences. The compounds were identified as (1*S**,3*S**,4*S**,7*E*,11*Z*)-3,4-epoxy-13-oxo-7,11,15-cembratriene, (1*S**,3*S**,4*S**,7*E*,11*E*)-3,4-epoxy-13-oxo-7,11,15-cembratriene, (3*E*,7*E*,11*Z*)-13-oxo-3,7,11,15-cembratetraene, (3*E*,7*E*,11*E*)-13-oxo-3,7,11,15-cembratetraene, (1*S**,3*S**,4*S**,7*E*,11*E*)-3,4-epoxy-14-oxo-7,11,15-cembratriene, (1*S**,3*S**,4*S**,14*R**,7*E*,11*E*)-3,4-epoxy-14-hydroxy-7,11,15-cembratriene, (7*E*,11*E*)-3,4-epoxy-7,11,15-cembratriene, and (−)-cembrene-A. The application of ^{13}C NMR spectroscopy to the determination of stereochemistry is discussed.

The soft corals or alcyonaceans are known to be a source of interesting marine natural products[1] which include sesquiterpenes,[2] cembranoid diterpenes,[3] polyhydroxylated sterols,[4] and pregnanes.[5] Some cembranoid diterpenes from soft corals are known to be toxic and have been cast in the role of deterrents to predation by reef fishes.[1] We wish to report the isolation and identification of eight cembranoid diterpenes from an unidentified soft coral[6] which was collected at Canton Island in the South Pacific.

Silica gel chromatography of the chloroform-soluble material from the combined acetone and 15% methanol in chloroform extracts of the soft coral gave a series of fractions from which the ketones 1 and 2 and the hydrocarbon 8 were obtained in high purity. Chromatography of one of the mixed fractions on silver nitrate impregnated silica gel gave two pure compounds, the ketones 3 and 5, and a mixture of the ketone 4 and the epoxide 7 which could only be separated after reduction of the ketone 4. The alcohol 6 was isolated from a mixture with the ketone 2 as the corresponding acetate. The molecular formulas, optical rotations, and yields of the compounds isolated are summarized in Table I.



1 2 3 4 5 6 7 8

The ketone 1 was shown to have the molecular formula $C_{20}H_{30}O_2$ by high-resolution mass measurement. The infrared band at 1690 cm^{-1} and the UV absorption at 236 nm (ϵ 3000) both suggested the presence of an α,β-unsaturated ketone. The ^1H NMR spectrum contained signals at δ 5.68 (1 H, t, J = 6.5 Hz) due to the β proton on an α,β-unsaturated ketone, 5.08 (1 H, t, J = 7 Hz) assigned to the vinyl proton on a trisubstituted olefinic bond, 4.85 (1 H, bs) and 4.74 (1 H, bs) for the terminal methylene protons and four methyl signals at 1.84, 1.80, 1.67, and 1.21 ppm. When recorded in $CDCl_3$ solution, the ^1H-NMR spectrum contained an unresolved proton multiplet at δ 2.84 and a signal at 2.64 (1 H, t, J = 6.5 Hz) which could be assigned to an α-epoxy proton. When recorded in C_6D_6 solution, the ^1H-NMR spectrum of 1 contained three mutually coupled signals at δ 3.06 (1 H, m, J = 7 Hz, H_c), 2.77 (1 H, dd, J = 17, 7 Hz, H_a), and 2.58 (1 H, dd, J = 17, 7 Hz, H_b)

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