Journal of Natural Products
Vol. 48, No. 2, pp. 273-278, Mar-Apr 1985

PARTIAL SYNTHESIS VIA INDOLE ALKALOIDS: A NEW HEXACYCLIC DERIVATIVE OF (−)-TETRAHYDROALSTONINE

BERNARD MOMPON,* THIERRY VASSAL, and PHILIPPE POIRIER

Laboratoires d'Etudes et de Recherches Synthelabo, 31 avenue Paul Vaillant Couturier, 92220 Bagneux, France

ABSTRACT.—Oxidation of (−) tetrahydroalstonine **5** with *t*-butyl hypochlorite affords the enamine **7**. Compound **7** reacts with formaldehyde to give, after reduction with sodium borohydride, a hexacyclic product (**8**) and a non-cyclized product (**9**). The structures of these compounds have been established by spectroscopic analysis, mainly ^{1}H and ^{13}C nmr. A mechanism is proposed to explain the cyclization.

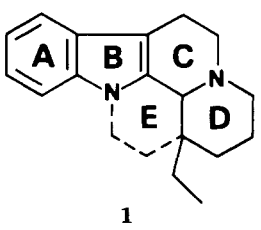
The eburnane group of indole alkaloids (**1**) has long been associated with interesting pharmacological properties. (+)-Vincamine, (−)-eburnamonine, and some of their derivatives have been shown to be useful in the treatment of certain cerebrovascular diseases (1,2) and consequently have been the object of numerous synthetic efforts.

Strategies employed for the synthesis of these natural alkaloids frequently involve the reaction of an enamine of type **2** with a suitable electrophile that permits formation of the E-ring (3-6). Such enamines have also been used for the synthesis of other pentacyclic compounds (7-9). Thus, Potier *et al.* have prepared compound **3** from enamine **2a** by reaction with formaldehyde followed by a subsequent reductive step (10).

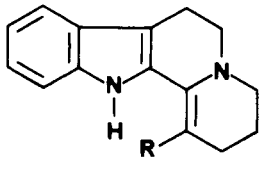
The present paper describes an extension of the above methodology to the synthesis of the novel heterocycle **8** via an enamine **7** derived from the natural product (−)-tetrahydroalstonine (**5**). The isolation of compound **9** offers an explanation of the cyclization mechanism (**7**↦**8**).

RESULTS AND DISCUSSION

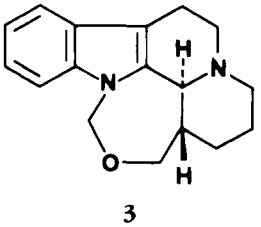
Oxidation of (−)-tetrahydroalstonine (**5**) with *t*-butyl hypochlorite afforded the stable iminium salt (**6** (11,12).[1] Treatment of this salt with NH_3 gave the unstable enamine **7** which was successively treated with HCHO, perchloric acid, and boro-



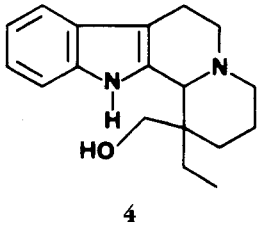
1



2a R=H
2b R=C_2H_5



3



4

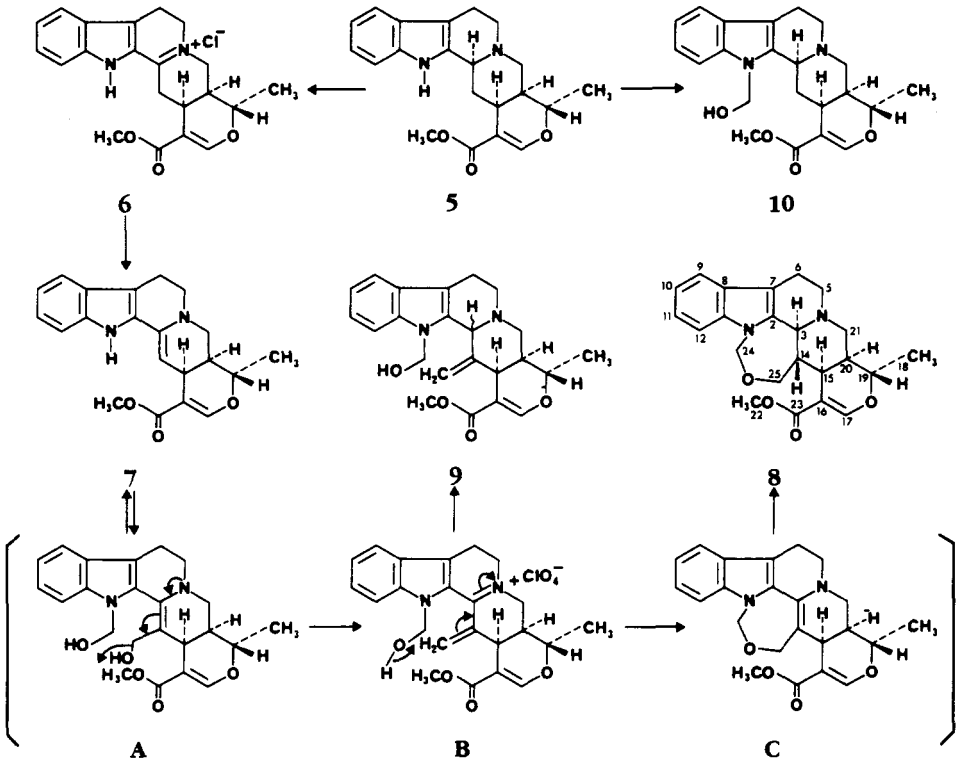
[1]Oxidation by *t*-butyl hypochlorite was preferred over mercuric acetate because of reported superior yields (13,14).

hydride as described by Potier *et al.* (10). Two new products, **8** and **9**, were obtained, and these were isolated chromatographically.

The structure of the hexacyclic derivative **8**, $C_{23}H_{26}N_2O_4$, was deduced from the following data: microanalysis, ms (molecular ion at *m/z* 394) and ^{13}C-nmr spectroscopy [signals at 77.7 and 77.9 ppm (15)] demonstrated the presence of an extra oxygen atom and two extra methylene groups.

The presence of an oxygen-containing ring [cf. product **3** (10)] is indicated by the ^{1}H-nmr spectrum. The D_2O exchangeable indole NH signal is now absent and two doublets at 5.88 and 5.08 ppm (AB system, $J_{AB}=11$ Hz) and two resolved doublets of doublets at 4.17 and 3.70 ppm (AB part of an ABX system; $J_{AB}=13$ Hz; $J_{AX}=10$ Hz and $J_{BX}=3.5$ Hz) are observed.

Compound **8** probably arises from reduction of the iminium salt derived from compound **C** (Scheme 1) thereby giving rise to two new asymmetrical centers at C-3 and C-14[2] together with the generation of a *cis*- or *trans*-quinolizidine ring conformation.



SCHEME 1

Protons H-3, H-14, H-15, H-19, and H-20 were identified in the ^{1}H-nmr spectrum by double resonance experiments and coupling constants (in particular $J_{3,14}=10$ Hz; $J_{14,15}=11$ Hz; $J_{15,20}=4$ Hz; $J_{19,20}=9$ Hz) were measured. The observed chemical shifts and coupling constants suggest the following configuration (17): H-3, α; H-14, β; H-20, α and H-19, β.

The presence of Bohlmann bands at 2820-2600 cm^{-1} in the compound's ir spectrum ($CHCl_3$) indicated a *trans*-diaxal relative conformation of the N-4 lone pair and the vicinal hydrogen H-3 (18,19).

[2]The numbering system is of the biogenetic type (16).

In order to confirm the hexacyclic structure **8**, Potier's compound (**3**) was prepared (10). All the spectroscopic properties, in particular the ^{13}C-nmr data (Table 1), were in agreement with the presence of the extra ring (C-24: 77.5 and 77.7 ppm in **3** and in product **8**, respectively, against 66.9 and 68.0 ppm for the non-cyclized compounds **9** and **10**) and confirm the proposed stereochemistry [C-3: 65.8 and 66.2 ppm in **3** and product **8**, respectively; C-6: 22.5±0.5 ppm in **3, 5, 9, 10,** and **8** (15)].

TABLE 1. Carbon-13 Chemical Shifts of Compounds **3, 5, 8, 9,** and **10**[a]

Atoms	Compounds				
	3	**5**	**8**	**9**	**10**
C-2	136,1	134,8	135,9[b]	132,9	136,7
C-3	65,8	60,0	66,2	61,3	59,9
C-5	53,8	53,6	54,7	49,6	52,8
C-6	22,5	22,0	22,7	22,3	22,7
C-7	111,0	107,9	111,7	106,3	111,6[b]
C-8	127,0	127,3	126,9	128,1	128,6
C-9	118,8	118,1	118,9	118,9	119,1
C-10	119,8	119,3	120,0	120,5	121,1
C-11	122,0	121,2	122,3	122,7	122,7
C-12	109,1	111,0	109,2	110,3	110,3[b]
C-13	136,9	136,2	136,1[b]	138,1	138,9
C-14	42,4	34,5	47,7	146,5	35,4
C-15	28,1	31,5	34,0	42,0[b]	32,5
C-16	—	109,6	108,4	111,2	110,3[b]
C-17	—	155,8	157,3	157,9	157,0
C-18	—	18,6	19,5	18,6	18,9
C-19	—	72,7	74,0	73,2	73,3
C-20	25,3	38,6	39,0	39,8[b]	38,8
C-21	56,2	56,3	57,5	54,9	56,8
C-22	—	51,3	52,0	51,6	51,7
C-23	—	168,1	169,5	169,2	169,2
C-24	77,5	—	77,7[c]	66,9	68,0
C-25	79,1	—	77,9[c]	114,8	—

[a]Chemical shifts in ppm from internal TMS in $CDCl_3$ solution except compound **9** in 1:1 $CDCl_3$-CD_3OD.

[b, c]These assignments may be interchanged within any column.

Compound **9** was shown by microanalysis and ms (molecular ion at $m/z=394$) to be isomeric with **8**, but other spectroscopic properties preclude the compound from being a stereoisomer of **8** and suggest instead the noncyclized structure **9**.

The ^{1}H-nmr spectrum of **9** differs from that of **8** in that signals due to H-14 at 2,10 ppm and the protons of the C-25 methylene at 3,70 and 4,17 ppm are absent. Instead, two broad signals at 4,68 ppm (1H) and 4,80 ppm (1H) are observed, which are compatible with the presence of an exocyclic methylene group (20), which is attached to C-14 because the two protons H-3 and H-15 have now become allylic in nature, thereby explaining their paramagnetic shifts by 0.85 ppm and 1.10 ppm, respectively, compared to their chemical shifts in compound **8**.

The two protons of the N-CH_2OH group resonate at 5.38 and 5.50 ppm (AB quartet; $J_{AB}=11.5$ Hz) and the presence of a hydroxyl function being confirmed by the ir spectrum in $CHCl_3$ (free and bonded OH at 3704 cm^{-1} and 3546 cm^{-1}, respectively).

The ^{13}C-nmr spectrum is in agreement with the proposed structure **9** (Table 1) in particular by the presence of two additional signals with respect to **5** at 66.9 ppm

[C-24: cf 68.0 ppm observed for the N-CH_2OH of compound **10**] and 114.8 ppm [exocyclic methylene group (20)].

Double resonance proton nmr experiments confirm that the configurations of the asymmetric centers at C-19, C-20, and C-15 remain unchanged [$J_{19,20}=10$ Hz; $J_{20,15}=5$ Hz] (17). The configuration at C-3 remains to be defined since the two empirical rules governing the chemical shift of the proton H-3 (21) and the size of the coupling constant $J_{3,14}$ (21) cannot be applied (H-3 is deshielded by the exocyclic double bond at C-14 and there is no H-14).

The presence of Bohlmann bands 2815-2760 cm^{-1} in the solution phase ($CHCl_3$) ir spectrum of compound **9** favors a *trans*-diaxal relative conformation of the N-4 lone pair and the vicinal hydrogen H-3 (18,19).

The reaction of HCHO and the enamine **7** obtained from (−)-tetrahydroalstonine (**5**) affords, after treatment with perchloric acid and sodium borohydride, the expected oxa-E homoeburnane type, hexacyclic product **8**. This product probably arises from the nonisolated intermediate **C** (Scheme 1), which, in acid, rearranges to an iminium salt that is readily reduced by borohydride. The resulting product has a *trans-trans*-configuration (i.e., a *trans*-diaxial configuration of the N-4 lone pair and of H-3 and a relative *trans*-configuration of H-3 and H-14). The other reaction product, compound **9**, presumably results from the condensation of HCHO with the indole nitrogen and with C-14 of the enamine **7** affording initially the intermediate **A** (Scheme 1). Dehydration of **A** would afford the iminium salt **B** which on borohydride reduction would afford compound **9**.

The isolation of compound **9** is, however, significant in that it suggests an explanation of the cyclization mechanism leading to **8**. This mechanism, which presupposes a dehydration step (i.e., **A**↦**B**), is further supported by the fact that the enamine **2b** when reacted with HCHO in an analogous way affords exclusively compound **4** (22). The presence of the ethyl group in effect prevents formation of the exocyclic double bond and subsequent cyclization.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points were determined on a Büchi 510 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. The ir spectra were recorded with a Perkin-Elmer 177 instrument. The uv spectra were measured in 95% EtOH solution using a Beckman DK-2A spectrophotometer. Mass spectra were obtained on a V.G. Micromass 7070F (70 eV, 200°). Microanalyses were obtained with a Perkin-Elmer 240 analyser coupled with a Tektronix 31 calculator. ^{1}H-nmr spectra were determined on a Bruker WP 200 SY in $CDCl_3$ solution. Chemical shifts are expressed in ppm with respect to internal TMS and coupling constant in Hz (s=singlet, d=doublet, t=triplet, q=quadruplet, m=multiplet, br=unresolved broad signal). ^{13}C-nmr spectra were measured on a Bruker WP 80. Tlc was carried out on Merck 60F-254 silica gel plates using mixtures of $CHCl_3$-MeOH, 99:1 and 97:3; spots were revealed by uv and by Dragendorff's reagent.

PREPARATION OF ENAMINE **7**.—*Iminium salt* **6**: *(19α, 20α)-16,17-didehydro-16-(methoxycarbonyl)-19-methyloxayohimbanium chloride*.—Freshly distilled triethylamine (7.5 ml) was added to a stirred solution of tetrahydroalstonine (**5**) (10 g) in CH_2Cl_2 (250 ml), cooled, and maintained at −10°. *t*-Butyl hypochlorite (3 ml) in CH_2Cl_2 (250 ml) was then added dropwise. Stirring was continued for a further 30 min after completion of the addition; then the solution was washed three times with H_2O (300 ml), dried (Na_2SO_4), and the solvent removed in vacuo. The amorphous residue (10.5 g) was dissolved in 1% methanolic HCl (6 ml of HCl in 600 ml of MeOH), and the resulting solution was heated at reflux for one h.

After partial evaporation of the MeOH, the solution was diluted with 2 liters of ice H_2O and extracted three times with CH_2Cl_2 (500 ml). The extracts were washed with H_2O, dried (Na_2SO_4), and evaporated to afford 10.4 g of the iminium salt **6**. This solid, mp 180-200°, could be kept without any special precautions.

Calculated for $C_{21}H_{22}N_2O_3$ HCl: C, 65.20; H, 5.99; N, 7.24; Cl, 12.14%. Found: C, 65.12-65.12; H, 5.78-5.84; N, 7.08-7.13; Cl, 11.87%.

Enamine **7**: *Methyl-(19α, 20α)-3,4,16,17-tetrahydro-19-methyloxayohimban-16-carboxylate*.—An

aqueous solution of the above iminium salt was basified with aqueous NH_3, and the mixture ws extracted with CH_2Cl_2. The dried (Na_2SO_4) solution was evaporated to dryness, and the residue was taken up with MeOH. Compound **7** crystallized out, mp 190-195°, M^+=350 ($C_{21}H_{22}N_2O_3$). This enamine decomposed rapidly in solution, in air, and on heating.

PREPARATION OF **8** AND **9**.—The enamine **7** (8 g) was in MeOH (400 ml), heated to 60° under N_2, and 40% aqueous HCHO (30 ml) was added. After 20 min, 70% perchloric acid (15 ml) was added, and the mixture cooled to 15° (ice bath). Sodium borohydride (12 g) was then added portionwise over one h. The reaction mixture was concentrated to 50 ml and the residue diluted with H_2O (2 liters). The resulting solution was basified with NH_3 and extracted with CH_2Cl_2 (3×500 ml). The combined extracts were washed and dried (Na_2SO_4). The residue, after evaporation of the solvent, was chromatographed on silica gel (60 merck, 200 g). Elution was carried out with toluene containing increasing amounts of $CHCl_3$ and then with $CHCl_3$-MeOH. Compound **8**, 4.2 g, was eluted with a 7:3 mixture of toluene-$CHCl_3$ and was recrystallized from CH_2Cl_2-Et_2O. Compound **5**, tetrahydroalstonine, 1.3 g, was then eluted with a 6:4 mixture of toluene-$CHCl_3$ and was recrystallized from 8:2 mixture CH_2Cl_2-Et_2O. Finally, compound **9** was eluted with a 9:1 mixture of $CHCl_3$-MeOH to give 1.08 g after crystallization.

Tetrahydroalstonine (**5**)*: Methyl (19, 20)-16,17-didehydro-19-methyloxayohimban-16-carboxylate.*—Mp 231° and $[\alpha]^{20}D$=−106° (c=1.08, $CHCl_3$) spectroscopic and chromatographic properties (uv, ir, ^1H and ^{13}C nmr) were identical to that of the starting product.

Compound **8***: Methyl {7aS-(7a,8,11a)}-5,6,7a,11a,11b,11c-hexahydro-8-methyl-7H,8H,12H,14H-9,13-dioxa-6a, 14a-diazabenz{2,3} azuleno {1,8,7,cde} anthracene-11-carboxylate.*—Mp 225°; $[\alpha]^{20}D$=−32.4° (c=1.03, $CHCl_3$); ir ($CHCl_3$) 2820, 2750 cm^{-1} (Bohlmann bands), 1695 cm^{-1} (C=O), and 1620 cm^{-1} (C=C); uv λ max (EtOH) 292 nm (ε=6300), 282 nm (ε=7750), 227 nm (ε=42650); ^1H nmr (200 MHz, $CDCl_3$, ppm) 3.50 (1H, br, $J_{3,14}$=10 Hz, H-3); 3.04-2.60 (4H, m, H-5 and H-6); 2.10 (1H, tdd, $J_{14,25}$=10 Hz, $J_{14,3}$=10 Hz, $J_{14,15}$=11 Hz and $J_{14,25'}$=3.5 Hz, H-14); 2.54 (1H, dd, $J_{15,20}$=4 Hz and $J_{14,15}$=11 Hz, H-15); 7.58 (1H, s, H-17); 1.40 (3H, d, $J_{18,19}$=6.5 Hz, H-18); 4.70 (1H, qd, $J_{18,19}$=6.5 Hz and $J_{19,20}$=9 Hz, H-19); 1.57 (1H, m, H-20); 3.04-2.80 (1H, m) and 3.10 (1H, dd, $J_{21,21'}$=12 Hz and $J_{21',20}$=2.5 Hz) H-21; 3.70 (3H, s, H-22); 5.08 (1H, d, $J_{24,24'}$=11 Hz) and 5.88 (1H, d, $J_{24',24}$=11 Hz) H-24; 3.70 (1H, dd, $J_{25,25'}$=13 Hz and $J_{25,14}$=10 Hz) and 4.17 (1H, dd, $J_{25',25}$=13 Hz and $J_{25',14}$=3.5 Hz) H-25; 7.45 (1H, d); 7.26 (1H, d); 7.18 (1H, t); and 7.08 (1H, t) Ar; ^{13}C nmr (Cf. Table 1); eims *m/z* 394 (M^+; 100%), 393 (M^+-H; 59%), 362 (M^+-CH_3OH; 11.5%), 198 (17.4%), 168 (15.3%), and 55 (9.7%). Calculated for $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64; O, 16.22; N, 7.10. Found: C, 70.19; H, 6.63; O, 16.14; N, 7.15.

Compound **9***: Methyl (19α, 20α)-14,16-didehydro-1-hydroxymethyl-14-methylene oxayohimban-16-carboxylate.*—Mp 214°; $[\alpha]^{20}D$=−101° (c=0.6, $CHCl_3$-MeOH, 9:1); ir ($CHCl_3$) 3400 cm^{-1} (OH), 2815-2760 cm^{-1} (Bohlmann bands), 1705 cm^{-1} (C=O), 1620 cm^{-1} (C=C) and 910 cm^{-1} (C=CH_2); uv λ max (EtOH) 291.5 nm (ε=5600), 281 nm (ε=7300), 275 nm (ε=7200), and 228.5 nm (ε=34500); ^1H nmr (200 MHz, $CDCl_3$, ppm) 4.35 (1H, brs, H-3); 2.96-2.64 (4H, m, H-5 and H-6); 3.44 (1H, brd, $J_{15,20}$=5 Hz and $J_{15,25}$<1 Hz, H-15); 7.66 (1H, s, H-17); 1.40 (3H, d, $J_{18,19}$=6 Hz, H-18); 4.25 (1H, qd, $J_{18,19}$=6 Hz and $J_{19,20}$=10 Hz, H-19); 1.76 (1H, m, H-20); 3.15 (1H, d, $J_{21,21'}$=13 Hz, H-21) and 3.30 (1H, dd, $J_{21',21}$=13 Hz and $J_{21',20}$=4 Hz, H-21); 3.70 (3H, s, H-22); 5.38 (1H, d, $J_{24,24'}$=11.5 Hz, H-24) and 5.50 (1H, d, $J_{24',24}$=11.5 Hz, H-24); 4.68 (1H, brs, H-25) and 4.80 (1H, brs, H-25); 7.47 (1H, d, Ar.); 7.44 (1H, d, Ar.); 7.20 (1H, t, Ar.); and 7.12 (1H, t, Ar.); ^{13}C nmr (Cf. Table 1); eims; *m/z* 394 $M^{+\cdot}$; 8.3%), 364 (M^+-CH_2O; 100%), 363 (M^+-CH_2OH; 54.8%), 349 (20%), 209 (12.8%), 182 (12%), and 168 (10%). Calculated for $C_{23}H_{26}N_2O_4$: C, 70.03; H, 6.64; N, 7.10. Found: C, 70.35; H, 6.73; N, 6.94.

PREPARATION OF **10**.—Formaldehyde 40% aqueous solution (300 ml) and HOAc (1.5 ml) were added to a solution of tetrahydroalstonine (10 g) in $CHCl_3$ (75 ml). After stirring for 24 h at 50°, the solution was diluted with ice H_2O (1 liter), basified with NH_3, and extracted with $CHCl_3$ (6×500 ml). The washed, dried extracts were evaporated to dryness. Recrystallization of the residue from CH_2Cl_2-Et_2O afforded 4.85 g of product **10**.

Compound **10***: Methyl (19α, 20α)-16,17-didehydro-3-hydroxymethyl-19-methyloxayohimban-16-carboxylate.*—Mp 171-172°; $[\alpha]^{20}D$=−186° (c=1, $CHCl_3$); ir ($CHCl_3$) 3600, 3450 cm^{-1} (OH), 2810, 2760 cm^{-1} (Bohlmann bands), and 1690 cm^{-1} (C=O); uv λ max (EtOH) 228 nm (ε=42000), 275 nm nm (ε=8800), 281 nm (ε=8700), and 291.5 nm (ε=6600); ^1H nmr (200 MHz, $CDCl_3$, ppm) 3.56 (1H, brd, $J_{3,14}$=12.5 Hz, H-3), 3.14-2.50 (4H, m, H-5 and H-6); 1.55 (1H, m, H-14) and 3.14-2.50 (1H, m, H-14); 3.14-2.50 (1H, m, H-15) 7.54 (1H, s, H-17); 1.40 (3H, d, $J_{18,19}$=6 Hz, H-18); 4.48 (1H, qd, $J_{19,18}$=6 Hz and $J_{19,20}$=10 Hz, H-19); 1.65 (1H, m, H-20); 3.14-2.50 (2H, m, H-21); 3.71 (3H, s, H-22); 5.56 (2H, s, H-24); 7.48-7.35 (2H, m, Ar.) amd 7.25-7.05 (2H, m, Ar.); ^{13}C nmr (Cf. Table 1); eims *m/z* 382 ($M^{+\cdot}$; 14%), 381 (M^+-H; 9.7%), 352 (M^+-CH_2O; 100%), 351 (M^+-CH_2OH; 69.4%),

337 (22.9%), 251 (10%), 223 (14.6%), and 156 (42.3%). Calculated for $C_{22}H_{26}N_2O_4$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.06, 69.11; H, 6.95, 6.72; N, 7.26, 7.26.

PREPARATION OF **3** (10).—Trans-*1, 12b octahydro-1,2,3,4,6,7,12,12b-methanooxymethanol-1, 12-indolo 2,3a quinolizine*.—mp 148-149° (EtOAc); ir ($CHCl_3$) 2860-2760 cm^{-1} (Bohlmann bands); ^1H nmr (200 MHz, $CDCl_3$, ppm) 3.11 (1H, brd, $J_{3,14}$=9.8 Hz, H-3); 3.16-2.87 (2H, m, H-5); 2.72-2.56 (2H, m, H-6); 2.02-1.55 (1H, m, H-14); 0.97 (1H, qd, $J_{15,15'}$=12.5 Hz, $J_{15,14}$=12.5 Hz, $J_{15,20}$=12.5 Hz and $J_{15,20'}$=5 Hz, H-15) and 2.02-1.55 (1H, m, H-15); 2.37 (1H, td, $J_{21,21'}$=11.5 Hz, $J_{21,20}$=11.5 Hz, $J_{21,20'}$=3.2 Hz, H-21) and 3.16-2.87 (1H, m, H-21); 5.83 (1H, d, $J_{24,24'}$=11.5 Hz, H-24) and 4.96 (1H, d, $J_{24',24}$=11.5 Hz, H-24); 4.01 (1H, dd, $J_{25,25'}$=12.8 Hz and $J_{25,14}$=3.4 Hz, H-25) and 3.43 (1H, dd, $J_{25',25}$=12.8 Hz and $J_{25',14}$=10.5 Hz, H-25); 7.59 (1H, brd, Ar.); 7.25 (1H, brd, Ar.); 7.15 (1H, td, Ar.); and 7.06 (1H, ddd, Ar.); ^{13}C nmr (Cf. Table 1); eims *m/z* 268 ($M^{+\cdot}$; 100%), 267 (M^+-H; 87.5%), 237 (M^+-CH_2OH; 11.8%), and 168 (7.7%). Calculated for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 75.87; H, 7.72; N, 10.34.

ACKNOWLEDGMENTS

The authors thank Dr. Michael Dimsdale and Dr. Jonathan Frost for helpful suggestions and translation of this manuscript.

LITERATURE CITED

1. H. Hauth and B.P. Richardson, *Ann. Rep. Med. Chem.*, **12** 49 (1977).
2. G. Bartholini, E.T. Mackenzie, H. Depoortere, and J.P. Nowicki, "Drugs and Acute Cerebral Ischaemia as Related to Physiological and Pathological Mechanisms," in: *Etats Déficitaires Cérébraux Liés à l'Age*, Ed. by R. Tissot, Bel-Air VI Symposium, Geneva, Switzerland, October 1980.
3. G. Rossey, A. Wick, and E. Wenkert, *J. Org. Chem.*, **47**, 4745 (1982).
4. E. Wenkert and B. Wickberg, *J. Amer. Chem. Soc.*, **87**, 1580 (1965).
5. H.P. Husson, T. Imbert, C. Thal, and P. Potier, *Bull. Soc. Chim. France*, 2013 (1973).
6. A. Buzas, C. Hérisson, and G. Lavielle, *C. R. Acad. Sc. Paris*, **283C**, 763 (1976).
7. R.N. Shut, F.E. Ward, and T.J. Leipzig, *J. Org. Chem.*, **34**, 330 (1969).
8. H.P. Husson, T. Imbert, C. Thal, and P. Potier, *Bull. Soc. Chim. France*, 2010 (1973).
9. T. Sevenet, C. Thal, P. Potier, and H.P. Husson, *French Patent* (1972) no. 2190113: *Chem. Abstr.*, **87**, 1368y (1974).
10. C. Thal, R. Besselievre, H.P. Husson, and P. Potier, *French Patent*, (1975) no. 2315277: *Chem. Abstr.*, **87**, 117989s (1977).
11. N. Finch and W.I. Taylor, *J. Amer. Chem. Soc.*, **84**, 1318 (1962).
12. L.J. Dolby and G.W. Gribble, *J. Org. Chem.*, **32**, 1391 (1967).
13. Y. Rolland, J. Granier, J. Mahuteau, and J. Poisson, *C. R. Acad. Sc. Paris*, **285**, 583 (1977).
14. E. Wenkert and D.K. Roychaudhuri, *J. Org. Chem.*, **21**, 1315 (1956).
15. E. Wenkert, C. Chang, H.P.S. Chawla, D.W. Cochran, E.W. Hagaman, J.C. King, and K. Orito, *J. Am. Chem. Soc.*, **98**, 3645 (1976).
16. J. Le Men and W.I. Taylor, *Experientia*, **21**, 508 (1965).
17. M. Lounasmaa and S.K. Kan, *Tetrahedron*, **36**, 1607 (1980).
18. F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958).
19. F. Bohlmann, *Angew. Chem.*, **69**, 641 (1957).
20. B. Mompon, G. Massiot, and R. Toubiana, *C. R. Acad. Sc. Paris*, **279 C**, 907 (1974).
21. W.F. Trager, C.M. Lee, and A.H. Beckett, *Tetrahedron*, **23**, 365 (1967).
22. C. Szantay, L. Szabo, G. Kalaus, E. Karpeti, and L. Szporny, *Belgian Patent*, (1975) no. 828621; *Chem. Abstr.*, **84**, 90138n (1976).

Received 6 August 1984