ALKALOIDS OF *GUATTERIA MELOSMA* AND *CLEISTOPHOLIS PATENS*

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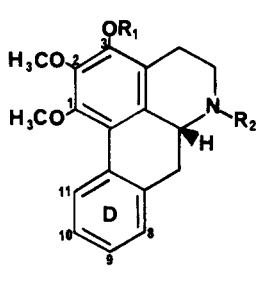
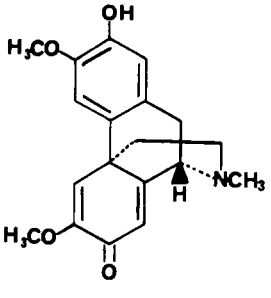
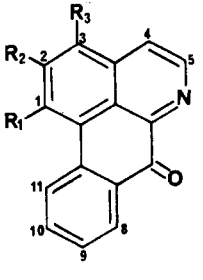
Abstract.—Fractionation and chromatography of an ethanol extract of the stembark of *Guatteria melosma* Diels (Annonaceae) afforded the new noraporphine alkaloid, 3-hydroxynornuciferine (**1**) and its corresponding oxoaporphine alkaloid, isomoschatoline (**2**). The latter alkaloid was also isolated from an ethanol extract of the stembark of *Cleistopholis patens* Engl. & Diels (Anonaceae). The structure of 3-hydroxynornuciferine (1,2-dimethoxy-3-hydroxynoraporphine) (**1**) was confirmed by a consideration of its spectral data and that obtained on its *N,O*-diacetyl (**5**) and N-methyl (**6**) derivatives. The latter derivative was identical (ir, ^{1}H-nmr, ms, [α] D) to 3-hydroxynuciferine (**6**). A consideration of the spectral data of isomoschatoline (**2**), its *O*-methyl (**8**) and *O*-acetyl (**9**) derivatives indicated that the alkaloid was 1,2-dimethoxy-3-hydroxyoxoaporphine. Reduction and subsequent acetylation of the alkaloid afforded a product that was identical (ir, ^{1}H-nmr, ms) to *N,O*-diacetyl-3-hydroxynornuciferine (**5**). In addition, the morphinandienone alkaloid, pallidine (**3**) was isolated from *G. melosma*; the oxoaporphine alkaloid, liriodenine (**4**) was isolated from both *G. melosma* and *C. patens*; and an uncharacterized alkaloid, CPA 1, was isolated from *C. patens*.

Guatteria melosma and *Cleistopholis patens* are Annonaceous plants native to South America and West Africa, respectively. In recent reports from our laboratories, two novel 7,7-dimethyltetradehydroaporphine alkaloids, melosmine and melosmidine, and a new oxoaporphine alkaloid, oxoanolobine, were isolated from *G. melosma* (1, 2). To our knowledge, no previous phytochemical studies have been reported on *C. patens*.

This paper presents the isolation and characterization of the noraporphine alkaloid, 3-hydroxynornuciferine (**1**) from *G. melosma* and its corresponding oxoaporphine alkaloid, isomoschatoline (**2**), from both *G. melosma* and *C. patens*. In addition, pallidine (**3**) and liriodenine (**4**) were isolated from *G. melosma*, while liriodenine (**4**) and the uncharacterized CPA 1 (mp>250°; M$^+$ *m/z* 291) were isolated from *C. patens*.







1 R_1, R_2 = H

5 R_1, R_2 = $COCH_3$

6 R_1 = H ; R_2 = CH_3

3

2 R_1, R_2 = OCH_3 ; R_3 = OH

4 $R_1 + R_2$ = OCH_2O ; R_3 = H

7 R_1, R_3 = OCH_3 ; R_2 = OH

8 R_1, R_2, R_3 = OCH_3

9 R_1, R_2 = OCH_3 ; R_3 = $OCOCH_3$

10 R_1, R_3 = OCH_3 ; R_2 = $OCOCH_3$

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Ethanolic extracts of the stembark of each plant were partitioned in the usual manner (1). Chromatography of the non-quaternary alkaloid fraction resulted in the isolation of alkaloids.

3-Hydroxynornuciferine (**1**) was isolated as white needles (52 mg); mp 173°, M^+ *m/z* 297 (67%) for $C_{18}H_{19}NO_3$. The alkaloid was levorotatory and exhibited a uv spectrum characteristic of an aporphine alkaloid (3). The bathochromic shift upon the addition of base indicated the phenolic nature of the alkaloid. The ^{1}H-nmr spectrum was indicative of a 1,2,3-trisubstituted noraporphine. The complex groups of aromatic protons δ 8.17–8.32 (1H, m) and 7.15–7.30 (3H, m) were assigned to the unsubstituted D-ring of the noraporphine. Singlets at δ 3.95 (3H) (C–2) and 3.70 (3H) (C–1) were assigned to two aromatic methoxy groups. The spectrum also indicated that the alkaloid did not possess an *N*-methyl [No δ 2.5 (3H, s)] group and that C–3 was substituted (No δ 6.5 aromatic singlet). The mass spectrum exhibited a base peak at $M^+ - 1$ (*m/z* 296) and a retrograde Diels-Alder rearrangement loss of 29 amu [*m/z* 268 (15%)], both characteristic of a noraporphine alkaloid (4).

Acetylation of the alkaloid (acetic anhydride/pyridine) afforded an *N,O*-diacetyl derivative (**5**) (M^+ *m/z* 381) whose spectra were consistent with a 1,2,3 trisubstituted-noraporphine. These data indicated that the alkaloid was 1,2-dimethoxy-3-hydroxynoraporphine (3-hydroxynornuciferine) (**1**). This proposal was confirmed by *N*-methylation (formaldehyde/sodium borohydride) to 3-hydroxynuciferine (**6**). The product was identical (ir, uv, ^{1}H-nmr, ms, [α] D) to an authentic sample[2].

Isomoschatoline (**2**) was isolated as red cuboidal crystals [mp 245° (MeOH), M^+ *m/z* 307 (100%)] which appeared as a blue spot when applied to a silica gel thin layer plate. Its uv and ir spectra (1662 cm^{-1}) were characteristic of an oxoaporphine alkaloid (5, 6). The bathochromic shift in the uv spectrum indicated that the alkaloid was probably phenolic. The mass spectral fragmentation of this alkaloid was similar to that of moschatoline (**7**) (7). The ^{1}H-nmr spectrum indicated that this compound was a 1,2,3-trisubstituted oxoaporphine. The aromatic AB system at δ 9.12 (1H, d, $J=6$ Hz) and 8.88 (1H, d, $J=6$ Hz) was assigned to the C–5 and C–4 protons, respectively; the complex aromatic system at δ 9.30 (1H,d, $J=8$ Hz), 8.60 (1H, d, $J=8$ Hz), 8.07 (1H, m) and 7.72 (1H, m) was assigned to the C–11, C–8, C–10 and C–9 protons, respectively. A singlet at δ 4.33 (6H) was assigned to two aromatic methoxy groups.

Methylation (diazomethane) of isomoschatoline (**2**) afforded an *O*-methyl derivative (**8**) (M^+ *m/z* 321) identical (ms, ir, ^{1}H-nmr) to an authentic sample of *O*-methylmoschatoline (**8**). This confirmed that isomoschatoline (**2**) was a 1,2,3-substituted oxoaporphine alkaloid containing two methoxy groups and one hydroxy group. Acetylation (acetic anhydride/pyridine) of isomoschatoline (**2**) afforded an *O*-acetyl derivative (**9**) (M^+ *m/z* 349) which was not identical (mp, ir, ^{1}H-nmr) with authentic[3] *O*-acetylmoschatoline (**10**). This indicated that isomoschatoline (**2**) was either 2,3-dimethoxy-1-hydroxyoxoaporphine or 1,2-dimethoxy-3-hydroxy-oxoaporphine. The uv spectrum of isomoschatoline (**2**) showed a bathochromic and hyperchromic shift in base indicating that the phenolic hydroxy group was at C–1 or C–3 (8). A comparison of the ^{1}H-nmr spectra of isomoschatoline (**2**), moschantoline (**7**), *O*-methylisomoschatoline (*O*-methylmoschatoline) (**8**), *O*-acetyl-isomoschatoline (**9**) and *O*-acetylmoschatoline (**10**) indicated that the hydroxy group should be at C–3. This was confirmed when isomoschatoline (**2**) was reduced (zinc/acetic acid) and subsequently acetylated (acetic anhydride/pyridine) to afford a product (**5**) which was identical (ir, uv, ^{1}H-nmr, ms) to *N,O*-diacetyl-3-

[2]This synthetic compound was kindly supplied by Dr. Michael P. Cava, Department of Chemistry, University of Pennsylvania, Philadelphia, PA.

[3]Sample kindly supplied by Dr. I. R. C. Bick, Department of Chemistry, The University of Tasmania, Australia.

hydroxynornuciferine (**5**) previously prepared in this study. Thus, isomoschatoline was 1,2-dimethoxy-3-hydroxyoxoaporphine (**2**).

EXPERIMENTAL[4]

PLANT MATERIAL.—The plant material used in this study consisted of the stembark of *Guatteria melosma* Diels (Anonaceae) collected in Peru in July, 1974, and *Cleistopholis patens* Engl. & Diels (*Oxymitra patens* Benth.) collected in Ghana in May, 1974. Herbarium specimens are on deposit at the National Arboretum, U.S.D.A. Acc. No.—PR-80719 and PR-80805, respectively.

ISOLATION OF ALKALOIDS FROM *G. melosma*.—The extraction and fractionation of *G. melosma* has been described, previously (1). Elution of column A (1) with chloroform-methanol (92:8) afforded a fraction (4.27 g) which was chromatographed over two successive silica gel columns (100 g, 3 x 30 cm) packed in chloroform-methanol (7:1). Elution with the same solvent afforded 3-hydroxynornuciferine (**1**) (64 mg).

The isolation of isomoschatoline (**2**) has been described previously as the uncharacterized alkaloid, GMA 1 (1).

Elution of column A (1) with chloroform-hexane (8:2) afforded a residue (1.72 g) which was chromatographed over a silica gel column (60 gm, 3 x 22 cm). Elution with chloroform-methanol (7:1) afforded liriodenine (**4**) (5 mg). Further elution of the column afforded pallidine (**3**) (15 mg).

EXTRACTION AND FRACTIONATION OF *C. patens*.—Dried ground stembark (33 kg) of *C. patens* Diels was placed in a stainless steel percolator and extracted with ethanol (600 liters) until the extract gave a negative test with Dragendorff's reagent (9). The ethanol, when concentrated in a wall evaporator and evaporated to dryness, yielded a syrupy residue (1.19 kg). The ethanol extract was dissolved in chloroform (15 liters) and extracted with 2% aqueous hydrochloric acid (15 liters x 5). The chloroform was dried over anhydrous sodium sulfate and evaporated to leave a dark brown residue (Fraction A—582 g). The combined aqueous acidic layers were basified to pH 9 with concentrated ammonium hydroxide and extracted with chloroform (62 liters x 3). The chloroform extracts were pooled, dried over anhydrous sodium sulfate, and evaporated to leave a brown non-quaternary alkaloid residue (Fraction B—8.2 g).

ISOLATION OF ALKALOIDS FROM *C. patens*.—Fraction B was dissolved in chloroform, adsorbed onto silicic acid (35 g) and chromatographed over a silicic acid column (350 g, 5 x 68 cm) prepared from a slurry in hexane-chloroform (1:1). Elution was begun with hexane-chloroform (1:1), and the polarity increased by the addition of chloroform and subsequently methanol (column A).

Thin layer chromatographic analysis of the fraction eluted with chloroform-methanol (8:2) revealed the presence of two alkaloid spots (R_f 0.70 and 0.15; chloroform-methanol-ammonium hydroxide, 50:10:1). This fraction (0.85 g) was dissolved in benzene-methanol (85:15) and chromatographed over a silica gel-celite (4:1) column (48 g, 2.2 x 65 cm) prepared from a slurry in benzene-methanol (9:1). Elution with the same solvent was initiated with 200 fractions (5 ml) being collected. Fractions 40–85 yielded liriodenine (**4**) (35 mg), while fractions 96–160 afforded isomoschatoline (**2**) (60 mg).

Thin layer chromatographic analysis of the fraction eluted with chloroform-methanol (6:4) (column A) revealed the presence of one alkaloid spot (R_f 0.2; chloroform-methanol-ammonium hydroxide, 50:10:2) together with other non-alkaloid constituents. This fraction (2.2 g) was dissolved in ethanol and applied to a preparative high pressure liquid chromatographic silica column. Elution was begun with ethanol, and collection of the fraction with a red color afforded CPA 1 (12 mg) (M^+ m/z 291).

3-HYDROXYNORNUCIFERINE (**1**).—3-Hydroxynornuciferine (**1**) was isolated as white cuboid crystals that turned green on standing (64 mg); mp 173° dec; $[\alpha]^{29}D$ −31° (c 2.48, MeOH); uv λ max (MeOH) 221 nm (log ε 3.36), 284 (3.22), 297 (sh) (3.09); uv λ max (MeOH+OH^-) 215 (3.33), 226 (3.30), 317 (3.28), uv λ max (MeOH+H^+) same as MeOH spectrum; ir ν max (KBr) 3315, 2940, 2840, 1588, 1568, 1468, 1450, 1438, 1420, 1360, 1352, 1320, 1310, 1245, 1200, 1115, 1085, 1050, 1033, 982, 850, 820, 800, 790, 770, 750, 730, 695, 645 cm^{-1}; ^1H-nmr ($CDCl_3$) 8.17–8.32 (1H, m) (C–11), 7.15–7.30 (3H, m) (C–8,9,10), 3.95 (3H, s) (C–2 methoxy), 3.70 (3H, s) (C–1 methoxy);

[4]Melting points were determined on a Thomas-Hoover Uni-melt Capillary Apparatus and are corrected. Optical rotations were measured on a Perkin-Elmer model 241 Polarimeter. Ultraviolet absorption spectra were obtained on a Perkin-Elmer model 202 Recording Spectrophotometer. Infrared spectra were taken on a Perkin-Elmer model 157 Infrared Recording Spectrophotometer. The ^1H-nuclear magnetic resonance spectra were taken on a 60MHz Hitachi Perkin-Elmer model R–24 High Resolution Spectrometer with tetramethylsilane as the internal standard and chemical shifts recorded in δ (ppm) units. Low resolution mass spectra were taken on a LKB–900 Mass Spectrometer. High pressure liquid chromatography was done on a Waters-Prep LC/System 500 Liquid Chromatograph with a single Prep PAK–500/Silica catridge. The adsorbents used for column chromatography were 100 mesh silicic acid (Mallinckrodt) and silica gel D–O (CAMAG)-acid washed celite (Mallinckrodt) (4:1). Thin layer chromatography was done on 5 x 20 cm or 10 x 20 cm glass plates coated with 0.30 mm of silica gel DF–O (CAMAG) and activated at 110° for one hour. Alkaloids were visualized by spraying with Dragendorff's reagent (9). All solvents were evaporated under reduced pressure at 40°.

ms *m/z* 298 (17%), 297 (M^+, 67), 296 (100), 282 (30), 280 (33), 268 (15), 266 (25), 250 (17), 237 (25), 222 (10), 210 (12), 194 (12), 180 (22), 165 (45).

PREPARATION OF *N,O*-DIACETYL-3-HYDROXYNORNUCIFERINE (**5**).—Acetic anhydride (1 ml) was added to a solution of 3-hydroxynornuciferine (**1**) (20 mg) in pyridine (1 ml) and set aside at room temperature for 24 hours. The solution was chilled, and cold distilled water (5 ml) added. The aqueous solution was extracted with chloroform (5 ml x 3). The chloroform extracts were pooled, dried over anhydrous sodium sulfate and evaporated to an oily residue. The residue was placed on a silica gel column (10 g, 1.5 x 15 cm) and eluted with chloroform-methanol (9:1). Forty (5 ml) fractions were collected. Fraction 3-8 yielded N,O-diacetyl-3-hydroxynornuciferine (**5**) as a pale yellow oil (12 mg); $[\alpha]^{23}D$ −37° (c 0.46, MeOH) uv λ max (MeOH) 222 nm (log ε 3.17), 275 (2.93); ir ν (KBr) 2960, 2930, 2860, 1770, 1740, 1650, 1550, 1490, 1450, 1410, 1370, 1350, 1250, 1205, 1160, 1125, 1075, 1050, 1035, 1020, 980, 950, 935, 890, 850, 800, 760, 735 cm^{-1}; ms *m/z* 382 (4%), 381 (M^+, 23), 322 (25), 321 (23), 280 (56), 279 (20), 267 (100), 251 (10), 233 (6), 180 (12), 165 (30), 152 (45).

PREPARATION OF 3-HYDROXYNUCIFERINE (**6**).—Formalin (37%, 0.5 ml) was added dropwise with stirring to a solution of 3-hydroxynornuciferine (**1**) (24.8 mg) in methanol (3 ml). After one hour of stirring, sodium borohydride (50 mg) was added slowly and stirring was continued for one hour. After evaporation, the resulting residue was diluted with water (20 ml) and acidified with dilute hydrochloric acid to pH 3. It was then basified with ammonium hydroxide to pH 9 and extracted with chloroform (10 ml x 4). The combined chloroform extracts were dried over anhydrous sodium sulfate and evaporated to residue (22.8 mg). The residue was placed on a silica gel column (1 g; 0.5 x 8 cm) and eluted with chloroform-methanol (8:2). Fifty fractions (0.25 ml) were collected. Fractions 12–13 were combined to yield 3-hydroxynuciferine (**6**) as a pale yellow amorphous residue (6 mg); $[\alpha]^{29}D$ −56° (c 0.36, MeOH); uv λ max (MeOH) 215 nm (log ε 3.14), 222 (3.15), 283 (2.95), 295 (sh) (2.86); uv λ max (MeOH+OH^-) 214 nm (log ε 3.31), 230 (sh) (3.18), 316 (3.13); uv λ max (MeOH+H^+) same as MeOH spectrum; ir ν max (KBr) 3400 (br), 2940, 2860, 2800, 1592, 1498, 1470, 1453, 1438, 1420, 1378, 1355, 1228, 1205, 1120, 1090, 1060, 1015, 982, 880, 865, 820, 760, 700, 680, 650 cm^{-1}; ^{1}H-nmr ($CDCl_3$) 8.2–8.4 (1H, m) (C–11), 7.15–7.3 (3H, m) (C–8,9,10), 3.98 (3H, s) (C–2 methoxy), 3.70 (3H, s) (C–1 methoxy), 2.55 (3H, s) (*N*-methyl); ms *m/z* 312 (19%), 311 (M^+, 98), 310 (100), 309 (84), 296 (68), 294 (70), 280 (40), 268 (36), 249 (14), 237 (41), 194 (19), 178 (20), 165 (36), 147 (38). The product was identical (uv, ir, ^{1}H-nmr, ms, [α] D) to authentic 3-hydroxynuciferine (**6**).

ISOMOSCHATOLINE (**2**).—Isomoschatoline (**2**) was isolated as red cuboidal crystals (100 mg); mp 245° (MeOH); HCl mp (>300°); $[\alpha]^{29}D$ 0° (c 0.5, MeOH); uv λ max (MeOH) 230 nm (log ε 4.10), 283 (4.26), 363 (2.96), 467 (3.53); uv λ max (MeOH+OH^-) 219 (4.28), 308 (4.32), 604 (3.63); uv λ max (MeOH+H^+) 222 (4.28), 288 (4.25), 545 (3.31); ir ν max (KBr) 3450 (br), 1662, 1598, 1580, 1560, 1545, 1478, 1470, 1388, 1308, 1260, 1200, 1090, 1045, 1035, 988, 975 cm^{-1}; ^{1}H-nmr (TFA) 9.33 (1H, d, J=8 Hz) (C–11), 9.12 (1H, d, J=6 Hz) (C–5), 8.88 (1H, d, J=6 Hz) (C–4), 8.60 (1H, d, J=8 Hz) (C–8), 8.07 (1H, m) (C–9), 7.72 (1H, m) (C–10), 4.33 (6H, s) (C–1,2 methoxys); ^{1}H-nmr (CD_3OD) 4.05 (3H, s) (C–1 methoxy), 4.11 (3H, s) (C–2 methoxy); ms *m/z* 308 (21%), 307 (M^+, 100), 293 (5), 292 (24), 265 (3), 264 (18), 260 (7), 249 (10), 221 (10), 193 (4), 165 (7), 164 (6), 153.5 (M^{++}, 3).

PREPARATION OF *O*-METHYLISOMOSCHATOLINE (*O*-METHYLMOSCHATOLINE) (**8**).—Treatment of isomoschatoline (**2**) (10 mg) with excess ethereal diazomethane[5] for 24 hours followed by evaporation yielded a yellow residue. The residue was chromatographed on a silica gel-celite column (10 g, 1.5 x 15 cm) packed and eluted with benzene-methanol (85:15). Fourteen fractions (2 ml) were collected with fractions 9–13 pooled to afford *O*-methylisomoschatoline (**8**) as a yellow amorphous residue (8 mg); ir ν max (KBr) 3440 (br) 2940, 2850, 1660, 1595, 1580, 1540, 1488, 1480, 1465, 1390, 1330, 1310, 1260, 1255, 1200, 1155, 1112, 1090, 1055, 1042, 1000, 970, 935, 905, 845, 838, 815, 795, 775, 755, 700, 685, 672, 640 cm^{-1}; ^{1}H-nmr ($CDCl_3$) 4.21 (3H, s) (C–3 methoxy), 4.12 (3H, s) (C–2 methoxy), 4.08 (C–1 methoxy); ^{1}H-nmr (CD_3OD) 4.10 (6H, s) (C–1,2 methoxys), 4.20 (3H, s) (C–3 methoxy); ms *m/z* 322 (24%), 321 (M^+, 100), 307 (11), 306 (44), 292 (6), 291 (13), 279 (4), 278 (21), 264 (5), 263 (23), 249 (4), 248 (14), 235 (10), 234 (6), 221 (5), 220 (25), 192 (8), 164 (15), 163 (4), 160.5 (M^{++}, 6), 145.5 (6).

The product was identical (ir, ^{1}H-nmr, ms) to authentic O-methylmoschatoline (**8**) available in our laboratory.

PREPARATION OF *O*-ACETYLISOMOSCHATOLINE (**9**).—Acetic anhydride (1 ml) was added to a solution of isomoschatoline (**2**) (20 mg) in pyridine (1 ml) and set aside at room temperature for 24 hours. The solution was then chilled, and cold distilled water was added (5 ml). The aqueous solution was then basified with concentrated ammonium hydroxide to pH 9 and extracted with chloroform (5 ml x 3). The chloroform extracts were combined, dried over anhydrous sodium sulfate and evaporated; a yellow solid residue was obtained. The residue was chromatographed on a silica gel column (25 g, 3 x 15 cm) packed with benzene-methanol (10:1). Elution with benzene-methanol (10:1) and collection of the yellow band (30 ml) afforded *O*-acetylisomoschatoline (**9**) as fine yellow needles (15 mg); mp 193–4° dec. ($CHCl_3$); uv λ max (MeOH) 212 nm (log ε 4.38), 236 (4.42), 268 (4.49), 315 (sh) (3.73), 422 (3.89); uv λ max (MeOH+OH^-) 213 (4.48), 227 (sh) (4.38), 307 (4.57), 610 (3.85); uv λ max, (MeOH+H^+) 212 (4.36), 241 (4.39), 277 (4.44), 374 (sh) (3.64), 470 (3.56); ir ν max (KBr) 2930, 2850, 1768, 1665, 1610, 1585, 1480, 1465, 1395, 1370, 1335, 1310, 1260, 1200, 1170, 1150, 1115, 1085, 1035, 1005, 965, 924, 880, 845, 815, 755, 692 cm^{-1}; ^{1}H-nmr ($CDCl_3$) 9.14 (1H, dd, J=8, 2Hz) (C–11), 9.00 (1H, d, J=5Hz) (C–5),

[5]Diazald—Aldrich Chemical Co.

8.57 (1H, dd, J=8, 2Hz) (C-8), 7.89 (1H, d, J=5Hz) (C-4), 7.63 (1H, m) (C-9), 7.48 (1H, m) (C-10), 4.08 (3H, s) (C-1 methoxy), 4.05 (3H, s) (C-2 methoxy), 2.55 (3H, s) (C-3 acetoxy); ms m/z 350 (3%), 349 (M^+, 14), 309 (3), 308 (21), 307 (100), 293 (4), 292 (20), 278 (4), 264 (13), 260 (6), 249 (6), 223 (5), 221 (7), 220 (6), 184 (4), 168 (7), 165 (7), 164 (7), 141 (7), 140 (4), 139 (5), 137 (4), 128 (4), 115 (8), 77 (15), 43 (2). *O*-Acetylisomoschatoline (**9**) was not identical (mp, ir, ^{1}H-nmr) with authentic[3] *O*-acetymoschatoline (**10**).

PREPARATION OF *N,O*-DIACETYL-3-HYDROXYNORNUCIFERINE (**5**) FROM ISOMOSCHATOLINE (**2**). REDUCTION AND ACETYLATION OF ISOMOSCHATOLINE (**2**).—A solution of isomoschatoline (**2**) (75 mg) in acetic acid-water (2:1, 3 ml) was treated with zinc powder (4.5 gm) and concentrated hydrochloric acid (9 ml) (10). The reaction mixture was refluxed at 100° for 2 hours. The acidic solution was then basified to pH 8 with concentrated ammonium hydroxide and extracted with chloroform (10 ml x 4). The combined chloroform extracts were dried over anhydrous sodium sulfate and evaporated to yield a residue (71 mg). Acetic anhydride (1 ml) was added to a solution of the residue in pyridine (2 ml) and set aside at room temperature for 24 hours. The solution was chilled, and cold distilled water (5 ml) was added. The aqueous solution was basified to pH 9 with concentrated ammonium hydroxide and extracted with chloroform (10 ml x 3). The combined chloroform extracts were dried over anhydrous sodium sulfate and evaporated to yield a residue (41 mg). The residue was chromatographed on a silica gel column (15 g, 2 x 18 cm). Elution with chloroform-methanol (88:12) first yielded *N,O*-diacetyl-3-hydroxynornuciferine (**5**) (7 mg) and then starting material (isomoschatoline) (**2**) (10 mg). The product (**5**) was obtained as a pale yellow amorphous residue; $[\alpha]^{29}$D 0° (c 0.3, MeOH); ^{1}H-nmr ($CDCl_3$) 8.3–8.4 (1H, m) (C-11), 7.2–7.35 (3H, m) (C-8,9,10), 3.90 (3H, s) (C-2 methoxy), 3.71 (3H, s) (C-1 methoxy), 2.37 (3H, s) (C-3 acetoxy), 2.16 (3H, s) (*N*-acetyl). The product was identical (^{1}H-nmr, ms, ir, uv) to authentic *N,O*-diacetyl-3-hydroxynornuciferine (**5**).

PALLIDINE (**3**).—Pallidine (**3**) was isolated as an amorphous residue: $[\alpha]^{29}$D −29° (c 1.0, MeOH). The substance was identical (ir, uv, $[\alpha]$ D) to an authentic[6] sample.

LIRIODENINE (**4**).—Liriodenine (**4**) was isolated as yellow needles; mp 282–3°. The substance was identical (mmp, ir, uv) to an authentic sample available in our laboratories.

ACKNOWLEDGMENTS

The authors express their appreciation to Drs. Norman R. Farnsworth and Geoffrey A. Cordell, School of Pharmacy, University of Illinois at the Medical Center, Chicago, Illinois, for providing the plant material used in this study, and to Drs. Cava, Bick and Shamma for providing reference samples.

Received 25 January 1982

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[6]Sample kindly supplied by Dr. Maurice Shamma, Department of Chemistry, Pennsylvania State University, State College, PA.