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ALKALOIDS FROM THE LEAVES OF *PHYLLANTHUS DISCOIDEUS*

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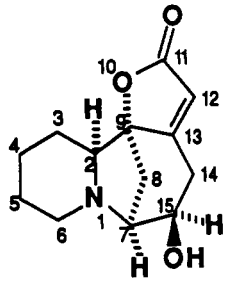
ABSTRACT.—A new alkaloid, the 14,15-dihydroallosecurinine-15β-ol [**1**], was isolated from the leaves of *Phyllanthus discoideus* and identified by spectral data and physical analysis.

Phyllanthus discoideus (Baill.) Müll Arg. (Euphorbiaceae) is a small tree widely used in tropical West Africa in local medicine. The leaves are used as a tonic and in various infectious diseases. The bark is given mainly as a purgative and antipyretic (1,2). Several alkaloids have been isolated from the root bark (3–6). Two alkaloids, securinine and allosecurinine, have been reported from the stem bark and leaves of the Nigerian species (7). In the present work, we report the isolation of five alkaloids from the leaves of samples from the Ivory Coast.

The powdered leaves of *P. discoideus* were extracted with H_2O (room temperature), and the aqueous extracts, after concentration, were basified and extracted with $CHCl_3$. After conventional acid/base extraction of the $CHCl_3$ extracts, the alkaloids were isolated by column, centrifugal tlc, and preparative chromatography on Si gel. Four known compounds were identified as securinine, dihydrosecurinine, viroallosecurinine [**2**] and norsecurinine [**3**] by comparison with published data (mp, $[\alpha]_D$, uv, ir, ms, ^1H nmr, and ^{13}C nmr) (8–15). The uv, ir, ms, and ^1H-nmr spectrum of viroallosecurinine and the ^{13}C-nmr spectra of viroallosecurinine and norsecurinine have not been published in previous papers and accordingly are reported here. Spectral data of a new compound, **1**, were in agreement with the structure of a 14,15-dihydroallosecurinine-15β-ol.

The ir spectrum of **1** showed absorption at 3467 cm^{-1} attributable to a hydroxyl



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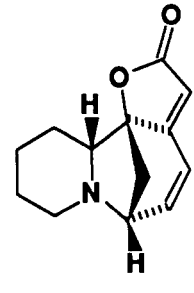

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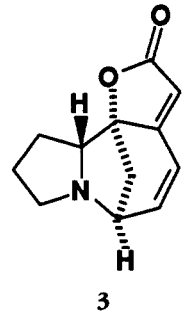

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group. The eims of compound **1** showed major peaks at *m/z* $[M]^+$ 235, 191, 163, 140, 134, 84, 44. These fragments suggested that the alkaloid belongs to the *Securinega* type with a hydroxyl group. The most important peak at *m/z* 191 was formed by loss of CH_2CHOH. These fragments agreed with the formula $C_{13}H_{17}NO_3$ (16,17). In the ^{1}H-nmr spectrum, the position of a hydroxyl at C-15 was given by a signal centered at δ 3.0 and attributable to a CH-C*H*OR-CH_2 system (12,16,17). The triplet at δ 5.63 (J = 2 Hz) was attributable to H-12 and confirmed the 15β position of the hydroxyl group (16,17). The ^{13}C-nmr spectrum in $CDCl_3$ and the induced shifts with Eu(fod)$_3$ confirmed the securinine skeleton (13) and the presence of a hydroxyl group at the C-15 position (Table 1).

TABLE 1. Shift Assignments for Alkaloid **1**.

Carbon	Chemical shift ($CDCl_3$ ppm)	Chemical shift with Eu(fod)$_3$ (1 mol ratio, ppm)	Induced shift (Δ ppm)
C-11	174.62 s	177.69	3.07
C-13	173.73 s	175.97	2.24
C-12	109.53 d	111.97	2.44
C-15	67.95 d	69.20	1.25
C-14	28.89 t	28.60	1.71

Only three compounds with the securinine skeleton containing a hydroxyl group have been identified previously: 14,15-dihydroviroallosecurinin-15α-ol (securinol A), 14,15-dihydroviroallosecurinin-15β-ol (securinol B), and 14,15-dihydroallosecurinin-14-ol (securinol C) (12,16,17). These compounds are different from **1**, according to the mp and [α]D.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp's were taken on a Reichert microscope and were uncorrected. The uv spectra were obtained with a Hewlett-Packard 8451 A spectrophotometer and the ir spectra with a Perkin-Elmer PE 983 spectrophotometer. A Brucker WM 250 spectrometer was used to record ^{1}H-nmr (250 MHz) and ^{13}C-nmr (62.89 MHz) spectra. Optical rotations were measured with a Perkin-Elmer model 141 polarimeter in EtOH solution. Ms were measured at 70 eV, 3500 V in a Varian LKB 20.91 mass spectrophotometer.

PLANT MATERIAL.—The plant material was collected from the Ivory Coast. A voucher specimen was deposited in the Herbarium of the Faculté des Sciences Pharmaceutiques, Université Toulouse III, France.

EXTRACTION AND PURIFICATION OF THE ALKALOIDS.—The air-dried, powdered leaves (1 kg) of *P. discoideus* were extracted with H_2O at room temperature (5 × 5 liters). The extracts were concentrated, basified to pH≃8, and extracted with $CHCl_3$ (5 × 500 ml). The organic layer was extracted with 1 N H_2SO_4. The aqueous acid layer was basified to pH 8 and extracted with $CHCl_3$ (5 × 500 ml). The evaporated $CHCl_3$ extract (5 g) was subjected to Si gel (300 g) cc (35 × 600 mm) and eluted with $CHCl_3$ followed by $CHCl_3$/MeOH mixtures of increasing polarity. Fractions of 100 ml were collected, and the fractions with similar composition were combined. The $CHCl_3$-MeOH (99:1) fraction was re-chromatographed on a Si gel column and eluted with *n*-PrOH-H_2O (70:30) to afford **1**. The $CHCl_3$-MeOH (98:2) fraction contained securinine that was crystallized from EtOH. The $CHCl_3$-MeOH (96:4) fraction was rechromatographed by centrifugal tlc with $CHCl_3$-MeOH (99.5:0.5 to 99:1) as eluent to afford dihydrosecurinine and viroallosecurinine [**2**]. Norsecurinine [**3**] contained in the $CHCl_3$-MeOH (90:10) fraction was isolated by centrifugal tlc with $CHCl_3$-MeOH (95:5) as eluent and preparative tlc on Si gel with hexane-Me_2CO (90:10) as eluent.

14,15-DIHYDROALLOSECURININ-15β-OL [**1**].—$C_{13}H_{17}NO_3$; crystallized from *n*-PrOH (orange-yellow); mp 157–158°; $[\alpha]^{25}D$ −96° (c = 0.48, EtOH); uv λ max (MeOH) nm 220; ir ν max (KBr) cm^{-1} 3467, 1806, 1756, 1645, 1400, 1260, 1166, 1088, 1022, 905, 855, 685; ms *m/z* (rel. int.) $[M]^+$ 235 (46), 207 (21), 205 (5), 191 (83), 176 (21), 163 (23), 140 (45), 134 (25), 110 (92), 84 (48), 78 (19), 55 (76), 44 (25), 39 (100); ^{1}H nmr ($CDCl_3$) δ 5.63 (1H, t, J = 1.87 Hz, H-12), 3.70 (1H, broad s, H-7), 3.23 (1H, broad s, 15-OH), 3.00 (1H, dt, J_1 = 19.6 Hz, J_2 = 2.5 Hz, H-15), 2.77 (2H, m, 2 × H-6),

2.70–2.59 (2H, m, 2 × H-14), 2.33 (1H, d, J = 10.5 Hz, H-8α), 2.10 (1H, dd, J_1 = 10.5 Hz, J_2 = 3.5 Hz, H-8β), 1.95–1.30 (7H, m, H-2, 2 × H-3, 2 × H-4, 2 × H-5); ^{13}C nmr ($CDCl_3$) δ 174.62 (s, C-11), 173.73 (s, C-13), 109.53 (d, C-12), 83.90 (s, C-9), 67.95 (d, C-15), 65.47 (d, C-2), 59.87 (d, C-7), 52.98 (t, C-6), 35.76 (t, C-8), 26.89 (t, C-14), 26.06 (t, C-3), 25.21 (t, C-5), 24.73 (t, C-4).

VIROALLOSECURININE [**2**].—$C_{13}H_{15}NO_2$; crystallized from *n*-PrOH (orange-yellow plates); mp 135–136°; $[\alpha]^{25}D$ +990° (c = 0.98, EtOH); uv λ max (MeOH) nm 256; ir ν max (KBr) cm^{-1} 1812, 1797, 1752, 1627, 1253, 1178, 1076, 906, 860, 694; ms *m/z* (rel. int.) $[M]^+$ 217 (4.0), 134 (11), 106 (28), 100 (23), 84 (100), 78 (46), 55 (30); ^{1}H nmr ($CDCl_3$) δ 6.79 (1H, dd, J_1 = 9.1 Hz, J_2 = 5.5 Hz, H-15), 6.63 (1H, d, J = 9.1 Hz, H-14), 5.70 (1H, s, H-12), 3.88 (1H, t, H-7), 3.63 (1H, dd, J_1 = 12.9 Hz, J_2 = 3.6 Hz, H-2), 2.72 (2H, m, 2 × H-6), 2.65 (1H, dd, J_1 = 9.8 Hz, J_2 = 4.2 Hz, H-8α), 1.90 (1H, d, J = 9.8 Hz, H-8β), 1.66–1.08 (6H, m, 2 × H-3, 2 × H-4, 2 × H-5); ^{13}C nmr ($CDCl_3$) δ 172.44 (s, C-11), 167.32 (s, C-13), 148.53 (d, C-15), 122.40 (d, C-14), 108.65 (d, C-12), 91.45 (s, C-9), 60.51 (d, C-2), 58.55 (d, C-7), 43.36 (t, C-6), 42.43 (t, C-8), 21.90 (t, C-4), 20.80 (t, C-3), 18.21 (t, C-5).

NORSECURININE [**3**].—$C_{12}H_{13}NO_2$; oil; $[\alpha]^{25}D$ −246° (c = 0.98, EtOH); uv λ max (MeOH) nm 258; ir ν max (KBr) cm^{-1} 1800, 1751, 1629, 1247, 1217, 1107, 1070, 960, 855, 688; ms *m/z* (rel. int.) $[M]^+$ 203 (4), 134 (12), 106 (30), 85 (60), 83 (71), 78 (47), 70 (100); ^{1}H nmr ($CDCl_3$) δ 6.74 (1H, dd, J_1 = 9 Hz, J_2 = 5.5 Hz, H-15), 6.47 (1H, d, J = 9 Hz, H-14), 5.65 (1H, s, H-12), 3.61 (1H, t, J = 6.5 Hz, H-7), 3.28 (1H, m, H-5), 3.22 (1H, dd, J = 15 Hz, H-2), 2.57 (2H, m, H-5, H-8α), 1.70 (1H, d, J = 10.5 Hz, H-8β), 1.99–1.77 (4H, m, 2 × H-3, 2 × H-4); ^{13}C nmr ($CDCl_3$) δ 172.61 (s, C-11), 168.32 (s, C-13), 143.71 (d, C-15), 120.24 (d, C-14), 107.63 (d, C-12), 91.72 (s, C-9), 64.92 (d, C-2), 59.60 (d, C-7), 55.10 (t, C-5), 35.61 (t, C-8), 29.16 (t, C-3), 26.64 (t, C-4).

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