

TWO NEW TERTIARY INDOLE ALKALOIDS OF *STRYCHNOS DECUSSATA*

AJIBOLA A. OLANIYI¹ and WENCHE N. A. ROLFSEN²

*Department of Pharmacognosy, Faculty of Pharmacy, Box 579, Biomedical Center,
University of Uppsala, S-751 23 Uppsala, Sweden*

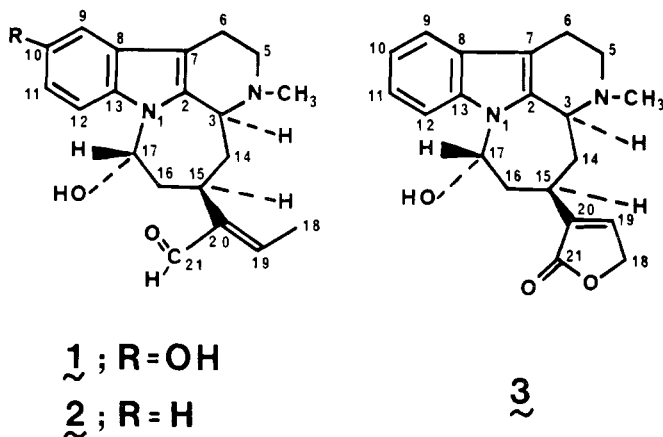
ABSTRACT.—From the chloroform fraction of the stem bark of *Strychnos decussata* (Pappe) Gilg (Loganiaceae), two new tertiary indole alkaloids, 10-hydroxyakagerine (1) and akagerinelactone (3), have been isolated. The structures of the alkaloids have been elucidated by means of their spectral data, particularly ¹H-nmr and ¹³C-nmr.

In a recent publication, we reported the isolation of five tertiary indole alkaloids, three of which were new, from the stem bark of *Strychnos decussata* (1). In continuation with our studies of the convulsant and muscle-relaxant constituents of *S. decussata*, we have now isolated two more indole alkaloids from the chloroform fraction of the stem bark.

RESULTS AND DISCUSSION

The proposed structures are presented in the figure.

Alkaloid 1 analyzed for C₂₀H₂₄N₂O₃ (M⁺, 340.1795); C₂₀H₂₄N₂O₃ requires 340.1787. The alkaloid's uv spectrum, which was strikingly similar to that of 10-hydroxy-17-O-methylakagerine, showed a bathochromic shift on addition of alkali, suggesting the presence of a phenolic function. The ir spectrum showed absorption peaks at 3280 cm⁻¹ (—OH) and at 1665 cm⁻¹ (—C=O). A comparison of the ms of alkaloid 1 with that of akagerine (2) showed a constant difference of 16 mass units higher values for the fragments containing the aromatic moiety in alkaloid 1. The ¹H-nmr spectrum of alkaloid 1 exhibited signals for an aldehydic proton at δ9.22 (1H, *s*), an ethylidene chain at δ6.52 (1H, *q*) and δ2.04 (3H, *d*), and three aromatic protons in the region δ7.10–6.62. This is almost identical with the ¹H-nmr spectrum of 10-hydroxy-17-O-methylakagerine, except for the absence of



¹Present address: Dept. of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Ife, Ile-Ife, Nigeria.

²To whom correspondence should be addressed.

a three-proton singlet for a methoxy group in **1**, suggesting that alkaloid **1** is 10-hydroxyakagerine.

Alkaloid 3 analyzed for $C_{20}H_{22}N_2O_3$ (M^+ , 338.1655); $C_{20}H_{22}N_2O_3$ requires 338.1657. The uv spectrum of this alkaloid was typical of akagerine-like compounds (1). The ir spectrum of alkaloid **3** showed a strong absorption at 1735 cm^{-1} , suggesting the presence of an α,β -unsaturated lactone. The $^1\text{H-nmr}$ spectrum of alkaloid **3** was very similar to that of akagerine, differing only in the protons of the side chain, H-18, H-19 and H-21. The signals due to the aldehydic proton, $\delta 9.24$ (1H, *s*), and the ethylidene chain protons, $\delta 6.43$ (1H, *q*) and $\delta 2.03$ (3H, *d*), present in the $^1\text{H-nmr}$ of akagerine were replaced by a two-proton triplet and a one-proton multiplet resonating at $\delta 4.80$ and $\delta 7.12$, respectively, in the spectrum of alkaloid **3**. The assignments of the spectrum were carried out by decoupling experiments, further supporting a lactone ring in alkaloid **3**. Irradiating the signals at $\delta 4.80$ and at $\delta 7.12$ revealed coupling between H-18 and H-19. Further decoupling studies showed long range coupling both between $\delta 3.45$ (H-15) and $\delta 7.12$ (H-19) and between $\delta 3.45$ and $\delta 4.80$ (H-18). The $^{13}\text{C-nmr}$ spectrum of alkaloid **3** was also similar to the spectrum of akagerine-like compounds, except for the carbons in the side chain. The signals for C_{18} (CH_3 , 15.1), C_{19} (CH , 150.7), C_{20} (C , 147.8), and C_{21} (H-C=O- , 195.0) in akagerine disappeared in the $^{13}\text{C-nmr}$ spectrum of alkaloid **3**; the following signals were observed instead: CH_2 (70.23), CH (144.11), C (138.21) and C (173.40), respectively. The signals of the $^1\text{H-nmr}$ and $^{13}\text{C-nmr}$ of alkaloid **3** are in full accord with the replacement of the ethylidene-aldehyde side chain in akagerine by a lactone ring in alkaloid **3**, for which the name akagerinelactone has been given.

Further evidence for the presence of a lactone ring was provided by positive color reactions with reagents for the detection of an unsaturated lactone group.

Comparing the values of the $^1\text{H-nmr}$ and $^{13}\text{C-nmr}$ spectra of akagerinelactone and akagerine, it is most likely that the configuration at the asymmetric carbons C-3, C-15 and C-17 are the same in the two alkaloids.

No pharmacological testing of the two new alkaloids was performed due to the limited amount of material isolated.

EXPERIMENTAL³

Details of plant collection, extraction and chromatographic procedures have been reported elsewhere (1).

10-HYDROXYAKAGERINE (1).—Purified by preparative tlc using cyclohexane-chloroform-diethylamine (50:40:10) as mobile phase, 10-hydroxyakagerine was obtained as a pale brown powder (8.5 mg) mp $154\text{--}156^\circ$. It gave uv: λ max ($\log \epsilon$) (ethanol): 230.5 (4.38), 280 (3.93), 308 (sh, 3.60) and 312 (3.52) nm; λ max ($\log \epsilon$) (addition of KOH): 232 (4.74), 279 (3.89) and 322 (3.54) nm; ir: ν max (KBr): 3280, 2900, 2820, 1665, 1620, 1460, 1360, 1210, 1150, 1100, 900, 830 and 785 cm^{-1} ; ms: m/z (%): 340 (11, M^+), 322 (17), 293 (7), 276 (5), 253 (14), 214 (7), 202 (16), 201 (100), 200 (27), 187 (10), 172 (11), 160 (6), 159 (6), 144 (5) and 143 (2); $^1\text{H-nmr}$ (CDCl_3): 89.22 (1H, *s*, H-21), 7.10 (1H, *d*, $J=9\text{ Hz}$, H-12), 6.70 (1H, *d*, $J=2\text{ Hz}$, H-9), 6.62 (1H, *dd*, $J=9\text{ Hz}$, 2Hz, H-11), 6.52 (1H, *q*, $J=7\text{ Hz}$, H-19), 6.04 (1H, broad *s*, H-17), 2.48 (3H, *s*, N-CH_3) and 2.04 (3H, *d*, $J=7\text{ Hz}$, H-18) ppm.

³The uv spectra were run on a Shimadzu MPS-5000 UV-VIS spectrophotometer, the ir spectra on a Jasco-IRA-I-spectrophotometer and the ms spectra on an LKB 9000 instrument at 70 eV with direct inlet system. $^1\text{H-nmr}$ spectra were run on a Jeol 100 MHz spectrometer and the $^{13}\text{C-nmr}$ spectrum was recorded on a Varian 100 MHz instrument at 25.2 MHz in the Fourier transform mode. Melting points were determined with a Leitz mikroskopheitztisch 350. Preparative thin-layer chromatography (tlc) was carried out on either precoated silica gel plates (0.25 mm, silica gel Si60 F₂₅₄, E. Merck) or on a 0.50 mm layer of silica gel (type 60, GF₂₅₄, E. Merck) spread on 20 x 20 cm glass plates.

Reagents used for the detection of unsaturated lactones on tlc: Keddes reagent [2], Baljets reagent [2], Raymonds reagent [3], Legals reagent [4] and hydroxyl ammonium chloride: ferric (III) chloride [4].

AKAGERINELACTONE (3).—On purification by preparative tlc using diethyl ether-ethanol-diethylamine (90:3:7) as mobile phase, *akagerinelactone* crystallized from ethanol/diethyl ether as colorless needles (17 mg), mp 184–186°. It gave uv: λ max (log ϵ) (ethanol) 222 (4.33), 276 (3.90), 283 (3.91) and 293 (3.80) nm; ir: ν max (KBr): 3350, 3000, 2900, 2820, 2760, 1735, 1640, 1600, 1460, 1380, 1350, 1310, 1270, 1200, 1190, 1090, 1060, 1040, 980, and 735 cm^{-1} ; ms: m/z (%): 338 (9, M^+), 323 (4), 320 (7), 214 (6), 198 (8), 186 (15), 185 (100), 183 (10), 171 (18), 169 (5), 156 (13), 144 (8) and 143 (6); ^1H -nmr: ($\text{CDCl}_3 + \text{CD}_3\text{OD}$): δ 7.58–7.16 (4H, *m*, H-9, H-10, H-11, H-12), 7.12 (1H, *m*, H-19), 6.30 (1H, *m*, H-17), 4.80 (2H, *t*, $J = 1\text{Hz}$, H-18) and 8.45 (1H, *m*, H-15) and 2.59 (3H, *s*, N- CH_3) ppm; ^{13}C -nmr: ($\text{CDCl}_3 + \text{CD}_3\text{OD}$) C-2 136.11, * C-3 60.04, C-5 50.58, C-6 19.63, C-7 108.38, C-8 126.34, C-9 118.39, C-10 121.79, C-11 119.68, C-12 108.68, C-13 135.40*, C-14 38.81, C-15 29.06, C-16 36.66, C-17 75.04, C-18 70.23, C-19 144.11, C-20 138.21, C-21 173.40 and N- CH_3 42.15 ppm.

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* (Assignment may be reversed.)