SHIHUNINE AND DIHYDROSHIHUNINE FROM *BANISTERIOPSIS CAAPI*

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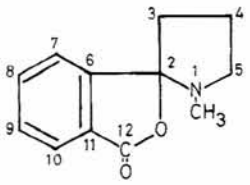
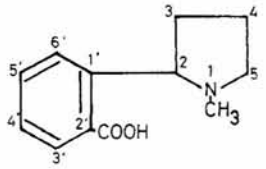
ABSTRACT.—Nine alkaloids of the β-carboline type have been isolated from *Banisteriopsis caapi* Morton (Malpighiaceae). Two new alkaloids of a different structural type, shihunine and dihydroshihunine, are reported here. The former had been isolated earlier from *Dendrobium lohohense* Tang. and Wang., and *D. pierardii* Roxb.; this is the first recorded natural occurrence of the latter, which possesses the S configuration.

Harmine, harmaline and tetrahydroharmine are well-known constituents of *Banisteriopsis cappi* (1, 2). In previous communications we reported the isolation of six new β-carboline alkaloids: harmine-*N*-oxide, harmic acid methylester, harmalinic acid, harmic amide, acetyl norharmine, and ketotetrahydronorharmine from this plant (3, 4). Now two additional alkaloids have been isolated and identified as the pyrrolidine bases shihunine (**1**) and S-(+) dihydroshihunine (**2**) (5–7).



1. Shihunine



2. Dihydroshihunine

RESULTS AND DISCUSSION

After isolation of the β-carboline alkaloids, the two new alkaloids were separated by column chromatography on silica gel and finally purified by preparative tlc.

Compound **1**, $C_{12}H_{13}NO_2$ by high resolution ms, mp [78–79° (lit. (6), 78.5–79°)] gave ir data identical to data for shihunine furnished by Prof. Inubushi. 200 MHz pmr showed better assignments for protons of pyrrolidine and benzene rings (6). The chemical shifts of cmr of this compound were the same as those given by Leete and Bodem (8). M^+ at *m/e* 203 [(intensity 8.9%)], on high and low resolution ms, was confirmed by fdms as $M+H^+$ at *m/e* 204; the base ion, *m/e* 158, $C_{11}H_{12}N$, was formed by decarboxylation on the cleavage of the phthalide ring and deprotonation of pyrrolidine ring. The second strong peak [(13.7%)], at *m/e* 103, C_8H_7, was formed by the loss of C_3H_5N from the pyrrolidine ring by fragmentation of the base ion. Shihunine was determined to be a racemic compound by $[\alpha]^{25}D-0°$ and no absorption of circular dichroism (cd) spectrum.

Ir and tlc data, ($C_{12}H_{15}NO_2$) high resolution ms, and mp [187–189° (lit. (6), 190–201°: (8), 185–190°)], for compound **2**, and for the compound formed by reduction of **1** with $NaBH_4$, were identical to data for dihydroshihunine furnished by Prof. Inubushi. The pmr and cmr substantiated this identification. $M+H^+$ appeared at *m/e* 205 in fdms and M^+ at 205 [(8.2%)] in low resolution ms. Peaks found for ions at *m/e* 190 [(52.0%)] and 172 [(27.9%)] can be accounted for by the loss of methyl and water from the molecular ion and the *m/e* fragment 190, respectively. The base ion was at *m/e* 84, $C_5H_{10}N$, corresponding to *N*-methyl pyrrolinium. The absolute configuration at C-2 of the pyrrolidine ring in dihydroshihunine ($[\alpha]^{25}D+234.7$) was established as S by the cd Cotten effect,

($[\theta]_{244}^{25}$+23200 in MeOH) as compared with those of S ($[\alpha]^{25}$D −32.5°, positive Cotten bands) and R ($[\alpha]^{25}$D+34.1°, negative Cotten bands) of α-phenetylamines (9). The cd spectrum of the synthetic dihydroshihunine ($[\alpha]^{25}$D0°) showed no absorption 220–350 nm, indicating a racemic compound.

Thus, the two compounds were shown to possess the pyrrolidine nuclei of shihunine and dihydroshihunine. Although shihunine had been previously isolated from *Dendrobium lohohense* Tang. and Wang. and *D. pierardii* Roxb., S-(+) dihydroshihunine is reported here for the first time as a constituent of the plant kingdom. It is noteworthy from the chemotaxonomic point of view that Orchidaceous bases have now been found in a typical hallucinogenic plant of the Amazonian Malpighiaceae.

EXPERIMENTAL[1]

ISOLATION.—The last fraction (200 mg), when eluted with chloroform-methanol on a silica gel column chromatography as described in former reports (3,4), gave two bases. These bases were separated by repeated column chromatography with chloroform-methanol gradients and, finally, by preparative tlc with methylene dichloride-methanol-water (8:6:2) and methylazanide-water (7:3). Each of the two separate bands obtained was extracted with chloroform-methanol (5:1), and the alkaloids were crystallized from chloroform and methanol.

CHARACTERIZATION OF SHIHUNINE.—Yield 0.0001%, mp 78–79°, $[\alpha]^{25}$D 0° (c: 0.55, $CHCl_3$), $C_{12}H_{13}NO_2$ (found 203.094, calc. 203.095) by high resolution ms; uv λ max ($CHCl_3$) (log ε) 280.5(2.576), 273(2.689), 266 sh (2.609), 242(2.754); ir ν ($CHCl_3$) 1740 cm^{-1}; pmr (200 MHz) ($CHCl_3$) δ 2.1–2.2(2H, m, H-3 or 4), 2.11(3H, s, N-CH_3), 2.36–2.5(2H, m, H-4 or 3), 3.10(1H, dt, J=9.0 and 7.8, H-5), 3.36(1H, dt, J=9.0 and 4.4, H-5), 7.43(1H, ddd, J=7.5, 1.1 and 0.8, H-7), 7.54 (1H, td, J=7.5 and 1.1, H-8 or 9), 7.67(1H, td, J=7.5 and 1.1, H-9 or 8), and 7.86(1H, ddd, J=7.5, 1.1 and 0.8, H-10); ms, m/e (%) M^+ 203(8.9), 158(100), 103(13.7); fdms, m/e M+H^+ 204; cd(c: 4.93×10^{-4}, $CHCl_3$) [θ] (nm) 0(220–350).

CHARACTERIZATION OF DIHYDROSHIHUNINE.—Yield 0.00003%, mp 187–189°, $[\alpha]^{25}$D 234.7 (c: 0.542, $CHCl_3$), $C_{12}H_{15}NO_2$ (found 205.107, calc. 205.112) by high resolution ms; uv λ max ($CHCl_3$) (log ε) 273(3.093), 242.5(3.339); ir ν (KBr) 1613 cm^{-1}; pmr (200 MHz) ($CDCl_3$) δ 2–2.2 (4H, m, H-3 and 4), 2.45(3H, s, N-CH_3), 2.73(1H, like q, H-2), 3.60(2H, like td, H-5), 7.18(1H, dd, J=7.0 and 1.7, H-6'), 7.40(1H, td, J=7.0 and 1.7, H-4' or 5'), 7.42(1H, td, J=7.0 and 1.7, H-5' or 4') and 8.22(1H, dd, J=7.0 and 1.7, H-3'); cmr (22.6 MHz) (d_6-DMS) δ 21.52(t, C-4), 31.78(t, C-3), 37.40(q, N-CH_3 in $CDCl_3$ and CD_3OD), 53,59(t, C-5), 71.08 (d,C-2), 128.60(d, C-6'), 129.82(d, C-4'), 131.28(d, C-3'), 132.37(d, C-5'), 133.91(s, C-2'), 137.52(s, C-1'), and 170.18(s, C=O); ms, m/e (%) M^+ 205(8.2), 190(52.0), 172(27.9), 161(11.2), 160(9.9), 132(18.7), 84(100); fdms, m/e M+H^+ 206, cd(c: 5.85×10^{-5}, MeOH) [θ] (nm) 0(285), +4440(272 sh), +23200 (244), 0(227).

REDUCTION OF SHIHUNINE.—Shihunine (10 mg) was dissolved in 5 ml of methanol to which 10 mg of $NaBH_4$ in 5 ml methanol was added, and the resulting solution was allowed to stand overnight at 25°. The methanol was removed, and the residue was partitioned between chloroform and water. The chloroform solution, upon evaporation, gave a crystalline product which was confirmed as dihydroshihunine by ir. $[\alpha]^{25}$D 0° (c: 0.092, $CHCl_3$); cd(c: 2.0×10^{-3}, MeOH) [θ] (nm) 0(220–350). The measurements of $[\alpha]^{25}$D and cd values of authentic S-(−) and R-(+) α-phenethylamines (Tokyo Kasei Co. Ltd.) were performed. S one: $[\alpha]^{25}$D −32.5 (c: 0.658, $CHCl_3$); cd(c: 3.39×10^{-3}, MeOH) [θ] (nm) 0(271), +295(267), +94(264), +395(261), +189(258), +265(255), +183(252); and R one: $[\alpha]^{25}$D+34.1 (c: 0.625, $CHCl_3$); cd(c: 3.64×10^{-3}, MeOH) [θ] (nm) 0(271), −313(267), −104(264), −346(261), −181(258), −258(255), −153(252).

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[1]Melting points were determined on a Büchi micro melting point instrument and are uncorrected; uv spectra were recorded with the Hitachi 124 spectrometer; ir analyses were done on KBr discs, nujol mulls and $CHCl_3$ (film 0.1 mm) with the Hitachi 215 instrument. Field desorption mass spectra were examined on the JEOL JMS D100 spectrometer. Low and high resolution mass spectra were obtained on the JEOL JMS 01SG spectrometer. ^1H nmr spectra were measured with the Varian XL-200 spectrometer, and ^{13}C spectra were measured on the Varian XL-200 and NEVA NV-21 spectrometers in $CDCl_3$ solutions unless stated otherwise. Optical rotations were taken with the JASCO DIP-181 digital polarimeter. Cd spectra were recorded on the JASCO J-500C spectropolarimeter. Tlc analyses and preparative tlc were carried out on precoated plates with 0.25 and 0.5 mm layers of silica gel G with fluorescence indicator, respectively (E. Merck). Components were visualized under uv 254 nm and sprayed by Dragendorff's reagent.

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