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INDOLE ALKALOIDS FROM *UNCARIA GAMBIR*

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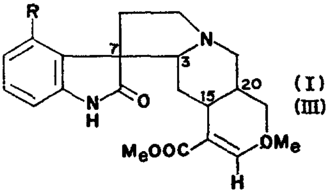
Plant. *Uncaria gambir* Roxb. *Source*. Botanical Gardens of Singapore. *Uses*. Manufacture of tannin. *Previous work*. Gambirine and dihydrocorynantheine from the leaves.[1] Chan[2] reported also the isolation of gambirdine and isogambirdine from the stems of *U. gambir*.

The methanolic extract of the leaves was treated with NH_4OH and extracted with Et_2O. Chromatography of the extract through silica gel with hexane/Et_2O mixtures gave, besides gambirine and dihydrocorynantheine, a mixture of rotundifoline (I) and isorhynchophylline (II), rhynchophylline (III) and a new alkaloid (A). The difficult[3] separation of isorhynchophylline and rotundifoline was accomplished by preparative TLC on silica gel with $Et_2O/HCOOH$ (99:1), then with Et_2O alone (3 runs). The three oxindole alkaloids were identified by m.p., UV, IR, MS and NMR spectra, CD curves, equilibration of II and III with 50% AcOH, and comparison with authentic samples. Gambirine was converted into rotundifoline in low yield with $Pb(AcO)_4$ in CH_2Cl_2,[4] thus confirming its stereochemistry.

The unknown alkaloid (A), purified by rechromatography through silica gel, has m.p. 300° (dec), R_f 0·56 (CHCl–Et_3N 9:1), 0·03 (Et_2O) on silica gel, grey spot on TLC with $Ce(SO_4)_2$, green with $FeCl_3$, violet Adamkiewicz reaction, mass 736 (analysis: C, 67·71; H, 7·05; N, 8·49%) UV: 230, 275, 291 and 300 nm (ε 76 000, 13 400, 11 800, 8700) in 95% EtOH, NMR (acetone-*d*, Fig. 1): 2 indole NH at 9·43 and 9·52 δ, unsubst. indole (7·0–7·5), 2 *ortho* protons (AB) at 6·66 (J = 8 Hz), a singlet at 7·38 (1 H), two CH–O or CH–N protons at 4:11 and 4:71, 3 OMe at 3·61, 3·73, 3·80, 25 H between 1·0 and 4·0, and a Me (unsymm. triplet at 0·9 δ). These data are consistent with a dimeric indole structure. The presence of a fragment including the carbons 15–20 of a dihydrocoryantheine is suggested by the conjugated doublet at 5·85 and 6·10 μ in the IR,[5] by the absence of a minimum in UV around 250 nm, and by the unsymmetrical triplet of the methyl group.[6] The shift of the



(I) R=OH, 7=A; (II) R=H, 7=B;
(III) R=H, 7=A; in all cases 3α,15α,20β.

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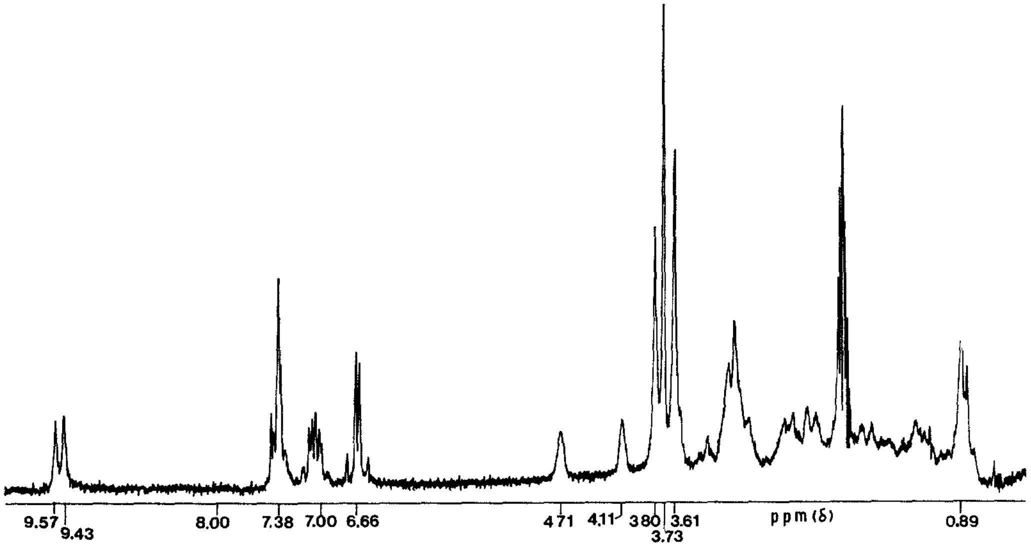

FIG. 1.

aromatic ortho protons (6·66 δ) could suggest that there are two OR substituents, probably in the positions 4 and 6 of an indole, consistently with the long wavelength maximum in UV. The proton at 4·71 δ, which is shifted downfield by CF_3COOH, is most probably attributed to a C_3–H (yohimbine nomenclature) and with equatorial orientation, that means a C/D ring *cis* junction. Selenium dehydrogenation afforded harman, norketoyobirine and nordehydroketoyobirine, identified by UV and MS spectra. Attempts to carry on degradations or derivatizations on 1–5 mg scale failed. Neither a 220 MHz NMR spectrum nor spin-decoupling experiments gave further details, due to the overlapping of the high-field signals.

Thus, on the basis of the available data, it can only be suggested that the compound is a dimeric indole alkaloid, one of the moieties being a dihydrocorynantheine-type substituted in 9 and 12 with two OR groups, and the other a yohimbine-type one. No further work is planned, due to lack of supply of material.

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Key Word Index—Uncaria gambir; Rubiaceae; indole alkaloids; rotundifoline; isorhynchophylline; rhynchophylline.