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STEROID ALKALOIDS OF SARACOCOCA PRUNIFORMIS LINDL.

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In view of the recent report on the occurrence of pro-aporphines (1) and pyrrocolines (2) in Euphorbiaceae several species of this family have been examined. Of these Saracococa pruniformis Lindl. appears to be interesting as it produces in its leaves steroid alkaloids of pregnane derivatives occurrence of which has been observed only in Apocynaceae (3) and Buxaceae (4).

The leaves of S. pruniformis are reported to contain a steroid alkaloid saracocine, the structure of which has been tentatively proposed as 3β-dimethylamino-20β-methyl-N-acylamino-Δ^5-preganene (I) (5).

Recently we have isolated two new steroid alkaloids, saracodine, m.p. 190-92° (yield, 0.001%) and saracodinine, m.p. 136° (yield, 0.0001%) from the same source besides saracocine, m.p. 235-36° (yield, 0.002%) and a neutral component, m.p. 246-8° (yield, 0.1%).

The structure and stereochemistry of saracodine and saracocine have been completely established.

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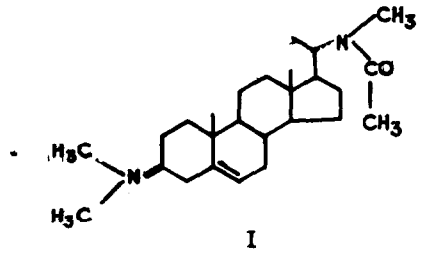
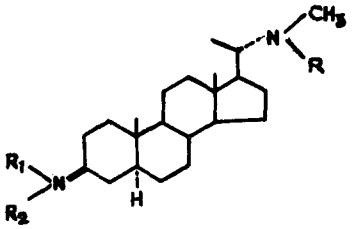
The leaves were successively extracted with petrol (b.p.60-80°) and chloroform. The chloroform extract of the defatted leaves was partitioned between the same solvent and 5% aqueous acetic acid to give a weak base fraction. The latter and the crude alkaloid mixture (weakly basic) from petrol extract of the leaves on thin layer chromatogram disclosed three Dragendorff-staining components. This mixture on chromatography over Brockmann alumina (eluted with petrol and ether mixture and ether) resolved into saracodinine, saracodine and saracocine. But it was extremely difficult to separate the closely similar alkaloids, saracocine and saracodine, the latter being a saturated base. The purity of saracodine was tested from an examination of its TLC, n.m.r. and mass spectra.

The base, saracodine crystallises from acetone in flakes, m.p. 190-92°. The elementary analysis of saracodine indicated the empirical formula $C_{26}H_{46}N_2O$. Mass spectrometry verified (molecular ion peak at m/e 402) this conclusion. It does not exhibit any characteristic UV absorption but its IR spectrum in chloroform discloses the presence of $-\overset{|}{C}-CH_3$ (7.35 μ), $N-CH_3$ (7.12 μ) and an amide linkage (6.15 μ) further proof of which was provided by chemical evidence and n.m.r. spectrum. In conformity with the amide structure saracodine undergoes hydrolysis with 10N H_2SO_4 in a sealed tube to a desacylcompound $C_{24}H_{44}N_2$, m.p. 94-96° which on subsequent N-methylation with formic acid and formaldehyde furnished the dimorphic dimethylchonemorphine (IIa), m.p. 108-9° and 123-24°, $[\alpha]_D^{30}$ + 24°, prepared from chonemorphine shown to be 3β-amino-20α-dimethylamino-5α-pregnane (IIb) (6) synthesised by Chatterjee and Das (7). This eventually

settles the structure of saracodine as 3β-dimethylamino-20α-methyl-N-acylamino-5α-pregnane (II).



I



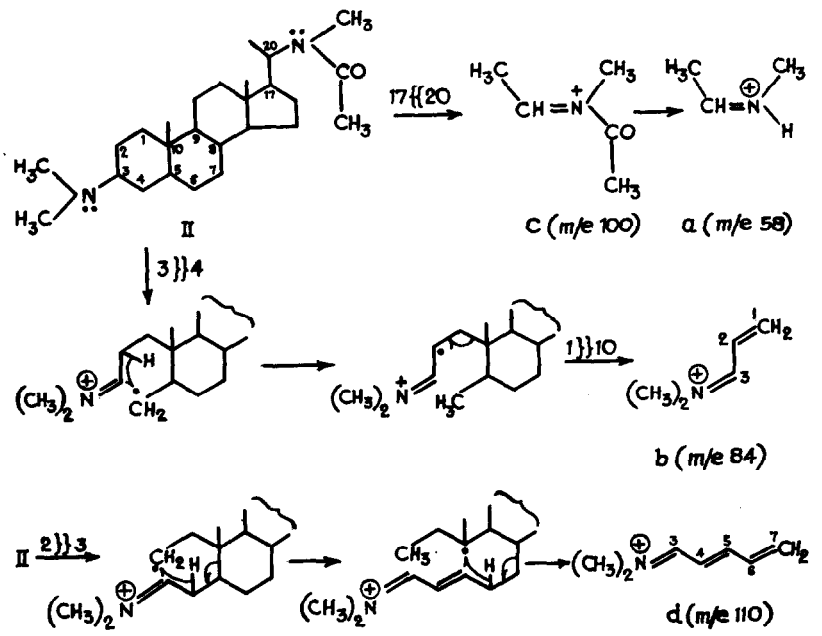
I : R = -CO·CH_3; R_1 = R_2 = CH_3

IIa: R = R_1 = R_2 = CH_3

IIb: R = CH_3; R_1 = R_2 = H

The n.m.r. spectrum of saracodine is in excellent agreement with the structure (II). The n.m.r. spectrum shows a total of 45 ± 1 protons corresponding to $C_{26}H_{46}N_2O$ with six proton signal at 7.80τ for $N(CH_3)_2$ grouping, the chemical shift for methyl groups at C_{10} and C_{18} being around 9.23 and 9.25τ; the doublet (J = 7.0 cps) centered at 8.8τ is the expected position for secondary methyl group (C_{20}), the three proton signal for methyl group (N-CO.CH_3) attached to the amide nitrogen being discernible at downfield with a doublet at 7.72 and 7.27τ.

The mass spectrometry also provides an independent structure proof of saracodine. The mass spectra exhibit the substantial peaks at m/e 58, 84, 100 and 110 characteristic of C_3, C_{20}-aminopregnane derivatives (8) and associated with the generation of the fragments (a), (b), (c) and (d) [shown by arrows].



Saracodine, the structure of which is thus firmly established as (II) is recognised to be a close relative of saracocine (I). The latter upon catalytic hydrogenation in glacial acetic acid with Adams Catalyst shows an uptake of one molecule of hydrogen. Dihydrosaracocine thus produced is found to be identical with saracodine (TLC and IR spectra). Saracocine is therefore proved to be dehydro-saracodine, the location of unsaturation in saracocine at $\Delta^{5,6}$ being ascertained from mass spectrometry (9). The mass spectra exhibit three peaks (a), (b) and (c) showing the absence of peak, m/e 110 (d) because of the 5-6 double bond in saracocine which presumably facilitates the allylic fission across C3-C4.

It follows, therefore, that saracocine (I) has the same configuration as that of saracodine (II) in all its asymetric centres except C_5 and C_6.

The alkaloid, saracodinine so far investigated appears to be identical with Kurchessine (10) and further work on this base is in progress.

It might be mentioned in this connection that N-methyl-desacyl-epipachysamine-A (11) is identical (12) with dimethyl-chonemorphine (IIa) thereby suggesting the identity of epi-pachysamine-A (11) with saracodine.

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