Alkaloid Studies. Part LIV. Structure of Deoxytubulosine and Interconversion with Tubulosine

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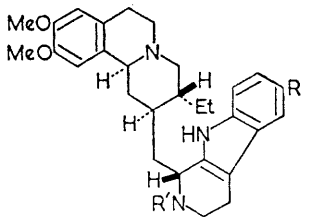
TUBULOSINE, isolated from *Pogonopus tubulosus* (DC.) Schumann (family *Rubiaceae*) has been assigned[1] the biogenetically novel structure (I) largely on the basis of physical measurements and especially a comparison of the mass spectra of the alkaloid and the racemic synthetic base (II).[2] Neither the stereochemistry nor the precise location of the phenolic group in the β-carboline portion of (I) was established at that time. Subsequently, it was found in our laboratory that an alkaloid isolated by Pakrashi[3] together with emetine and related bases[4] from *Alangium lamarckii* Thw. (family *Alangiaceae*) was identical with tubulosine (I). Through the courtesy of Dr. Pakrashi,[3] we were provided with a sufficient quantity of tubulosine to permit further chemical studies, the results of which now fully support our earlier structural assignment.[1]

Tubulosine (I) was transformed into its *ON*-ditosylate and desulphurised[5] with Raney nickel catalyst in boiling ethanol to deoxytubulosine *N*-tosylate (III), m.p. 145—150° [mass spectrum: M^+ 613 ($C_{36}H_{43}N_3O_4S$)], which proved to be identical in all respects with the *N*-tosylation product of a new alkaloid, $C_{29}H_{37}N_3O_2$, m.p. 230—232°, $[\alpha]_D$ −17° ($CHCl_3$), isolated in Pretoria from the South African plant *Cassinopsis ilicifolia* Kuntze (family *Icacinaceae*). Its mass spectrum, infrared spectrum, and thin-layer-chromatographic mobility were identical with those of the racemic synthetic[2] base (II) kindly provided by Professor Battersby. Recently, Battersby and his colleagues[6] have synthesized deoxytubulosine ($[\alpha]_D$ −24°) of established absolute configuration (II) and showed it to be identical with a specimen isolated from *Alangium lamarckii* Thw., which in turn had been shown to be identical with our material. The structure and stereochemistry of tubulosine is thus rigorously established in terms of structure (I) except for the location of the phenol function.

Some light on this remaining question was shed by dehydrogenation of tubulosine (I) in boiling water with maleic acid and palladium black,[7] which

[1] P. Brauchli, V. Deulofeu, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, 1964, **86**, 1895.
[2] A. R. Battersby, J. C. Davidson, and J. C. Turner, *J. Chem. Soc.*, 1961, 3899.
[3] S. C. Pakrashi, *Indian J. Chem.*, 1964, **2**, 468.
[4] H. Budzikiewicz, S. C. Pakrashi, and H. Vorbrueggen, *Tetrahedron*, 1964, **20**, 399.
[5] General method of G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, 1949, S178.
[6] A. R. Battersby, J. R. Merchant, E. A. Ruveda, and S. S. Salgar, *Chem. Comm.*, preceding paper.
[7] S. Akabori and S. Kojiro, *Ber.*, 1930, **63**, 2245.

led to a fluorescent product in which only the tetrahydro-β-carboline moiety had been aromatised [mass spectrum: M^+ 471 ($C_{29}H_{33}N_3O_3$)]. Its



(I) R=OH; R'=H
(II) R=R'=H
(III) R=H; R'=*p*-Me·C_6H_4·SO_2

ultraviolet absorption spectrum λ_{max} (EtOH) 208, 232, 291, and 297·5 mμ, log ε 4·52, 4·49, 4·10, 4·22; λ_{sh} (EtOH) 245, 260, and 286 mμ, log ε 4·30, 4·17, 4·09] closely resembles that[8] of 7-methoxy-2-methyl-β-carboline and differs significantly from those of the other position isomers.[8] It is for this reason that the phenolic hydroxyl group of tubulosine is placed in the indicated position (I).

It is noteworthy that the previously unknown ipecac-β-carboline hybrid structure typified by tubulosine (I) and deoxytubulosine (II) has now been encountered in three completely distinct plant families (*Rubiaceae*, *Alangiaceae*, and *Icacinaceae*).

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[8] G. G. Doig, J. D. Loudon, and P. McCloskey, *J. Chem. Soc.*, 1952, 3912.