

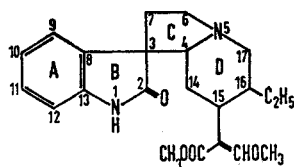
THE STRUCTURES OF THE ALKALOIDS FROM *MITRAGYNA* SPECIES OF GHANA

BY A. H. BECKETT AND A. N. TACKIE

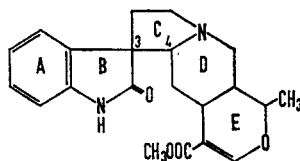
From the School of Pharmacy, Chelsea College of Science and Technology, London, S.W.3

Received May 1, 1963

THE known alkaloids, rhynchophylline, isorhynchophylline, mitraphylline and rotundifoline, were isolated in investigations on *Mitragyna* species of Ghana (Beckett, Shellard and Tackie, 1963). While the work was in progress, the structure of rhynchophylline and isorhynchophylline was elucidated as (I) (Seaton, Nair, Edwards and Marion, 1960); these alkaloids were shown to be isomeric about positions C(3) or C(4). More recently Finch and Taylor (1962) have provided convincing evidence that they are isomeric about C(3) and that the groups at C(15) and C(16) are *trans*. Meanwhile Wenkert, Wickberg and Leicht (1961) from N.M.R. spectra have deduced a *cis* arrangement of methoxymethylene and ester group about the double bond.



[I]



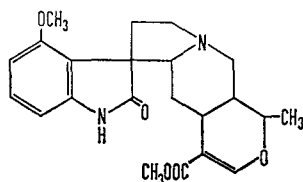
[II]

Recently the structure of mitraphylline has been established as (II) (Seaton, Tondeur and Marion 1958). Because oxidative rearrangement of the indole ajmalicine with known *trans* D/E junction gave mitraphylline (and isomitraphylline), this alkaloid must have the *trans* D/E junction (Shavel and Zinnis 1962, Finch and Taylor 1962). Evidence for the *trans* C/D junction was also presented.

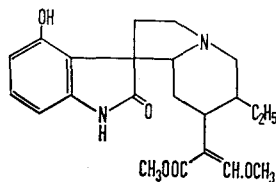
Rotundifoline, isolated from *M. rotundifoline* has previously been allocated the molecular formula $C_{22}H_{26}O_5N_2$ (Barger, Dyer and Sargeant, 1939; Ongley 1950). Hendrickson (1962) assumed this was correct and from available evidence tentatively suggested formula (III).

On more recent evidence, the molecular formula has been amended to $C_{22}H_{28}O_5N_2$ by Beckett and others (1963). Acid hydrolysis of rotundifoline yielded an alkaloid devoid of a methoxy group and further rendered formula (III) untenable. On the basis of ultra-violet and infra-red spectroscopy studies, N.M.R. spectra and mass spectrometry, we have now established the structure of rotundifoline as (IV), hydrolysis yielding the aldehyde (V) (Beckett and Tackie, 1963).

From *M. stipulosa* and *M. ciliata* another oxindole alkaloid, $C_{22}H_{23}O_5N_2$, was isolated by Beckett, Shellard and Tackie (1963). Unlike rotundifoline, of the same molecular formula, it was soluble in sodium hydroxide solution and its ultra-violet spectrum changed upon changing the pH of the solutions. Recently this alkaloid, now designated



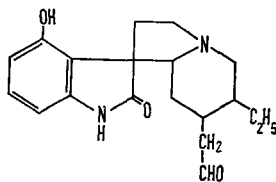
[III]



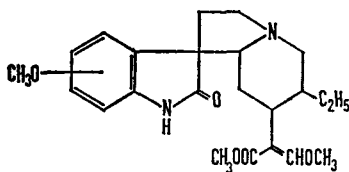
[IV]

isorotundifoline, was shown to be an isomer of rotundifoline. On the basis of pK_a values, rates of quaternisation, the formation of the same quaternary ammonium iodide from either isomer, ultra-violet and infra-red spectroscopy under different conditions, we conclude that these alkaloids, unlike rhynchophylline and isorhynchophylline, are isomeric about C_4 .

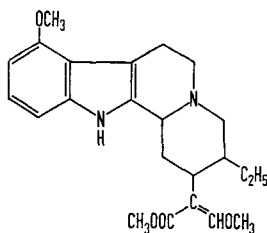
Two new oxindole alkaloids, $C_{23}H_{30}O_5N_2$, designed rhynchociline and ciliaphylline, were isolated from *M. ciliata* by Beckett, Shellard and Tackie (1963). It was subsequently found that isomerisation of ciliaphylline with acetic acid gave rhynchociline. Chemical and physico-organic data indicate that these isomers may be represented as (VI).



[V]



[VI]



[VII]

Available evidence indicates that the new indole alkaloid, mitraciliatine, probably has a structure closely related to mitragynine whose structure (VII) has been recently suggested by Joshi, Raymond-Hamet and Taylor (1963).

STRUCTURES OF ALKALOIDS FROM *MITRAGYNA* SPECIES OF GHANA

REFERENCES

- Barger, G., Dyer, E. and Sargeant, L. J. (1939). *J. org. Chem.*, **4**, 418.
Beckett, A. H., Shellard, E. J. and Tackie, A. N. (1963). *J. Pharm. Pharmacol.*, **15**, *Suppl.*, 158 T-169 T.
Beckett, A. H. and Tackie, A. N. (1963). *Chem. Ind.*, 1122-1123.
Finch, N. and Taylor, W. I. (1962). *J. Amer. chem. Soc.*, **84**, 1319-1320; 3871-3877.
Hendrickson, J. B. (1962). *Ibid.*, **84**, 650-653.
Ongley, P. A. (1950). Ph.D. Thesis, Glasgow University, Scotland.
Seaton, J. C., Nair, M. D., Edwards, O. E. and Marion, L. (1960). *Canad. J. Chem.*, **38**, 1035-1042.
Seaton, J. C., Tondeur, R. and Marion, L. (1958). *Ibid.*, **36**, 1031-1038.
Shavel, J. and Zinnes, H. (1962). *J. Amer. chem. Soc.*, **84**, 1320.
Joshi, T., Raymond-Hamet and Taylor, W. I. (1963). *Chem. and Ind.*, 597.
Wenkert, E., Wickberg, B. and Leicht, C. (1961). *J. Amer. chem. Soc.*, **83**, 5037.

The paper was presented by DR. BECKETT.