Tetrahedron Letters No.12, pp. 1525-1527, 1968. Pergamon Press. Printed in Great Britain.

ACROPHYLLINE AND ACROPHYLLIDINE

TWO NEW ALKALOIDS FROM ACRONYCHIA HAPLOPHYLLA

F. N. Lahey and M. McCamish

Department of Chemistry, University of Queensland, Brisbane,
Queensland, Australia

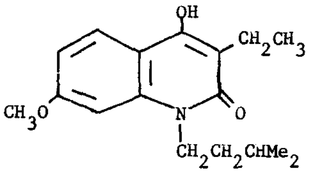
(Received in UK 31 October 1967)

Two alkaloids, first isolated from the bark of Acronychia haplophylla by McEwan[1] as alkaloid B, $C_{17}H_{17}NO_3$, and alkaloid C, $C_{17}H_{19}NO_4$, have been named acrophylline (II) and acrophyllidine (III) respectively and identified as new furoquinolones on the following evidence.

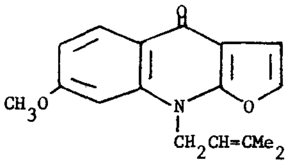
Acrophylline, $C_{17}H_{17}NO_3$, M.W.=283 (mass spectrum $M^{+\cdot}$=283), m.p. 120° (uncorr.) has an I.R.(nujol) 1620, 1595, 1540, 1505 cm^{-1} [2,3,4] and U.V. (ethanol) λmax mμ (log ε) 253(s)(4.66), 257.5(s)(4.69), 261(4.78), 290(s)(3.73), 320-25(4.03) which in 0.2M HCl collapses to 249(4.59) and 320(4.04)mμ, [2,5,6], characteristic of N-alkyl 4-furo[2,3-b]quinolones, evidence further corroborated by the alkaloid's rapidly turning pink in solution [2,7]. The N.M.R. (in $CDCl_3$, δ values relative to internal TMS) establishes the presence of methyl (3H, s, 3.83) and prenyl [$\underline{Me}_2C=$, 6H, 1.73, 1.89; $X-\underline{CH}_2-CH=$, 2H, d, 4.82; $CH_2-\underline{CH}=$, 1H, t, 5.15] attached to O- and N- but cannot differentiate between them [8,9,10]; furan protons (Hα, d, 7.22, J=2cps; Hβ, d, 6.99, J=2cps)[8] and three aromatic protons, one (d, 8.31, J=8.5cps) being peri to a carbonyl (strong deshielding) and demanding an ortho proton, the other two in an unresolved multiplet (6.83).

Reduction with palladium yields a tetrahydro derivative, whereas with Adams's catalyst hexahydroacrophylline is formed (mass spectrum $M^{+\cdot}$=289), m.p. 174° with I.R. 1630, 1580, minimum 1580-1460 cm^{-1} and U.V. 226, 243(s)(4.18), 251(4.13), 286(3.91), 316(4.18), 328.5(4.19) unaffected by acid, characteristic of 2-quinolones[2] substituted in the 7-position [11]. The N.M.R. shows, as new features from reduction, an isoamyl [$\underline{Me}_2CH-$, 6H, d, 0.97; $C-\underline{CH_2-CH}-C$, 3H, m, 1.75, $X-\underline{CH}_2-CH_2$, 2H, t, 4.25] and the hydrogenolytically created ethyl group [$\underline{CH}_3$, 3H, t, 1.11, J=7.5cps; $\underline{CH}_2$, 2H, q, 2.77, J=7.5cps].

The point of attachment of the alkyl side chains was substantiated by synthesis of hexahydroacrophylline. m-Anisidine was acetylated in Ac$_2$O-pyridine and the product N-alkylated in NaH/DMF and isoamyl bromide. The resulting oil was hydrolysed in 20% aqueous HCl to afford N-isoamyl-m-anisidine. (All products were isolated and gave satisfactory I.R. and N.M.R.). The N-alkyl anisidine and diethyl ethylmalonate, on refluxing in diphenyl ether, gave a compound m.p. 174°, whose TLC behaviour, I.R., U.V., N.M.R. and mass spectra were identical with those of the hexahydro-alkaloid which must therefore have structure I from which acrophylline must be II.

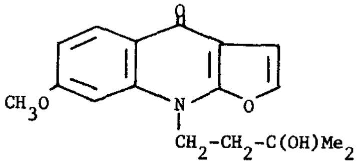


I



II

Acrophyllidine, $C_{17}H_{19}NO_4$, m.p. 177-78° has a U.V. identical to that of acrophylline, as is the N.M.R. save that the prenyl side chain has been hydrated [$\underline{Me}_2$C(OH)-, 6H, s, 1.40; CH$_2$-$\underline{CH}_2$-C, 2H, t, 2.03, J=8cps; X-$\underline{CH}_2$-CH$_2$-, 2H, t, 4.58, J=8cps]. That the side chain is attached to the nitrogen was shown by acid catalysed hydration of acrophylline to acrophyllidine, which therefore must be III.



III

These are the first recorded examples of (a) naturally occurring 4-furo[2,3-b]quinolones and (b) furoquinoline type alkaloids containing N-isoprenoid groups.

The detailed mass spectra, with those of several N-alkyl 4-furo[2,3-b]quinolones will be published subsequently.

REFERENCES

1. T. McEwan, M. Sc. Thesis, 1959.
2. H. Rapoport and K. G. Holden, J.Am.Chem.Soc., 82, 4395 (1960).
3. A. R. Katritzky and R. A. Jones, J.Chem.Soc., 2947 (1960).
4. L. J. Bellamy, Spectrochim.Acta., 16, 30 (1960).
5. F. W. Eastwood, G. K. Hughes and E. Ritchie, Aust.J.Chem., 7, 87 (1954).
6. F. Werny, "The Alkaloids of Platydesma Campanulata Mann", 26, University Microfilms, Inc., Ann Arbor, 1964.
7. e.g. R. H. Prager, E. Ritchie and W. C. Taylor, Aust.J.Chem., 14, 380 (1960).
8. A. V. Robertson, Aust.J.Chem., 16, 451 (1963).
9. S. Goodwin, N. J. Shoolery and L. F. Johnson, J.Amer.Chem.Soc., 81, 3065 (1959).
10. T. J. Batterham and J. A. Lamberton, Aust.J.Chem., 18, 859 (1965).
11. (a) T. Sato and M. Ohta, Bull.Chem.Soc.Japan, 31, 157 (1958).
    (b) F. N. Lahey and M. McCamish - unpublished results.

ACKNOWLEDGMENTS

We wish to thank the Commonwealth Government for a Post-graduate Award to one of us (M. McC.).