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CHLOROFORM-SOLUBLE ALKALOIDS OF THE ROOT BARK OF *FAGARA VIRIDIS*

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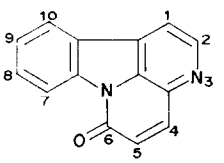
Abstract—Three alkaloids have been isolated from the root bark of *Fagara viridis* A. Cheval. (Rutaceae). One of these, canthin-6-one, is reported for the first time from an African species of *Fagara* while the others are the quaternary benzophenanthridine alkaloids chelerythrine and nitidine.

INTRODUCTION

OF THE three samples of bark from the West African species *Fagara viridis* A. Cheval. (syn. *F. fuscopilosa* Engl.) examined by Paris and Moyse-Mignon,[1] only one was reported to contain the furoquinoline alkaloid skimmianine. The other samples were said to contain an unidentified base (hydrochloride m.p. 245°) and small amounts of an orange-coloured alkaloid. Calderwood and Fish,[2] from TLC results only, postulated the presence in root bark of 5 alkaloids, including skimmianine, angoline and angolinine. More recently, however, angoline has been shown to be an artefact of chelerythrine[3] and angolinine to be probably identical with nitidine.[4]

RESULTS AND DISCUSSION

The major alkaloid of the root bark of *Fagara viridis* has been found to be canthin-6-one (I) and not skimmianine as previously reported.[1,2] This base on repeated recrystallization from dry methanol gave pale yellowish crystals (m.p. 162–163°). Accurate mass measurement gave a parent ion consistent with $C_{14}H_8N_2O$ and the complex UV spectrum (strong



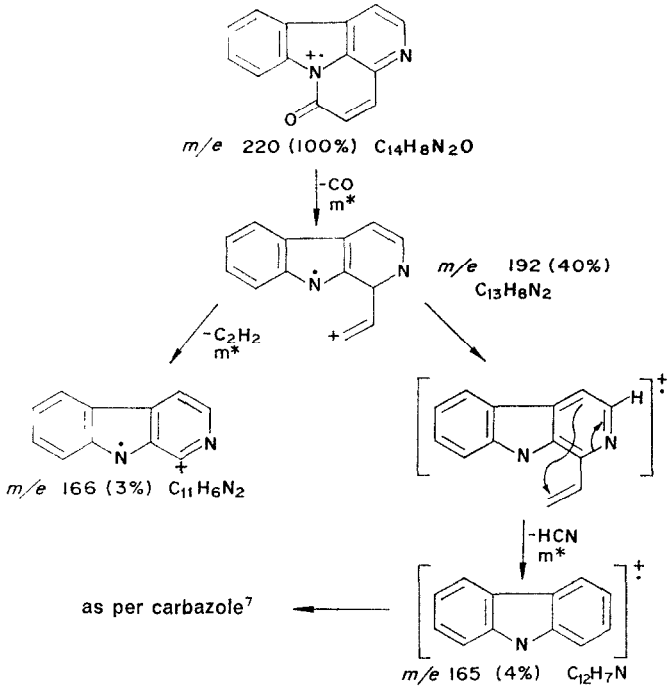
(I) Canthin-6-one

maxima at 362 and 380 nm) suggested a structure related to that of an extended carbazole.[5] The IR spectrum indicated the presence of a ketonic grouping.

[1] R. PARIS and H. MOYSE-MIGNON, *Ann. Pharm. France* **6**, 409 (1948).
[2] J. M. CALDERWOOD and F. FISH, *J. Pharm. Pharmac.* **18**, 119S (1966).
[3] L. FONZES and F. WINTERNITZ, *Phytochem.* **7**, 1889 (1968).
[4] F. FISH and P. G. WATERMAN, *J. Pharm. Pharmac.* **23**, 67 (1971).
[5] A. W. SANGSTER and K. L. STUART, *Chem. Rev.* **65**, 69 (1965).

A PMR study ($CDCl_3$) showed all peaks in the range τ 1·3–3·3, indicating the absence of any substitution pattern. Deuteration of the sample (D_2O) gave no change in the spectrum, suggesting that N-H groups were absent and that the system was completely aromatic. An AB system centred at $\tau = 3{\cdot}2$ (1H, doublet $J = 8$ c/s) and $\tau = 2{\cdot}15$ (1H, doublet $J = 8$ c/s) was assigned to protons at C-4 and C-5, respectively. A second AB system centred at $\tau =$ 1·35 (1H, doublet $J = 5$ c/s) and $\tau = 2{\cdot}30$ (1H, doublet $J = 5$ c/s) was similarly assigned to those protons at C-1 and C-2, respectively. A doublet at $\tau = 1{\cdot}6$ (1 H) was assigned to the C-7 proton whilst the remaining protons at C-8, C-9 and C-10 were found in a complex multiplet τ 2·2–2·8 (3 H). These results are compatible with those obtained by Kump *et al.* for tuboflavin.[6]

Significant peaks on the mass spectrum of canthin-6-one were at *m/e* 221 ($P^+ + 1$) 220 (P^+ 100%) 192, 166, 165, 139, 114. The formation of these are tentatively explained by Scheme 1, peaks at 165, 139 and 114 being compatible with the formation and breakdown of carbazole.[7]



SCHEME 1.

Canthin-6-one has previously been reported from two other species of the *Fagara/Zanthoxylum* complex, namely, *Fagara elephantiasis* Macf. (syn. *Zanthoxylum elephantiasis* Kr. and Urb.)[8] and *Zanthoxylum dominianum* Merr. and Perry (syn. *Zanthoxylum suberosum* C. T. White).[9,10] *Zanthoxylum caribaeum* Lam.[11] has been reported to have very similar alkaloids.

[6] C. KUMP, J. SEIBL and H. SCHMID, *Helv. Chim. Acta* **46,** 498 (1963).
[7] K. G. DAS, P. T. FUNKE and A. K. BOSE, *J. Am. Chem. Soc.* **86,** 3729 (1964).
[8] A. T. AWAD, J. L. BEAL, S. K. TALAPATRA and M. P. CAVA, *J. Pharm. Sci.* **56,** 279 (1967).
[9] J. R. CANNON, G. K. HUGHES, E. RITCHIE and W. C. TAYLOR, *Austral. J. Chem.* **6,** 86 (1953).
[10] G. B. GUISE, E. RITCHIE, R. G. SENIOR and W. C. TAYLOR, *Austral. J. Chem* **20,** 2429 (1968).
[11] D. D. CASA and C. M. SOJO, *J. Chem. Soc.* **C,** 2155 (1967)

Canthin-6-one has not been previously reported in any African *Fagara* species and it is noteworthy that this is the first African species so far investigated from which skimmianine is absent. Additionally, although skimmianine appears to be an extremely common alkaloid in all except the South American species of *Fagara*, it has not so far been reported from any of those species found to contain canthin-6-one. It thus appears possible that the biogenetic production of these two alkaloids may be mutually exclusive.

The previous report of skimmianine by Calderwood and Fish[2] may be attributed to the marked similarity in the behaviour of skimmianine and canthin-6-one in the chromatographic system which they used. Their original extract has been re-examined in the course of this work and the major alkaloid found to be canthin-6-one. It also seems probable that the unknown alkaloid (hydrochloride m.p. 245°) isolated by Paris and Moyse-Mignon[1] from two of their samples was canthin-6-one.

Small amounts of the benzophenanthridine alkaloids chelerythrine and nitidine have also been isolated. Sufficient chelerythrine was obtained to allow unequivocal identification but the quantity of nitidine was adequate only for identification by TLC and UV spectrum. The ratio in which these two alkaloids occur confirms the earlier report[2] in which they were formerly designated as angoline and angolinine, respectively.

EXPERIMENTAL

Plant Material

Root bark of *Fagara viridis* A. Cheval. was supplied by the Tropical Products Institute, London and verified at source in Nigeria. A voucher sample has been deposited at the Pharmaceutical Society Herbarium, Bradford.

Extraction

Powdered root bark (250 g) was extracted in a Soxhlet with petroleum ether (b.p. 40–60°) and $CHCl_3$. The extracts were concentrated under reduced pressure and partitioned with 1 N HCl. From the acid fraction of the petroleum ether extract a precipitate was produced on standing which when chromatographed on an alumina column (Woelm Activity II), eluting with $CHCl_3$/cyclohexane 70:30, gave separation of two compounds. These on recrystallization from EtOH/1 N HCl yielded chelerythrine (25 mg) and nitidine (7 mg) as the chlorides.

The acid fractions from both extracts were made alkaline with 0·880 ammonia and re-extracted into $CHCl_3$. Evaporation of the $CHCl_3$ under reduced pressure followed by repeated recrystallization from MeOH gave canthin-6-one (from petroleum ether extract 1·23 g; from $CHCl_3$ extract 260 mg).

Canthin-6-one. Isolated as pale yellowish needles m.p. 162–163° (MeOH); UV λ_{max}^{EtOH} 227, 251, 260, 268·5, 301, 346·5, 362 and 380 nm (log ϵ 4·23, 4·10, 4·08, 4·05, 3·89, 3·93, 4·14, 4·10) in agreement with published data.[12] IR (ν cm^{-1}) 1680 (carbonyl), 1630. Found M^+ = 220·0636, $C_{14}H_8N_2O$ requires 220·0636. Canthin-6-one picrate m.p. 260–261° (EtOH) (Lit. 262°). Cis-2-(1′-β-carbolyl) acrylic acid was prepared (m.p. 212°) (Lit. = 212–214°) from canthin-6-one according to the method of Hughes *et al.*[12] Canthin-6-one hydrochloride m.p. 242–244° (Lit. 245°).[12]

Chelerythrine chloride. Isolated as yellow needles, $C_{21}H_{18}O_4N^+$ Cl^-, m.p. 202–203° (EtOH–N HCl) identical with an authentic sample (mixed m.p., TLC, IR, UV); chelerythrine nitrate m.p. 240° (EtOH).

Nitidine chloride. Isolated as yellow–green needles, $C_{21}H_{18}O_4N^+$ Cl^-, identical with an authentic sample by TLC (3 systems) and UV spectrum.

The UV spectra were recorded in EtOH and the IR spectra in KCl. PMR (60 MHz) spectra were recorded on a Perkin–Elmer R 12 instrument with T.M.S. as internal standard. Mass spectra were determined on a double-focusing AEI MS902 spectrometer at 70 eV. M.ps (uncorrected) were determined on a Kofler hot stage.

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[12] H. F. HUGHES, E. R. NELSON and J. R. PRICE, *Austral. J. Sci. Res.* **5A**, 387 (1952).