drying ($Na_2SO_4$) were evaporated under reduced pressure to a crystalline mass. This was recrystallized from $Et_2O$ to give colourless needles of pseudoaconine, m.p. 88–90° (lit. m.p. 93–94°). IR (KBr) 3400 (0H), 2860, 2810, 1450, 1370, 1100, 1030, 980 and 925 $cm^{-1}$. The NMR spectrum showed signal for a methyl group at $\tau$ 8·91 (triplet, $N{-}CH_3CH_2$) and four methoxyl groups at 6·76, 6·70 and 6·58 (12H). (Found: C, 62·15; H, 8·53; N, 3·01; OMe, 25·63% Calc. for $C_{25}H_{41}O_8N$: C, 62·11; H, 8·49; N, 2·99; OMe 25·67%). The alkaline, aqueous solution was acidified with HCl and continuously extracted with $CHCl_3$. The extract after drying and evaporation yielded benzoic acid, m.p. 120°, either alone or on admixture with an authentic sample.

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## RUTACEAE

# CHLOROFORM-SOLUBLE ALKALOIDS OF *FAGARA LEPRIEURII*

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**Abstract**—The dried root and stem barks of *Fagara leprieurii* Engl. have yielded 1-hydroxy-3-methoxy-10-methylacridan-9-one, nitidine and chelerythrine together with the previously reported 1-hydroxy-2,3-dimethoxy-10-methylacridan-9-one and skimmianine.

## INTRODUCTION

THE BARK of *Fagara leprieurii* Engl. (syn. *F. angolensis* Engl.) has previously been shown to contain the furoquinoline alkaloid skimmianine[1] and 1-hydroxy-2,3-dimethoxy-10-methylacridan-9-one.[2] Although angoline and angolinine have also been reported,[3,4] angoline has more recently been shown to be 9-methoxychelerythrine, an artefact of chelerythrine,[5] while angolinine is probably identical with nitidine.[6]

We now confirm the presence of the benzophenanthridine alkaloids, chelerythrine (IV) and nitidine (V) and report the occurrence of 1-hydroxy-3-methoxy-10-methylacridan-9-one

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[1] K. H. PALMER, Ph.D. Thesis, Univ of Paris (1956).

[2] L. FONZES and F. WINTERNITZ, *Compt. Rend.* **266**, 930 (1968).

[3] K. H. PALMER and R. PARIS, *Ann. Pharm. France* **13**, 657 (1955).

[4] J. M. CALDERWOOD and F. FISH, *J Pharm. Pharmac.* **18**, 119S (1966).

[5] L. FONZES and F. WINTERNITZ, *Phytochem.* **7**, 1889 (1968).

[6] F. FISH and P. G. WATERMAN, *J Pharm. Pharmac.* **23**, 67 (1971).

(III). This is the first report of (III) from a natural source although it has previously been synthesized.[7]

## RESULTS AND DISCUSSION

The yellow colour, weak basicity and UV spectrum ($\lambda_{max}^{EtOH}$ 395 nm) of (III) indicated an acridone structure. It gave a negative chromotropic acid test for methylenedioxy groups[8] but a positive ferric chloride test, indicating a phenolic hydroxyl. The low IR absorption band ($\nu = 2650\ cm^{-1}$) was in agreement with the reported stretching frequency of 1-hydroxy substituted acridones.[9] Mass spectral analysis indicated a parent ion *m/e* 255 ($C_{15}H_{13}O_3N$) and the fragmentation pattern observed agreed with that published for 1-hydroxy-3-methoxy-10-methylacridan-9-one.[10] A PMR study in $CDCl_3$ revealed a one proton signal ($\tau = -4{\cdot}6$) which disappeared on exchange with $D_2O$. The lowfield $\tau$ value is indicative of the strong intramolecular bonding between the C-1 hydroxyl and the C-9 carbonyl substituents. The broad doublet ($\tau = 1{\cdot}7$ 1H) was assigned to the deshielded proton at C-8 and the multiplet ($\tau = 2{\cdot}2$–$2{\cdot}9$ 3H) to C-5H, C-6H and C-7H. The singlet ($\tau = 3{\cdot}9$ 2H) could, in the absence of methylenedioxy groups, only be assigned to protons at C-2 and C-4. Two three-proton singlets at $\tau = 6{\cdot}2$ (C-3 methoxyl) and $\tau = 6{\cdot}4$ (*N*-methyl) accounted for the remaining six protons. These results were in agreement with PMR data published on acridone alkaloids.[11] Compound (III) was identical in all spectroscopic detail with an authentic synthesized sample of 1-hydroxy-3-methoxy-10-methylacridan-9-one used for comparison.

The isolation of chelerythrine and the absence of angoline confirms the postulation of Fonzes and Winternitz[5] that angoline is an artefact produced from chelerythrine in alkaline conditions. Other similar artefacts have been reported from chelerythrine,[12] nitidine[13] and avicine.[14] The presence of angoline in five African species of *Fagara* reported by Calderwood and Fish[4] can probably be attributed to the extraction procedure used. Angoline has also been reported[1] from *F. parvifolia* A. Chev. and *F. xanthoxyloides* Lam. and these should now be reinvestigated to determine the true nature of the benzophenanthridines present.

Nitidine, the second benzophenanthridine compound isolated in this present work, had UV spectrum and TLC characteristics identical with those of an authentic sample of the previously reported angolinine.[3,4]

## EXPERIMENTAL

### *Plant Material*

Dried root and stem bark of *Fagara leprieurii* Engl. was collected in Nigeria, authenticated at source and supplied by the Tropical Products Institute, London. A voucher sample has been deposited at the Pharmaceutical Society Herbarium in the University of Bradford.

### *Extraction*

Powdered root bark (2·4 kg) and stem bark (3 kg) were successively extracted to exhaustion in a Soxhlet with light petroleum (b.p. 40–60°) and $CHCl_3$. The extracts were concentrated under reduced pressure at 40° and 60°, respectively.

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[7] G. K. HUGHES and E. RITCHIE, *Austral. J. Scient. Res.* **A4**, 423 (1951).
[8] S. W. GUNNER and T. HAND, *J. Chromatog.* **37**, 357 (1968).
[9] J. R. PRICE and J. B. WILLIS, *Austral. J. Chem.* **12**, 589 (1959).
[10] J. H. BOWIE, R. G. COOKS, R. H. PRAGER and H. M. THREADGOLD, *Austral. J. Chem.* **20**, 1179 (1967).
[11] J. A. DIMENT, E. RITCHIE and C. A. TAYLOR, *Austral. J. Chem.* **20**, 1719 (1967).
[12] F. G. TORTO, P. SEFCOVIC and B. A. DADSON, *Tetrahedron Letters* 181 (1966).
[13] H. R. ARTHUR, W. R. HUI and Y. L. NG, *J. Chem. Soc.* 1840 (1959).
[14] H. R. ARTHUR, W. R. HUI and Y. L. NG, *J. Chem. Soc.* 4007 (1959).

The concentrated light petroleum extract of the root bark (100 ml) gave a crystalline deposit (1·3 g) and TLC indicated the presence of several bases. The crystalline material (1 g) was subjected to column chromatography (Woelm Alumina, activity II) eluting with $CHCl_3$–cyclohexane (70:30). Separate fractions of eluate yielded I (45 mg) and a non-basic, Dragendorff positive, material (105 mg). Other bases were irreversibly adsorbed to the column. The remaining 300 mg of crystalline material, applied to a silica gel g (Kieselgel G)–Celite 545 (1:1) column: eluting with benzene–ethyl acetate (9:1), followed by (1:1), yielded two weakly basic compounds III (12 mg) and II (81 mg).

The supernatant light petroleum (Dragendorff positive) was extracted with 1 N HCl (2 × 40 ml, 3 × 20 ml). On standing, the yellow base IV (196 mg) precipitated in the bulked aqueous fraction.

The $CHCl_3$ extract was concentrated to 250 ml and TLC revealed the presence of bases I–IV and base V. The extract (50 ml), on shaking with 1 N HCl (2 × 50 ml, 3 × 25 ml) gave a precipitate (87 mg). Chromatography of the precipitate on alumina (Woelm, activity II), eluting with $CHCl_3$–MeOH (98:2), yielded IV (42 mg) and V (19 mg). The acid extract was made alkaline with ammonia, extracted with $CHCl_3$ and the presence of I in the $CHCl_3$ extract demonstrated by TLC. From the remaining 200 ml of the $CHCl_3$ extract, II (312 mg) and III (115 mg) were obtained by the same methods used on the light petroleum extract.

The extracts from the stem bark were treated similarly and the same bases were found although the percentages present were in all cases smaller. No additional alkaloids were found.

*Skimmianine* (I). Isolated as colourless needles m.p. 175–176° ($CHCl_3$–light petroleum), $\lambda_{max}^{EtOH}$ 250, 320, 332 nm (log $\epsilon$ 4 87, 3·90, 3 91); identical in all respects with an authentic sample (UV, IR and mixed m p.).

1-*Hydroxy*-2,3-*dimethoxy*-10-*methylacridan*-9-*one* (II). Isolated as long, fine, yellow needles m.p. 177–178° (benzene–ethyl acetate); $\lambda_{max}^{EtOH}$ 231, 246 (sh.), 265 (sh.), 275, 325, 399 nm (log $\epsilon$ 4·19, 4·33, 4 59, 4·71, 3·73, 3·80); undergoes a bathochromic shift in the presence of alkali; $\nu_{max}$ (OH) = 2650 $cm^{-1}$; identical in all respects with an authentic sample (UV, IR and mixed m.p.).

1-*Hydroxy*-3-*methoxy*-10-*methylacridan*-9-*one* (III). Isolated as yellow clusters m p. 174–176° (benzene–ethyl acetate); $\lambda_{max}^{EtOH}$ 223, 248, 263, 271, 295, 324, 395 nm (log $\epsilon$ 4 11, 4 40, 4 55, 4 61, 4 00, 3·77, 3·72); undergoes a bathochromic shift in the presence of alkali; $\nu_{max}$ (OH) = 2650 $cm^{-1}$ Found: $M^+$ 255·0891. $C_{15}H_{13}O_3N$ requires 255·0895; identical in all respects to an authentic sample (UV, IR, MS and mixed m.p.).

*Chelerythrine* (IV). Isolated as yellow needles m p. ($Cl^-$) 202–203° (2 N HCl–MeOH); $\lambda_{max}^{EtOH}$ 228, 272, 283 (sh ), 302 (sh ), 343 nm (log $\epsilon$ 4 26, 4 54, 4·47, 4·37, 4·17); identical in all respects with an authentic sample (UV, IR and mixed m.p.).

*Nitidine* (V). Isolated as yellow–green needles m.p. ($NO_3^-$) 276–278° (2 N $HNO_3$–EtOH), $\lambda_{max}^{EtOH}$ 231, 272, 281 (sh.), 303 (sh.), 329 nm (log $\epsilon$ 4·41, 4 47, 4 47, 4 39, 4 37; identical in all respects with an authentic sample (UV, IR and mixed m p.).

M.ps (uncorrected) were determined on a Kofler hot stage, UV spectra in EtOH and IR spectra in KCl. PMR spectra were recorded in $CDCl_3$ with T.M.S. as internal standard. Mass spectra were measured on an AEI MS 902 double-focussing spectrometer in the Department of Chemistry, University of Strathclyde.

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