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SHORT COMMUNICATION

ALKALOIDS OF *FAGARA MACROPHYLLA*

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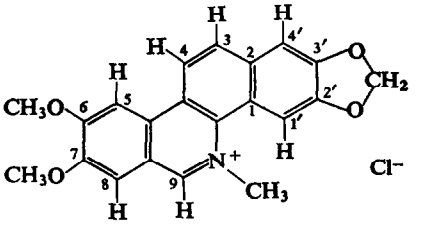
Abstract—Nitidine has been isolated, as the chloride, from *Fagara macrophylla*.

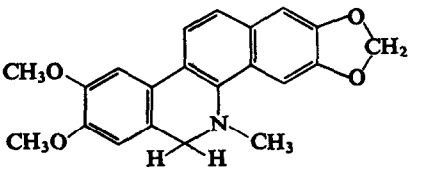
PARIS and Moyse-Mignon[1] isolated from *Fagara macrophylla* (Rutaceae) the furoquinoline alkaloid skimmianine, together with three unidentified alkaloids which they named alkaloid A, xanthofagarine and fagaridine.

We have recently described[2] the isolation from the plant of chelerythrine and dihydrochelerythrine, and have shown that alkaloid A is 9-ethoxychelerythrine, an artefact. We now report the identification of nitidine as the main alkaloidal constituent of the plant.

Root bark, moistened with ammonia, was extracted with ether. The concentrated extract was treated with dilute acetic acid and filtered. Basification of the acetic acid extract with ammonia gave a mixture of crude bases. The mixture was resolved by extraction with hot water into a small isoluble portion, which contained chelerythrine and dihydrochelerythrine, and a soluble portion, which contained the bulk of the basic material. Addition of hydrochloric acid to the soluble portion precipitated the basic material as nitidine chloride (identified by m.p. u.v., i.r.; elemental analyses and m.p. of acetate, pseudocyanide, nitrate).



(Ia)



(Ib)

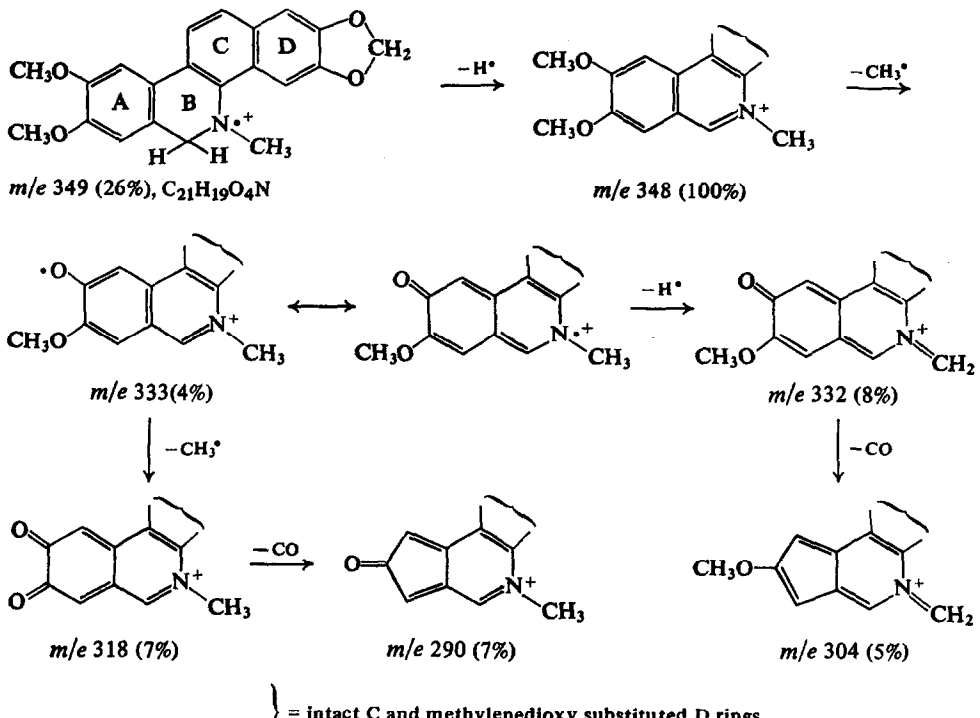
FIG. 1.

The NMR spectrum of nitidine chloride (Ia) in trifluoroacetic acid, with $Si(CH_3)_4$ as internal standard, show peaks for $-OCH_3$ (δ in ppm 4·19, 4·31), $\overset{+}{N}-CH_3$ (4·96), $-O-CH_2-O-$ (6·21), 9-position proton (9·37), protons 1′, 4′, 5, 8 (singlets at 7·49, 7·72, 8·09, 8·19), protons 3, 4 (doublets centred at 8·16, J=8 Hz, and 8·52, J=8 Hz).

[1] R. PARIS and H. MOYSE-MIGNON, *Ann. Pharm. Franc.* **9**, 479 (1951).
[2] F. G. TORTO, P. SEFCOVIC, B. A. DADSON and I. A. MENSAH, *Ghana Journal of Science* **9**, Nos. 1 and 2 (1969).

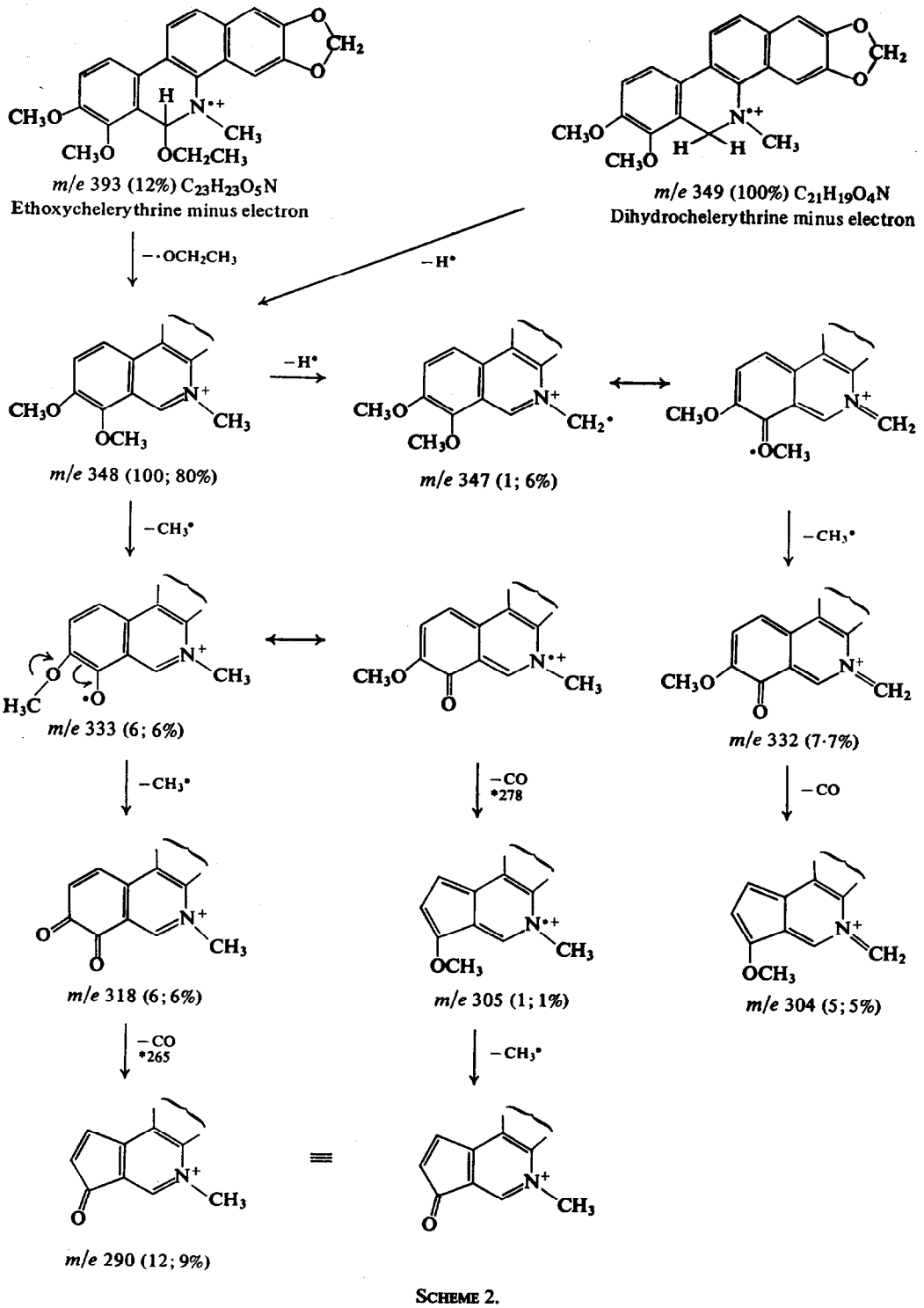
Reduction of nitidine chloride with $NaBH_4$ gave dihydronitidine (Ib) ($C_{21}H_{19}O_4N$ from exact mass determination, m.p., u.v., i.r.). The NMR in $CDCl_3$ show peaks for $=N-CH_3$ (2·58), $-OCH_3$ (3·88, 3·93), 9-position protons (4·12), $-O-CH_2-O-$ (5·99), protons 5, 8, 1′, 4′ (singlets at 6·76, 7·08, 7·28, 7·72), protons 3, 4 (doublets centred at 7·48, J=9 Hz, and 7·68, J=9 Hz). Significant peaks in the mass spectrum were at m/e 350, 349 (M^+), 348, 347, 334, 333, 322, 318, 304, 290, 174·5 (M^{2+}), 167, 166·5 (333^{2+}), 140, 123, 111, 109, 97, 94, 85, 83, 81, 71, 69, 57, 55.

The formation of the more important peaks in the mass spectrum of dihydronitidine may be tentatively explained as in Scheme 1, which is based largely on analogy with the mode of



SCHEME 1.

fragmentation of 9-ethoxychelerythrine and dihydrochelerythrine, the spectra of which show a number of metastable peaks and are therefore more readily interpreted, as in Scheme 2. The percentages after each m/e in the latter refer to fragments originating from ethoxychelerythrine and dihydrochelerythrine respectively. Where molecular formulae are given in the schemes they have been determined by high resolution measurements. Asterisks indicate transformations for which appropriate metastable ions, at the m/e values shown, were observed. The most notable feature of the mass spectra of the three compounds is the ready loss of $-OCH_2CH_3$, in the case of ethoxychelerythrine, or a hydrogen, in the case of the dihydro compounds, to give relatively stable aromatized ions, m/e 348, as highly abundant species.


m/e 393 (12%) C23H23O5N
Ethoxychelerythrine minus electron
m/e 349 (100%) C21H19O4N
Dihydrochelerythrine minus electron
−·OCH2CH3
−H·
m/e 348 (100; 80%)
−H·
m/e 347 (1; 6%)
−CH3·
−CH3·
m/e 333 (6; 6%)
m/e 332 (7·7%)
−CH3·
−CO
*278
−CO
m/e 318 (6; 6%)
m/e 305 (1; 1%)
m/e 304 (5; 5%)
−CO
*265
−CH3·
m/e 290 (12; 9%)

SCHEME 2.

Xanthofagarine, obtained by the procedure of Paris and Moyse-Mignon,[1] that is by treating a suspension of nitidine chloride in water with ammonia, is obviously a mixture of substances.[3] Thus it gave peaks in the mass spectrum which were shown by high resolution measurements to be due to dihydronitidine, $C_{21}H_{19}O_4N$, and oxynitidine, $C_{21}H_{17}O_5N$.

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[3] H. R. ARTHUR, W. H. HUE and Y. L. NG, *J. Chem. Soc.* 1840 (1959).