

PAGICERINE - A NEW INDOLE ALKALOID FROM PAGIANTHA CERIFERA (PANCHER ET SÉBERT) MARKGRAF (APOCYNACEAE)

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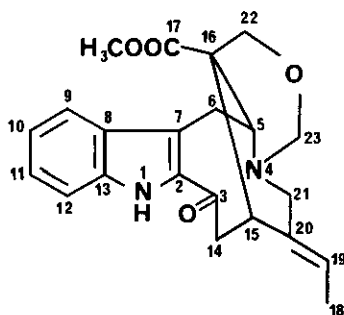
Abstract - A new 2-acylindole alkaloid, pagicerine (1) has been isolated from the stem bark of Pagiantha cerifera (Pancher et Sébert) Markgraf. Its structure has been elucidated on the basis of spectroscopic analyses. It is the first indole alkaloid to present an additional tetrahydro-1,3-oxazine ring.

Pagiantha cerifera (Pancher et Sébert) Markgraf is a small, variable tree growing throughout New-Caledonia¹. It is sometimes included in the genus Tabernaemontana L. as Tabernaemontana cerifera Pancher et Sébert². Various indole alkaloids had been previously isolated from the leaves of this species^{3,4} but the bark had not been so far investigated from a chemical point of view.

A thorough search for the alkaloidal constituents of the bark⁵ has now led to the isolation of a new alkaloid which is named pagicerine. The present paper describes the structure determination of pagicerine⁶.

Pagicerine (1) has been obtained as a colourless amorphous solid, $[\alpha]_D^{20} = -130^\circ$ (CHCl₃, c = 0.7) (contents : 0.002 % from the dried plant material). The empirical formula has been established by high resolution mass spectrometry as C₂₂H₂₄N₂O₄ (Found : 380.1735 ; Calcd. : 380.1736). The uv spectrum displayed characteristic absorptions at $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ) : 219(3.97), 241(4.03) and 316(4.06) associated with a 2-acylindole⁷. In good agreement with this statement, the ir spectrum showed typical bands at $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹ : 3320(NH) and 1730(C=O). The ¹H nmr

spectrum⁸ exhibits the characteristic signals of a 2,3-disubstituted indole, of an ethylidene group and of a carbomethoxy. This latter appears as a 3H-singlet at 2.49 ppm strongly shielded by the indole ring, as usual in the vobasine-vincadifine series^{7,9}. Moreover, an AB system representing two protons at 4.63 and 4.79 ppm ($J = 9.5$ Hz) suggests the presence of a tetrahydro-1,3-oxazine ring^{10,11}. The small *gem*-coupling constant between these two protons is typical to this ring where the bond angle of the CH_2 in position 2 is modified by interaction with the adjacent electron lone-pairs of the $\alpha\text{-O}$ and $\alpha\text{-N}$ atoms¹⁰. In good agreement with these elements, the ^{13}C nmr spectrum exhibits signals at 88.3 and 76.5 ppm typical to C-2 and C-6 in a tetrahydro-1,3-oxazine substituted at C-4 and C-5^{11,12}. The other signals of this spectrum are quite similar to those previously described in the vincadifine series^{13,14}. Compared to the ^{13}C nmr spectra of vincadifine itself¹⁴, only slight but significant increases in the chemical shifts of C-5, C-6 and C-15 signals could be noted. The above elements permitted depicting the structure of pagicerine as 1.



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From a biogenetic point of view, pagicerine may be considered as arising from voacarpine^{15,16} through N_b -condensation with formaldehyde. It is, to our knowledge, the first indole alkaloid to present an additional tetrahydro-1,3-oxazine ring. This type of ring is uncommonly encountered in the structures of natural products^{12,17}.

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5. The plant material has been collected at the Rivière Bleue (New Caledonia) in september 1983. Herbarium Samples (PUCH 642) are kept in the herbaria of the Centre ORSTOM de Nouméa.
6. A biogenetic alkaloid numbering is used in this paper, according to W.I. Taylor and J. Le Men, Experientia, 1965, 21, 508.
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8. Pagicerine (1) : ^1H nmr (270 MHz, CDCl_3 , TMS) : δ ppm = 9.17 (1H, s, D_2O exch., NH-1) ; 7.77 (1H, dd, J_{9-10} = 8 Hz, J_{9-11} = 1 Hz, H-9) ; 7.37 (2H, m, H-11, H-12) ; 7.20 (1H, m, H-10) ; 5.37 (1H, q, J_{18-19} = 7 Hz, H-19) ; 4.79 (1H, d, $J_{23a-23b}$ = 9.5 Hz, H-23a) ; 4.63 (1H, d, $J_{23a-23b}$ = 9.5 Hz, H-23b) ; 4.40 (1H, dq, $J_{21a-21b}$ = 16 Hz, J_{18-21a} = 1 Hz, H-21a) ; 4.12 (1H, t, J_{14-15} = 8 Hz, H-15) ; 3.90-3.60 (5H, m, H-5, H-14a, H-14b, H-22a, H-22b) ; 3.37 (1H, d, $J_{21a-21b}$ = 16 Hz, H-21b) ; 3.15 (1H, dd, J_{6a-6b} = 14 Hz, J_{5-6a} = 10 Hz ; H-6a) ; 2.80 (1H, dd, J_{6a-6b} = 14 Hz, J_{5-6b} = 7 Hz, H-6b) ; 2.49 (3H, s, COOCH_3) ; 1.75 (3H, dd, J_{18-19} = 7 Hz, J_{18-21a} = 1 Hz, CH_3 -18) - ^{13}C nmr (50 MHz, CDCl_3 , TMS, spin echo) : δ ppm = 189.6 (C-3) ; 173.0 (C-17) ; 138.6 (C-13) ; 136.9 (C-20) ; 134.5 (C-2) ; 128.3 (C-8) ; 127.1 (C-11) ; 121.1* (C-19) ; 120.8* (C-9) ; 119.0 (C-7) ; 116.7* (C-10) ; 112.0 (C-12) ; 88.3 (C-23) ; 76.5 (C-22) ; 58.8 (C-5) ; 50.9 (COOCH_3) ; 49.7 (C-21) ; 46.9 (C-16) ; 44.5 (C-14) ; 36.7 (C-15) ; 26.4 (C-6) ; 11.8 (C-18).
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