Tetrahedron Letters,Vol.28,No.19,pp 2123-2126,1987 0040-4039/87 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

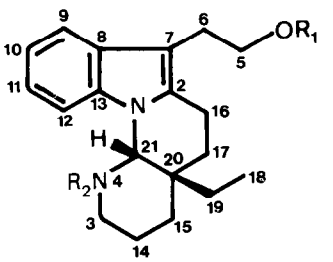
STRUCTURE OF GONIOMITINE, A NEW TYPE OF INDOLE ALKALOID

L. Randriambola, J.-C. Quirion, C. Kan-Fan and H.-P. Husson*

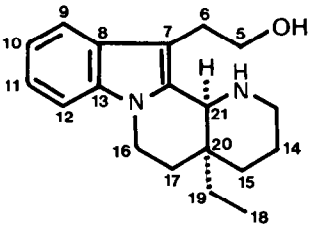
Institut de Chimie des Substances Naturelles, C.N.R.S., 91190 Gif-sur-Yvette (France)

Abstract *The structure 1 proposed for goniomitine, an indole alkaloid isolated from the root bark of Gonioma malagasy (Apocynaceae), was inferred from an analysis of its MS, ^1H and ^{13}C NMR spectral data. A biogenetic scheme is proposed to account for the formation of 1 from vincadifformine 9.*

Further work in the studies of the alkaloids of the genus Gonioma (Apocynaceae)[1] has resulted in the isolation of goniomitine 1 from the root bark of G. malagasy[2]. Following a classical extraction and purification method, goniomitine 1[3] was isolated



1 $R_1 = R_2 = H$: **goniomitine**
2 $R_1 = H$, $R_2 = Ac$
3 $R_1 = R_2 = Ac$



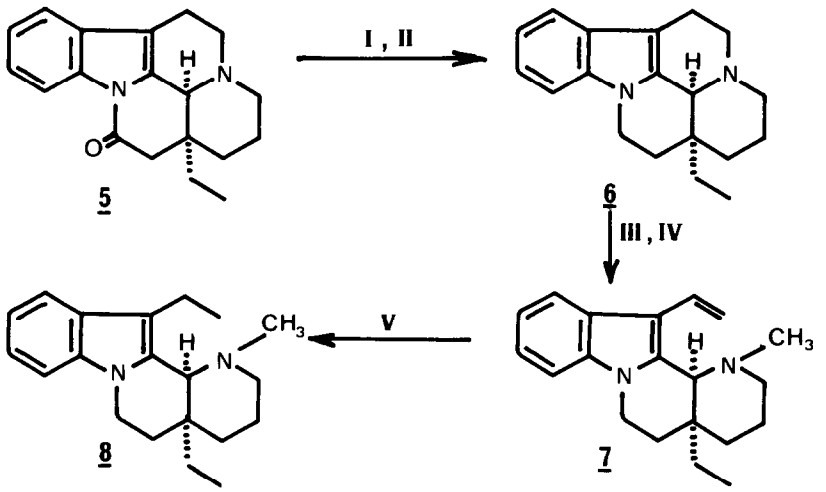
4

as a crystalline compound : m.p. 150°C (ether-methanol) ; $[\alpha]_D^{20}$: -80° ($CHCl_3$, c : 0.9). The molecular formula $C_{19}H_{26}N_2O$ was determined from its microanalysis and high resolution MS (exact mass $M^{+\cdot}$ 298.2080, calcd 298.2045). The spectroscopic properties of 1 revealed an indolic chromophore : λ_{max} (EtOH) 228 and 291nm, and OH and NH groups ν_{max} (neat) 3200 and 3450cm^{-1}. Chemical evidence for the latter functionalities was provided by the formation of an N-acetyl derivative 2 upon treatment of 1 with Ac_2O in MeOH and of an N,O-diacetyl derivative 3 with Ac_2O in pyridine[4].

Proton NMR at 400MHz showed clearly the presence of an ethyl group borne at a quaternary carbon centre (δ 0.86, t, 3H, J = 7Hz ; δ 1.20, m, 1H, J = 7Hz ; δ 1.56, m, 1H, J = 7Hz) and a hydroxyethyl moiety (δ 3.0, t, 2H ; δ 3.81, t, 2H) of tryptophol type as observed earlier for the alkaloid guettardine[5]. Of special interest was a ^1H NMR singlet at δ 4.86ppm for the C-21 proton.

The presence of the tryptophol moiety was confirmed by comparison of the ^{13}C NMR data for the natural product with those of analogues (see Table).

The chemical and physical properties summarised above led us to propose tentatively two possible structures 1 and 4 for the new alkaloid. The presence of eburnane type alkaloids in the same plant[6] prompted us to embark at first on the partial synthesis of 4 from vincamone 5. $LiAlH_4$ reduction of 5 followed by treatment of the resultant carbinol-

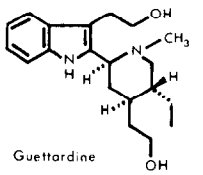


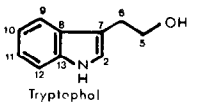
Reagents : (I) $LiAlH_4$, THF, Δ, 3h (II) HCOOH, Δ, 12h (III) ICH_3, CH_3OH, Δ, 12h (IV) AgOH, CH_3OH ; CH_2OH-CH_2OH, 140°C, 15min (V) H_2, Pd/C 10%, CH_3OH, 12h.

amine with refluxing HCOOH afforded 6 (86%). Hoffmann degradation of 6 methiodide led to the formation of the expected vinyl group of 7 (20% from 6). We encountered problems in the hydration of the double bond[7], which led us to prepare the desoxy analogue 8 instead, in order to compare the ^1H and ^{13}C NMR spectra of this series of indolic compounds. It became clear that the hypothetical formula 4 could on no account represent the structure of goniomitine. Indeed the key C-21 proton NMR signal of 7 and 8 ($\delta \sim 2.90$) is at higher field than observed for goniomitine ($\delta = 4.86$). An examination of the ^{13}C NMR spectra of 7, 8 and goniomitine also exhibited appreciable differences (see Table). It was thus clear that formula 1 should be considered as the structure of the new alkaloid[8]. A detailed examination of the ^{13}C NMR spectrum of 1 revealed that characteristic assignments could be made which took account of the proposed structure (see Table and Ref. 3). Important similarities were apparent between the spectrum of 1 and the spectra of tryptophol and guettardine[5]. Nearly identical chemical shifts for C-5, C-6, C-7, C-8, C-9, C-10, C-11 and C-13 were observed. A shielding (2.25ppm) of C-12 in 1 may be due to the substitution of the indole nitrogen. The resonance of C-21 at δ 71.1ppm is in contrast with C-21 of 7 and 8 ($\sim$ 64ppm) and is in good agreement with an aminal function[9].

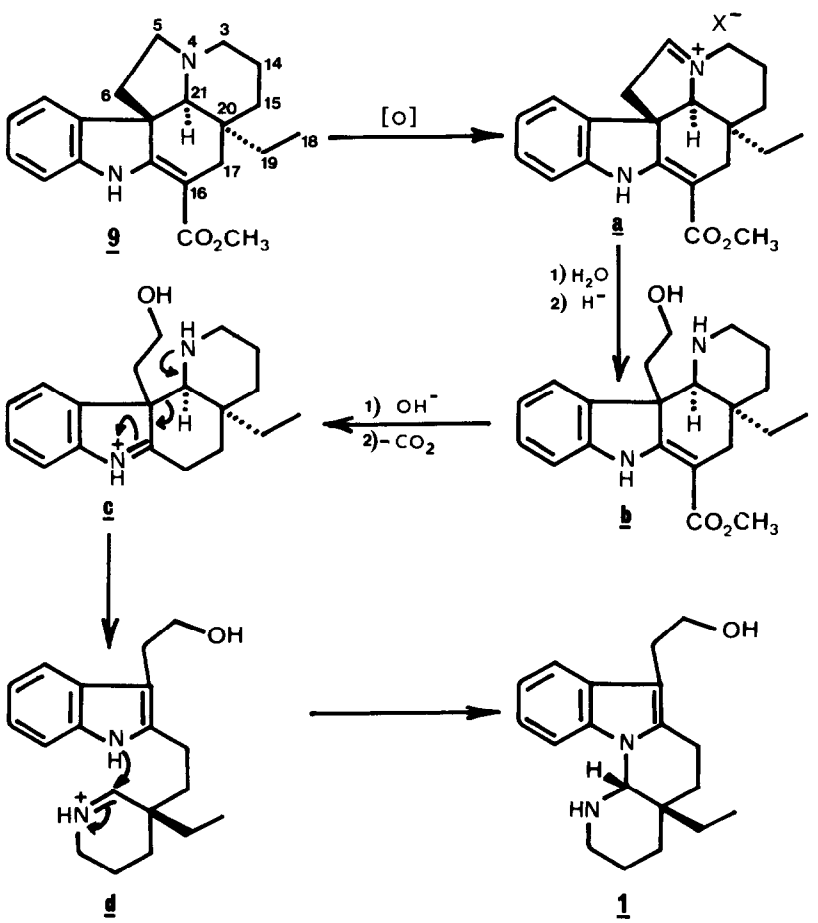
TABLE. ^{13}C NMR Chemical Shift Values (δ) in $CDCl_3$

	C-2	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C-12	C-13	C-21
Goniomitine 1	132.6	62.6	27.8	106.8	129.3	118.0	120.8	119.9	108.8	135.5	71.1
Guettardine	135.6	62.6	27.7	108.9	128.0	118.3	121.6	119.1	111.1	136.5	
Tryptophol		62.5	28.5	111.9	127.4	118.7	121.9	119.2	111.3	136.4	
Compound 7	136.0			114.1	126.2	120.4	121.8	120.5	109.7	137.6	63.9
Compound 8	132.6		17.7	126.9	128.6	119.0	121.2	119.0	109.5	137.8	64.6





Further support for structure 1 for goniomitine is obtained by the plausible biogenesis depicted in the Scheme. Goniomitine 1 may be derived from the Aspidosperma



skeleton of vincadifformine 9 by simple oxidative fission of the C-5, N-4 bond (9 → a → b) followed by decarboxylation (b → c), retro-Mannich reaction (c → d) and finally nucleophilic attack of the indole nitrogen on the resultant iminium ion (d → 1). The fact that Aspidosperma-eburnane alkaloids co-occur with goniomitine in the same plant[6] reinforces our structural and biogenetic proposals[11].

In conclusion, we have isolated from Gonioma malagasy goniomitine, a new alkaloid for which we are proposing structure 1. Previous work on G. kamassi[10] from South Africa[2] noted the isolation of alkaloids of unknown structure whose molecular weights were identical to those of goniomine and goniomitine. No data are available to draw a conclusion about the identity of alkaloids of the two plant species.

References and Notes

1 - First paper in this series : A. Chiaroni, L. Randriambola, C. Riche and H.-P. Husson, J. Am. Chem. Soc., 1980, 102, 5920.

2 - The plant grows in the South-West part of Madagascar. The genus Gonioma comprises only two species ; the other one, G. kamassi, is found in South Africa[10]. It is interesting to note the geographic distribution of this genus in relationship with the theory of plate tectonics.

3 - Goniomitine 1 : HR MS m/e (relative intensity) 298 ($C_{19}H_{26}N_2O$, 60), 280 ($C_{19}H_{24}N_2$, 35), 268 ($C_{18}H_{24}N_2$, 35), 267 ($C_{18}H_{23}N_2$, 100), 210 ($C_{15}H_{16}N$, 10), 208 ($C_{15}H_{14}N$, 10), 180 ($C_{13}H_{10}N$, 12), 156 ($C_{11}H_{10}N$, 14), 144 ($C_{10}H_{10}N$, 40), 143 ($C_{10}H_9N$, 21), 124 ($C_8H_{14}N$, 23), 110 ($C_7H_{12}N$, 11), 96 ($C_6H_{10}N$, 23) ; ^{13}C NMR ($CDCl_3$) : δ 7.3 (C-18), 18.5 (C-14)*, 20.8 (C-15)*, 21.8 (C-17)*, 27.8 (C-6), 28.7 (C-19), 33.8 (C-16), 35.3 (C-20), 45.4 (C-3), 62.6 (C-5), 71.1 (C-21), 106.8 (C-7), 108.7 (C-12), 118.1 (C-9), 119.9 (C-11), 120.8 (C-10), 129.3 (C-8), 132.6 (C-2), 135.4 (C-13). * Refers to carbon absorptions whose assignments may be interchangeable.

4 - Satisfactory IR, UV, ^1H and ^{13}C NMR spectra, HR MS or microanalyses were obtained for all compounds described.

5 - M.H. Brillanceau, C. Kan-Fan and H.-P. Husson, Tetrahedron Lett., 1984, 25, 2767.

6 - L. Randriambola and H.-P. Husson, unpublished results.

7 - Hydroboration and epoxidation reactions led to complex mixtures.

8 - We were unable to obtain an X-ray analysis of goniomitine due to the unsuitable nature of the crystals. We thank Mlle A. Chiaroni for her efforts.

9 - For compound 3 the ^{13}C-21 resonance is shielded to δ 60.8ppm and the C-21 ^1H singlet is deshielded to 5.46ppm with respect to 1.

10 - R. Kaschnitz and G. Spiteller, Monatsh. Chem., 1965, 96, 909.

11 - The absolute configuration as depicted in 1 is that of the Aspidosperma-Eburnane alkaloids found in the same plant[6].

(Received in France 17 February 1987)