NORMAVACURINE AND MINFIENSINE, TWO NEW ALKALOIDS WITH $C_{19}H_{22}N_2O$ FORMULA FROM *STRYCHNOS* SPECIES

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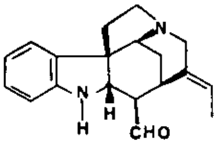
Abstract - Minfiensine and normavacurine are two novel $C_{19}H_{22}N_2O$ alkaloids from *Strychnos minfiensis, S. potatorum* and *S. longicaudata*. Minfiensine is characterized by a N-1 — C-3 bond instead of the usual N-1 — C-2 bond.

$C_{19}H_{22}N_2O$ formulae belong to secoiridoid deriving indole alkaloids, which have lost the methoxy-carbonyl unit without suffering further oxidation or reduction. Typical examples found in African Strychnos are 18-desoxy-Wieland-Gumlich aldehyde 1 from *S. dolichothyrsa* [1], *S. kasengaensis* [2] and *S. matopensis* [3] and normacusine B 2 from *S. dolichothyrsa* [4], *S. malacoclados* [5], *S. madagascariensis* [6], and *S. potatorum* [6]. We wish to report isolation and structural elucidation of two new bases having the same composition and gross carbon skeleton : normavacurine 3 from *S. minfiensis, S. potatorum* and *S. longicaudata* and minfiensine 4 from *S. minfiensis*. Erroneously alkaloid 3 from *S. longicaudata* was first given formula 5 of 1,2-dehydrodeacetylretuline [7].



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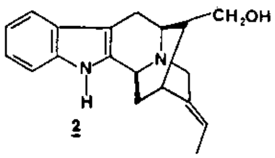

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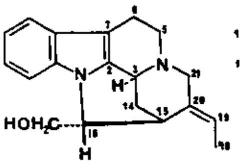

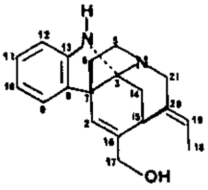

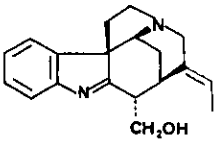

3
6 $N_4^+-CH_3$

4

5

Formulae 3 and 5 are characterized by the same array of protons and differ in the nature of their chromophores. Alkaloid 3 [8] was first thought to have an indolenine chromophore, owing to the lack of structure of its long wavelenght uv absorption band (λ=287 nm, log ε=3.6) but ^{13}C nmr, now available on the more abundant sample from *S. minfiensis*, unambiguously allows its identification as a N-substituted indole (Table I). In order to respect the proton arrangement (determined by a COSY experiment), the simplest way to obtain an indole is to shift C-3 and C-16 from C-7 and C-2 to C-2 and N-1 respectively, thus leading to structure 3 = normavacurine. The abnormal chemical shift of one of the H-21 (δ=1.03 ppm) is another evidence for its belonging to the pleiocarpamine series [9]. Further proof concerning the flat structure of 3 and the relative configurations of its asymmetric centers is provided by comparison of the ^{13}C nmr spectra of 3 and of mavacurine 6[10] (Table I).

	3	6[10]	4		3	6[10]	4
C-2	138.0	133.7	124.5	C-13	140.6	141.4	147.3
C-3	51.6	63.3	90.1	C-14	24.2	19.7	32
C-5	49.4	64.1	53.3	C-15	30.1	29.1	31.4
C-6	20.5	18.3	38.4	C-16	60.5	61.3	140.8
C-7	109.3	112.7	55.3	C-17	65.1	65.3	65.5
C-8	128.9	127.8	135.5	C-18	12.5	13.1	13.7
C-9	120.2	120.6	122.6	C-19	121.1	131.8	119.5
C-10	121.6	122.2	118.5	C-20	134.9	131.8	133.4
C-11	128.3	124.9	127.7	C-21	55.6	60.5	53.8
C-12	110.1	112.6	109.8				

Table I - ^{13}C nmr data for 3, 4 (75 MHz, $CDCl_3$) and 6[10].

Assignments of ^{13}C nmr spectra of 3 and 4 are based on C-H and H-H COSY experiments.

The mass spectrum of minfiensine 4[11] displays a molecular ion at m/z 294 (hrms : found : 294.1730, calcd for $C_{19}H_{22}N_2O$: 294.1731) and little fragmentation in the high masses range. Its uv spectrum shows three maxima at λ 213 nm (log ε : 3.98), 243 (3.54) and 295 (3.25), shifted at 212, 234 and 288 nm in acidic medium. The 300 MHz ^{1}H nmr spectrum shows signals for four aromatic protons, for a tryptamine unit and for a $N-CH_2-C=CH-CH_3$ unit ; it also shows at high field an ABX system with J_{AB}= 12Hz, and a vinylic proton long range coupling to a hydroxymethylene (δ=6.05 ppm, 1H and 4.10 ppm, 2H). The part of the ABX system (δ=3.41 ppm) also long range couples to the CH_2OH and to the vinylic proton of the ethylidene chain ; they can thus be assigned to H-15 and CH_2-17 of the skeleton of compound 1. In order to introduce a supplementary unsaturation, the N-1 to C-2 bond may be cleaved and to comply with ms data, N-1 is linked to C-3 which does not possess any hydrogen. This leads to structure 4 which is further supported by the ^{13}C nmr spectrum which shows ten olefinic or aromatic carbons and a deshielded signal for a C-3 substituted by two heteroatoms (δ=90.1 ppm) ; this situation also accounts for the hypsochromic shift of the uv spectrum recorded under acidic conditions. A NOESY experiment (600 ms mixing time) shows several meaningful correlations : H-2 — H-9, H-2 — H-17, H-17 — H-15 and H-15 — CH_3-18, thus bringing more evidences in favor of structure 4.

Whereas alkaloids 2 and 3 are members of well represented classes of alkaloids, there is no precedent for the isolation of a compound such as minfiensine 4. Its genesis is based upon two chemical events : a) ring cleavage between N-1 and C-2, and b) ring closure with formation of N-1 to C-3 bond. Event a) requires some activation of C-2 or C-16 which exists, for example, in 2,16 dehydroderivatives or in compounds with aldehyde or ester functions at C-17 and event b) demands oxidation of C-3 or of N-4, two related possibilities which are not rare among Strychnos alkaloids.

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8. Normavacurine 3 : amorphous solid, $(\alpha)_D$ =127° (c=0.67, $CHCl_3$) uv and ^{13}C nmr, see text ; ir ($CHCl_3$) : 3380 (br), 1640, 1610, 1450 cm^{-1} ; ms (rel. int.) : 294 (M^+, 80), 279 (5), 277 (2), 264 (35), 263 (100), 234 (30), 230 (15), 180 (50) ; ^1H nmr (300 MHz, $CDCl_3$) : 7.56 (dd, J=1.8, 7.2 Hz) ; 7.50 (dd, J=1.8, 7.0 Hz) ; 7.17 (m, 2H) ; 5.13 (d of quartets, J=2.0, 6.9 Hz, H-19) ; 4.22 (dd, J=5.5, 9.1 Hz, H-17) ; 4.10 (m, 2H, H-17+16) ; 3.78 (dd, J=2.2, 3.6 Hz, H-3) ; 3.28 (ddd, J=2.7, 10.3, 16.0 Hz, H-5) ; 3.24 (bs, H-15) ; 3.15 (ddd, J=2.7, 8.6, 15.0 Hz, H-6) ; 2.63 (ddd, J=6.1, 10.3, 16.0 Hz, H-5) ; 2.56 (ddd, J=2.2, 4.0, 13.5 Hz, H-14), 2.50 (br d, J=13.4 Hz, H-21) ; 2.18 (ddd, J=6.1, 8.6, 15.0 Hz, H-6) ; 1.96 (ddd, J=2.5, 3.6, 13.5 Hz, H-14) ; 1.57 (dd, J=2.3, 6.9 Hz, CH_3-18) ; 1.03 (d of quintets, J=13.4, 2.3 Hz, H-21).

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11. Minfiensine 4 : amorphous solid, uv and ^{13}C nmr, see text ; colour red upon Ce IV spraying, $(\alpha)_D$ =134° (c=0.82, $CHCl_3$) ; ms (rel. int.) : 294 (M^+, 100), 263 (15), 234 (15), 197 (20), 180 (25), 168 (25), 167 (20), 130 (15), 97 (20), 82 (55), ir ($CHCl_3$) : cm^{-1} : 3300, 1610, 1485, 1115, 1065, 1020, 750 ; ^1H nmr (300 MHz, $CDCl_3$) : 7.11 (dd, J=7.5, 1.4 Hz, H-9) ; 7.02 (dt, J=1.3, 7.5 Hz, H-11) ; 6.71 (dt, J=1.0, 7.5 Hz, H-10) ; 6.57 (ddd, J=7.5, 1.3, 1.0 Hz, H-12) ; 6.05 (t, J=1.4 Hz, H-2) ; 5.39 (quartet of quartets, J=7.2, 1.3 Hz, H-19) ; 4.10 (d, 2H, J=1.4 Hz, H-17) ; 3.68 (d of quintets, J=15.0, 1.6 Hz, H-21) ; 3.41 (br t, J=3.1 Hz, H-15) ; 3.30 (ddd, J=5.1, 7.2, 10.0 Hz, H- 5) ; 3.17 (d of quintets, J=15.0, 1.4 Hz, H-21) ; 2.63 (dt, J= 10.0, 7.6 Hz, H-5) ; 2.04 (m, 2H-6) ; 1.94 (m, 2H-14) ; 1.71 (dt, 3H, J=7.2, 1.4 Hz, CH_3-18).

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