STRUCTURE OF MATOPENSINE, A NOVEL DIMERIC INDOLE ALKALOID FROM *STRYCHNOS* SPECIES

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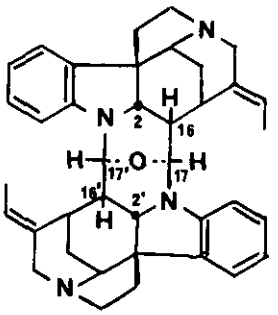
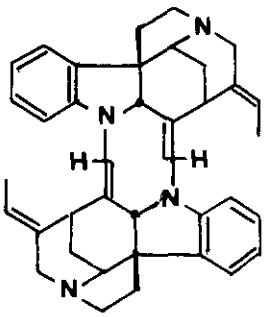
Abstract - A novel symmetrical bisindole alkaloid, matopensine, has been isolated from *Strychnos matopensis* and from *Strychnos kasengaensis*. Its structure has been elucidated by spectroscopic means including 401MHz ^{1}H NMR ; matopensine is 16S,16'S-dihydro-17R,17'R -oxybisnordihydrotoxiferine.

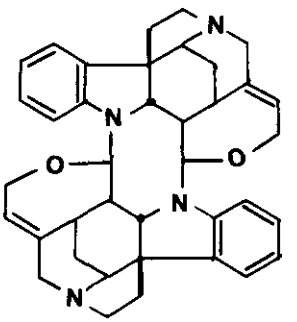
Among dimeric indole bases isolated from *Strychnos* species, there is a large group of alkaloids which are composed of two akuammicine-type subunits linked through N(1) and C(17) in an eight-membered ring system. Typical examples such as bisnordihydrotoxiferine 2, bisnor C alkaloid H and caracurine V 3 are combinations of Wieland-Gümlich and desoxy Wieland-Gümlich aldehydes[1]. A more complex picture is provided by bisnor C-curarine[1] where an oxygen atom links C(2) and C(2') and with C-calebassine[1] and bisnor C alkaloid D[2] where, in each, a supplementary bond is found between the C(17)s of the former and C(16)s of the latter. We now wish to report a novel dimer of similar type, exemplified by matopensine 1, where the C(17)s are joined through an ether bridge.



1 matopensine



2 bisnordihydrotoxiferine



3 caracurine V

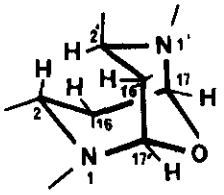
Matopensine was isolated simultaneously in our laboratory from two species of *Strychnos* from Zaire : *S.matopensis* S.Moore and *S.kasengaensis* De Wild[3]. Matopensine is an amorphous, non-polar compound (Rf=.8 ; $CHCl_3$/MeOH/NH_4OH : 94/5/1), which presents a red colouration with ceric(-IV) spray. Its elemental composition was determined as $C_{38}H_{42}N_4O$ by high resolution analysis of its mass spectrum molecular ion (observed value : 570.3366, calculated value for $C_{38}H_{42}N_4O$: 570.3359). The *UV spectrum of* 1 *displays maxima* at 217 nm (log ε:4.46), 263 (4.39) and 313 (3.95) ; it is reminiscent of the UV spectrum of caracurin V 3[4]. In the IR spectrum of 1, one remarks the absence of bands for NH,OH or CO vibrations ; a sharp absorption at 1605 cm^{-1} may be attributed to an indoline. Besides the molecular ion at m/z 570, the mass spectrum shows intense peaks at m/z 130,144 (100%), 121 and 122 indicating the presence of tryptamine and ethylpiperidine. Other prominent fragments at 277 and 279, analyzed for $C_{19}H_{21}N_2$ and $C_{19}H_{23}N_2$ and correspond to an akuammicine framework.

In the ^1H NMR spectrum of 1, obtained at 401MHz[5], signals appear for 21 protons; this is an indication of symmetry in the molecule (table 1). Among these protons, some are readily assigned as are the 4 aromatic protons and those of an ethylidene side chain (q at 5.35 ppm, d at 1.83 ppm, J=7Hz). At 5.3 ppm a narrow doublet (J=2Hz) features an olefinic proton or a carbinolamine proton (H-C-17) as in bisnor C alkaloid H (δ=5.3 ppm) ; another one-proton doublet appears at 4.11 ppm (H-C-2, J=5.5Hz). Multiple irradiations show these doublets to couple with a multiplet at 1.84 ppm (H-C-16). Systematic decoupling experiments performed on every single proton of the molecule allow the identification of the protons of the basic retuline skeleton.

Table 1 ^1H NMR spectrum of 1 (401MHz)

H	δ	Multiplicity	J(Hz)	H	δ	Multiplicity	J(Hz)
2	4.11	d	5.5	14	2.16	bd	14
3	3.14	bs		14'	1.81	bd	14
5	3.12	m		15	2.98	bs	
5'	2.9	dt	10,7,7	16	1.84	m	
6	2.48	dt	14,7,7	17	5.3	d	2
6'	2.0	dt	14,7,7	18	1.83	bd	7
9	7.14	d	8	19	5.35	bq	7
10	6.66	t	8	21	3.55	d	15
11	7.12	t	8	21'	3.13	bd	15
12	6.2	d	8				

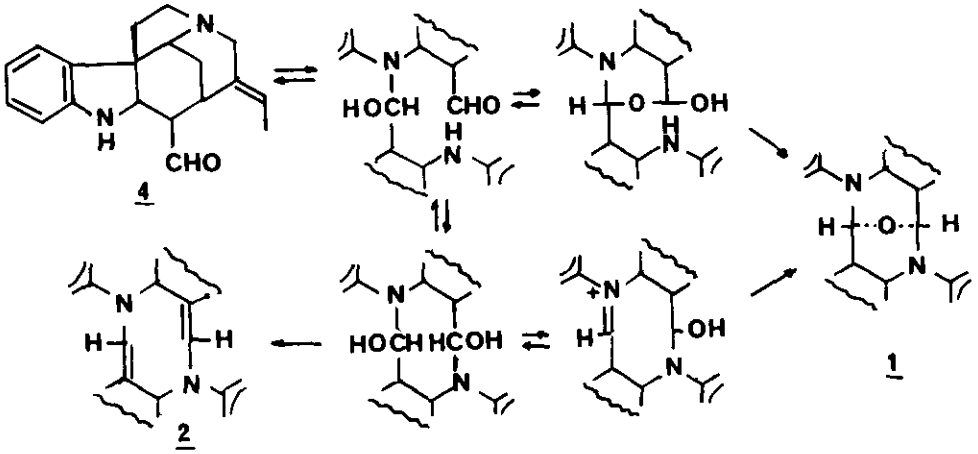
These data lead us to the conclusion that matopensine is a 16,16'-dihydro-17,17'-oxybisnordihydrotoxiferine. Examination of molecular models shows that the only configurations fitting the NMR coupling constants are 2βH,16βH (retuline series), C-17S, 2'βH, 16'βH, C-17'S. The oxazoline rings are in a chair conformation with H-2 axial, and H-16 and H-17 both equatorial ; this arrangement brings J_{2-16}(ax-eq) to 5.5Hz and J_{16-17} (eq-eq) to 2Hz. The value of J_{2-16} is slightly inferior to the value found by Angenot et al.[6] for retuline ; it is a result of a more severe deformation of the retuline ring C.



The element of symmetry of the molecule is a C_2 axis, which passes through the oxygen atom. The existence of a center or of a plane of symmetry was ruled out by the non-zero optical rotation of 1 ($(\alpha)_D$=+105°(c=0.6, MeOH)).

As far as biogenesis is concerned, it is not unreasonable to think that 1 originates from two desoxy Wieland-Gümlich aldehydes 4. The first step in the coupling would be the formation of a carbinolamine, which may further react with the remaining aldehyde to form a hemiketal ; its dehydration would yield the other six-membered ring of 1. Alternatively, an eight membered ring may be created, double dehydration of which results in bisnordihydrotoxiferine 2 formation whereas a single dehydration leads to matopensine 1.

In this respect, it is worth noting that in the two *Strychnos* species where 1 was found, it was accompanied by 2[7] ; to the best of our knowledge in the many isolations of 2 so far reported no mention has been made of another compound with similar TLC behaviour and which colours red with ceric spray (colouration of 2 with Ce IV is purple).



All efforts towards the chemical interconvertions of 1 and 2 have hitherto been in vain but prolonged acidic treatment transforms 1 into desoxy Wieland-Gümlich aldehyde 4.

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3 . Plant material was collected by one of us (C.D.) under the "Etude phytochimique de la flore du Zaïre" research project. We gratefully acknowledge support by "Ministère de la Coopération au développement de Belgique".

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5 . Due to the courtesy of Dr S.K.Kan, Université de Paris-Sud, Orsay, whom we thank.

6 . D.Tavernier, M.J.O.Anteunis, M.J.G.Tits and L.J.G.Angenot, Bull.Soc.Chim.Belg., 1978, 87, 595.

7 . Isolation of 1 and 2 from the stem bark of *S.kasengaensis*. Ground stem bark (880 g) is wetted with 500 ml of conc. NH_4OH half diluted in water and lixiviated overnight by means of 20 l of EtOAc. The organic solution is extracted by 2% aqueous H_2SO_4 ; the acid layer is separated, alkalized with NH_4OH and extracted by $CHCl_3$. The $CHCl_3$ solution is washed with water, dried over Na_2SO_4 and evaporated *in vacuo* ; one obtains 5.30 g of crude alkaloid mixture (6.03g/kg). Separation is obtained by medium pressure liquid chromatography on Sigel (Jobin-Yvon chromatospac - 10 bar). Column is eluted first with $CHCl_3$ (150 x 20 ml fractions) , then with a mixture of $CHCl_3$ and MeOH (99-1). Matopensine 1 is present in fractions 178-210 ; bisnordihydrotoxiferin 2 is found in fractions 220-237 along with isositsirikine.

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