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JANUSSINES A AND B FROM *STRYCHNOS JOHNSONII*

A CROSS POINT IN THE BIOGENESIS OF QUASIDIMERIC ALKALOIDS

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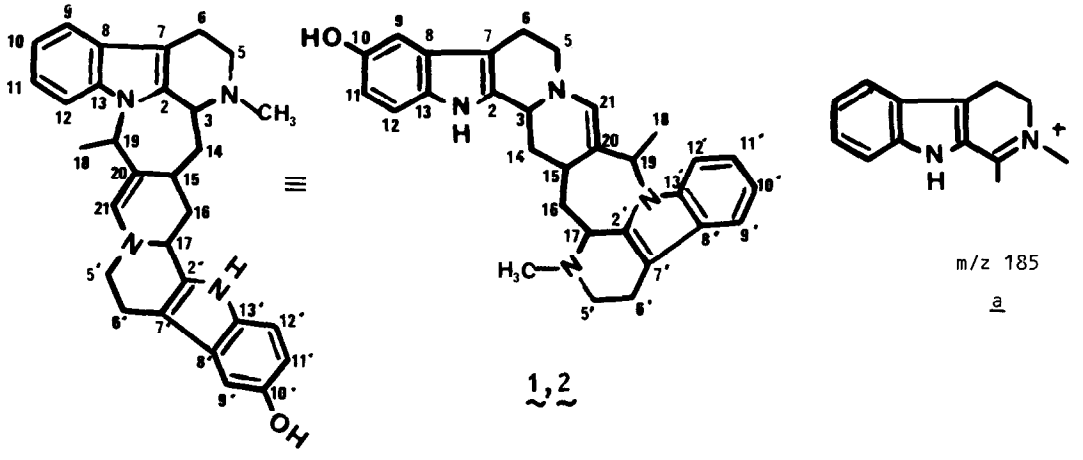
Summary : Two new quasidimeric alkaloids have been isolated from *Strychnos johnsonii*. According to the fashion they are looked at, they can be viewed as arising from akagerine or from cathenamine-type of alkaloids.

In the course of our investigations on African *Strychnos* alkaloids, we isolated two new isomeric bases - janussine A (1) and janussine B (2) from the root of *S.johnsonii*(1,2). Their novelty and uniqueness originate in their dual appearance and biosynthesis : akagerine or cathenamine type. Their structure was established as follows.



1,2

m/z 185

a

Their UV spectra were characteristic for an indole chromophore and were not modified at acidic pH ; their IR spectra were atypical (bands at 3420 cm^{-1}, NH and 1660 cm^{-1}, C=C). In mass spectrometry, molecular ions appeared at m/z 464 with a relatively low intensity (ca 20%) ; in both alkaloids, this ion was analyzed as $C_{30}H_{32}N_4O$ (calc. 464.2575, found : 464.2557 (1) and 464.2596 (2)). The unusual ratio between the number of carbon and nitrogen atoms indicated that the two alkaloids belong to the (small) class of "quasidimers", in

which a terpenic unit is linked to two tryptamines.

Complementary information was obtained in the 400MHz ^1H NMR spectra : unsubstituted indole nucleus, 10-or 11-substituted indole (ABX system, J_{AB}=2Hz, J_{AX}=7Hz), N-methyl group and $CH-CH_3$ unit (table I). The presence of an N-Me group and of MS fragments at m/z 185 (a) strongly suggested an akagerine (3) or a kribine (4) unit, unsubstituted on the aromatic ring.

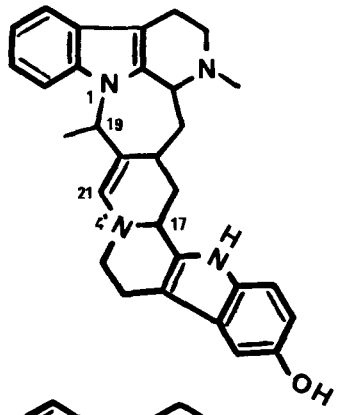
	1	2		1	2
H-11'	6.73	6.83	H-3 + H-17	4.1 + 3.78	
H-9'	6.72	6.61	N-Me	2.42	2.47
H-21	6.18	6.20	CH_3-18	1.65	1.51
H-19	4.93	4.91			

Table I

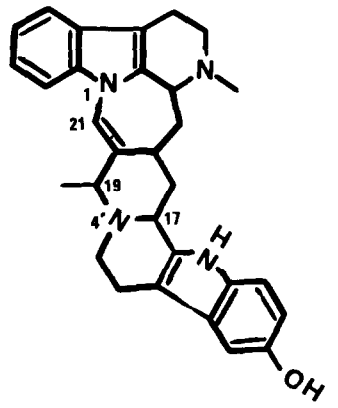
^1H NMR data for 1, 2

Examination of the ^{13}C NMR spectra of compounds 1 and 2 (table II) confirmed the existence of an unsubstituted indole, of a 10-hydroxy indole (5) and of a trisubstituted double bond (CH at 136.6 ppm ; C at 115.5 ppm). The aliphatic part of this spectrum consisted of $4CH, 6CH_2$ and $2CH_3$; two of the methylenes appeared at a high field (20.0 ; 20.9 ppm) consistent with the C-6 of tetrahydrocarbolines (6). Starting with fragment (a), simple biogenetic considerations led to possible structures I, II and III which differed in the attachment of N(1) and N(4') to C(17), C(19) and C(21). Structure III was eliminated on the basis of unappropriate ^1H chemical shifts and multiplicities. The key to the final structure determination was the recognition of the supplementary double bond as an enamine whose α-proton appeared as a singlet at δ6.18 ppm. When considering structures I and II, II would be expected to give a bathochromic shifted UV spectrum; as such a shift is not observed, only structure I is left. This choice was confirmed by the isolation from the same plant of compound 3, a compound with MS molecular ion at m/z 496. Salient physical data of 3 were : carbonyls at 1720 and 1655 cm^{-1} (IR), N-formyl carboline loss in the MS (ion at m/z 281) and protons at δ7.92 (s,NC<u>H</u>O), 5.51 (q,7Hz,H-19) and 5.27 (d,11Hz,H-17). Compound 3 is derived from 1 or 2 by autoxidation, a precedented fate of enamines (7).

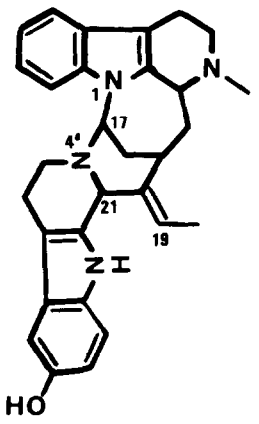
I



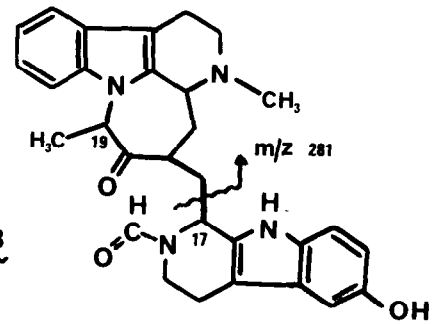
III



II



3



	1	2		1	2
C-2	135.9	135.9	C-18	21.2	21.2
C-3	57.9	58.1	C-19	53.5	52.1
C-5	50.3	50.7	C-20	107.8	111.5
C-6	22.4	20.0	C-21	139.2	136.6
C-7	105.3	105.3	C-2'	135.1	134.8
C-8	128.0	128.3	C-5'	53.8	53.7
C-9	118.4[a]	118.4	C-6'	20.3	20.9
C-10	119.0[a]	119.1	C-7'	107.5	107.6
C-11	121.3[a]	121.3	C-8'	126.7	126.7
C-12	111.2[b]	111.1	C-9'	102.7	102.7
C-13	136.1	135.8	C-10'	150.2	150.1
C-14	34.6	35.0	C-11'	109.8[b]	109.9
C-15	30.7	26.0	C-12'	111.9[b]	111.9
C-16	34.3	32.0	C-13'	131.8	131.5
C-17	57.2	57.7	N-Me	40.7	40.0

Table II : ^{13}C NMR data for 1, 2

a,b,c. values within the same volumn may be interchanged
the numbering corresponds to the formula drawn on the left of the first page of the article.

Beside the fact that janussines are novel alkaloids characterized by the rare enchainment of eight contiguous rings, 1 and 2 are unique because they can be viewed in two different manners, each with its own biogenetic background (see front page for representations). In the first representation 1 and 2 seem to derive from decussine(8)-mostuenine type (9) alkaloids ; in the second representation 1 and 2 are cathenamine-like alkaloids (10). As both types are represented in the plant (akagerine, akagerinelactone, desoxykribine, tetrahydroakagerine *vs* ajmalicinal, descarbomethoxy-gambirtanine), it is not possible to propose a unique biogenesis (and a numbering) for 1 and 2. The high density of functionnalization of the terpenic genitor secologanin (three aldehydes, one conjugated double bond and one ester) is the source of the diversity of indole alkaloids obtained by reaction with a single tryptamine (or tryptophan unit). The number of possibilities for reactions between secologanin and two tryptamines is large and it is therefore probable that the number of quasidimers isolated will rise.

References

1) Plant material was collected under the "Etude phytochimique de la flore du Zaïre" research project.

2) We thank Pr J.Lévy for suggesting the name of the janussines.
Janussine A (1) : (CR:brown), $(\alpha)_D$=+492°(c=0.5,MeOH) ; UV λ_{max}^{MeOH} nm (logε):228(4.31), 278(3.84) ; IR($CHCl_3$)cm^{-1}:3420,1660,1470,1385,1180 ; MS m/z(rel.int.):464(30),449(10), 420(10),295(15),277(50),265(65),198(25),185(90),182(60),143(100).
Janussine B (2) : (CR:brown) ; $(\alpha)_D$:+153°(c=0.2,MeOH) ; UV λ_{max}^{MeOH} nm (logε):228(4.44), 284(4.0),292(3.99) (sh) ; IR(KBr):3420,3400,1660,1460,1370,1330 ; MS same as above (some differences in the intensities).

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