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MAXONINE, A NOVEL ALKALOID FROM SIMIRA MAXONII

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Abstract: A novel alkaloid, maxonine, with an indole-pyrido-naphthyridine skeleton, has been isolated from *Simira maxonii*. Its structure was elucidated on the basis of 2D NMR spectral data.

During a screening of endemic flora in the tropical forest of Costa Rica harmane was isolated [1] from the roots of *Simira maxonii* (Rubiaceae). Further studies involving flash chromatography and preparative layer chromatography of the acid soluble portion afforded a novel alkaloid (1.2x 10^{-3}% of the roots), which was named maxonine, $C_{19}H_{13}N_3O$, and assigned the structure 1.

The physicochemical properties of maxonine were as follows: yellow oil, $[\alpha]_D^{20}$ -85 (c=0.2, $CHCl_3$); MS, M^+ 299 (45%), M - Me^+ 284 (100%); UV λ_{max}^{EtOH} nm (log ε): 250 (4.11), 305 (3.85), 419 (3.72). The IR spectrum ($CHCl_3$) showed the absorption due to a carbonyl group (1660 cm^{-1}). The ^1H NMR spectrum (Table 1) revealed the presence of a secondary methyl group (doublet at δ 1.64 ppm) coupled with a low field methine proton (δ 6.02 ppm). The remaining signals were noted in the aromatic region but an understanding of the complex pattern was achieved by a combination of different techniques. The results are summarized in Table 1.

The vicinal relationship between the resonances at δ 8.83 and 8.26 ppm as well as between the signals at δ 7.87 and 8.82 ppm was established by spin decoupling experiments. The correlation between each proton and its bearing carbon was achieved by an HETCOR [2] measurement, while the assignment of the quaternary carbons followed from the data of LONG-RANGE HETCOR [3] and a series of INEPTL [4] experiments.

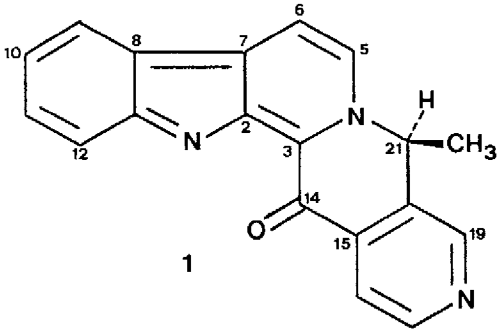
Table 1.

^{1}H and ^{13}C NMR spectral parameters* and relevant long-range ^{13}C-^{1}H connectivities of maxonine (1).

Carbon	δ_C	δ_H	$^{n}J_H$
2	135.02	-	$^{3}J_{H-6}$
3	135.13	-	$^{3}J_{H-21}$ $^{3}J_{H-5}$
5	140.63	8.83 (d,5Hz)	$^{2}J_{H-6}$
6	119.23	8.26 (d,5Hz)	$^{2}J_{H-5}$
7	133.46	-	$^{3}J_{H-5}$ $^{2}J_{H-6}$
8	121.16	-	$^{3}J_{H-10}$ $^{3}J_{H-12}$
9	122.50	8.23 (d,8Hz)	$^{3}J_{H-11}$
10	121.57	7.44 (m,8+5.5+2.5Hz)	$^{3}J_{H-12}$
11	130.15	7.78 (overlapped)	$^{3}J_{9}$
12	109.51	7.78 (overlapped)	$^{3}J_{H-10}$
13	140.84	-	$^{3}J_{H-9}$ $^{3}J_{H-11}$
14	190.64	-	$^{3}J_{H-16}$
15	145.25	-	$^{3}J_{H-19}$ $^{3}J_{H-21}$ $^{3}J_{H-17}$
16	123.84	7.87 (d,5Hz)	$^{2}J_{H-17}$
17	150.74	8.82 (d,5Hz)	$^{2}J_{H-16}$ $^{3}J_{H-19}$
19	148.73	8.94 (s)	$^{3}J_{H-16}$
20	132.78	-	$^{3}J_{H-16}$ $^{2}J_{H-19}$ $^{2}J_{H-21}$
21	54.09	6.02 (q,6.8Hz)	$^{2}J_{Me}$ $^{3}J_{H-19}$
22	21.29	1.65 (d,6.8Hz)	$^{2}J_{H-21}$

* 100.6 and 399.9 MHz, $CDCl_3$, TMS as internal reference.

The lowest field proton at δ 8.94 is long-range coupled with the carbons C-15, C-17 and C-20. Analogous connectivity was found between H-16 and C-19,thus suggesting the presence of a 3,4-disubstituted pyridine nucleus. The signals at δ 145.25 and 132.78 were now assigned to the bridgehead carbons C-15 and C-20, respectively. The connection of D and E rings was established by a concerted use of LONG-RANGE HETCOR and NOE difference experiments. The protons H-16 and H-19 displayed long-range correlation peaks with the carbons C-14 and C-21 of the D ring. Selective irradiation of the signal at δ 8.94 (H-19) caused considerable NOE enhancement of the resonance at δ 6.02 (H-21). These data require that these protons remain in the same plane with the methyl group oriented out of the plane. Again, on the basis of long-range correlations with protons H-5 and H-21, the carbon resonance at δ 135.13 was assigned to C-3,the common carbon between the C and D rings. The assignment of the two remaining C ring quaternary carbons (C-2 and C-7) was based on their long-range correlation with protons H-5 and H-6. Data for the attachment of rings A and B (a modified indole unit) were obtained as follows. The most characteristic high field resonance at δ 109.51, was attributed [5] to C-12 in ring A while the signals of the carbon atoms and protons attached thereto were assigned by proton-proton decoupling and heteronuclear correlation experiments.



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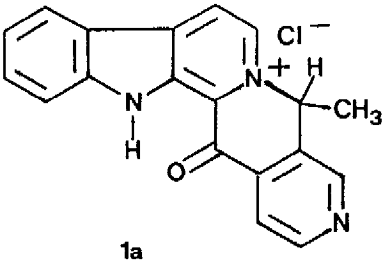
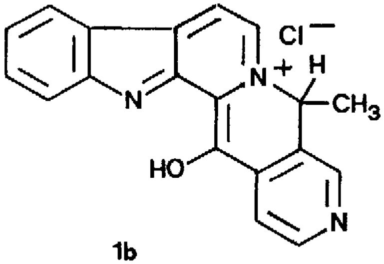


1a



1b

In conclusion, the structure 1 was assigned to maxonine. Similar compounds, namely anhydronium bases, are described in the literature [6-8] and show a typical behaviour in the UV spectra. Neutral and acid solutions exhibit the same longer wavelenght absorbance at 287-292 nm, whereas the addition of diluted alkali causes a bathochromic shift to 418-444 nm [7,8]. By contrast, the addition of alkali did not change the UV spectrum of maxonine, whilst a bathochromic shift to 461 nm was obtained with diluted HCl. This value cannot be displayed by a structure 1a, commonly assigned to anhydronium bases in acid environment, but would be rather compatible with a structure 1b, where the conjugation is extended by the participation of a further double bond. The structures of malindine [9], isolated from *Strychnos decussata*, and cadamine [10], isolated from *Anthocephalus cadamba*, differ from that of maxonine only in the oxidation state of the rings C and D.

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