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A NEW ALKALOID, 4-HYDROXYSTRYCHNINE, FROM AFRICAN SPECIES STRYCHNOS ICAJA BAILL.

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The root of young Strychnos icaja plants is used in Equatorial Africa as ordeal poison and as ingredient in arrow poison (1). From the leaves of S. icaja Bisset has recently isolated eleven alkaloids, belonging to five different structural groups, but neither strychnine nor substituted strychnine derivatives were isolated (2). Based on this and previous investigations it was concluded that little is known about the chemistry and pharmacodynamics of African Strychnos species and furthermore that strychnine and brucine have never been demonstrated with certainty to be present (3).

However, our pharmacological investigation showed that none of the alkaloids isolated by Bisset (2) could be responsible for the toxic effect of the plant (4,5).

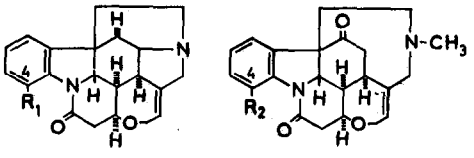
The pharmacological active alkaloid fraction A was isolated as described in ref. 4 and 5 and separated into two alkaloids, A_1 and A_2 (5).

Alkaloid A_1 crystallized from ethanol, m.p. 271-3°; $[\alpha]_D^{20} = -131°$ (c=1.0 in $CHCl_3$). The UV, IR and NMR spectra of A_1 were superimposable with those of authentic strychnine, m.p. 272-3°; $[\alpha]_D^{20} = -134°$ (c=1.0 in $CHCl_3$). Mixed m.p. unchanged. Mass spectrum: (M^+) 334 (base peak), peaks at m/e 319, 180, 162, 144, 143, 130, 120 and 107. Thus, alkaloid A_1 is strychnine (I). This is the first time that strychnine is ever proved with certainty to be present in an African Strychnos species.

The second alkaloid A_2, crystallized from ethanol, m.p. 276°. Mass spectrum: (M^+) 350 (also base peak), and very little fragmentation except

the "indole"peaks at m/e 160, 159 and 146 (16 mass units higher than corresponding peaks in strychnine, indicating a hydroxylated indole nucleus). The minor fragmentation between the "indole"peaks and the mass peak is strikingly similar to the strychnine fragmentation. UV spectrum similar to that of vomicine (IV) without bathochromic shift in alkaline solution. NMR spectrum generally shows a shift to higher field than that of strychnine, especially in the aromatic region, where the signal for the C-4-proton is missing in the region 7.83-8.16 p.p.m. The protons at C-1, C-2, C-3 must be adjacent due to the complex signals in the aromatic region. At 11.70 p.p.m. a singlet corresponding to a hydroxyl group is present. The same singlet is found in vomicine (IV).

$[\alpha]_D^{20} = -8^\circ$ (c=0.7 in $CHCl_3$) for alkaloid A_2, when compared to strychnine (I), $[\alpha]_D^{20} = -134^\circ$, shows nearly the same change towards the dextrorotary region as vomicine (IV), $[\alpha]_D^{20} = +100^\circ$ does, when compared to icajine (III), $[\alpha]_D^{20} = -18^\circ$. It was concluded that A_2 is a new alkaloid: 4-hydroxystrychnine (II).



I R_1=H Strychnine
II R_1=OH 4-hydroxy-strychnine
III R_2=H Icajine
IV R_2=OH Vomicine

REFERENCES

1. F. Sandberg, Cahiers de la Maboké; 3, fasc. 1, 5 (1965)
2. N.G. Bisset, Alkaloids of some African species of Strychnos. Thesis submitted to the University of London for the degree of Ph.D. 1968
3. N.G. Bisset and A.J.M. Leeuwenberg, Lloydia, 31, 208 (1968)
4. F. Sandberg, E. Lunell, K.J. Ryrberg, Acta Pharm. Suec. 6, (1969). In press.
5. F. Sandberg, K. Roos, K.J. Ryrberg, K. Kristianson, ibid. 6, (1969). In press