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(+)-*N*-METHYLLAUROTETANINE-β-*N*-OXIDE FROM *GLOSSOCALYX BREVIPES*

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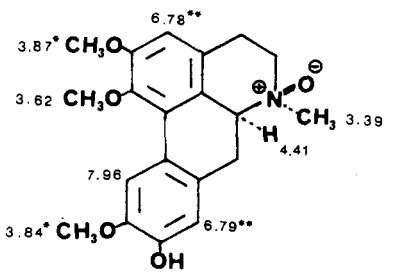
At least twelve naturally occurring aporphine *N*-oxides are known (1). However, the stereochemistry at the *N*-oxide center for only one of them, namely (−)-laurepukine, is known; the stereochemical determination resulting from an X-ray analysis (2,3).

In the course of a study of the chemical constituents of the Nigerian flora, we had occasion to investigate the alkaloids of *Glossocalyx brevipes* Benth., one of the four tropical West African species belonging to the small botanical family Siparunaceae. The plant yielded the new aporphine (+)-*N*-methyllaurotetanine-β-*N*-oxide (**1**), $C_{20}H_{23}NO_5$.

The 360 MHz ^{1}H-nmr spectrum of (+)-*N*-methyllaurotetanine-β-*N*-oxide in CD_3OD is presented around expression **1**. Three methoxyl singlets were present, the most upfield one, at δ 3.62, assignable to C-1. Three aromatic singlets were also in evidence, with the most downfield, at δ 7.96, due to H-11. The *N*-methyl signal was relatively downfield at δ 3.39, while H-6a appeared as a doublet of doublets at δ 4.41.



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^{1}H-nmr nOeds (nuclear Overhauser enhancement difference spectroscopy) (4) was used to settle the stereochemistry at the *N*-oxide center. Irradiation of the δ 3.39 *N*-methyl singlet led to a 10% enhancement of the δ 4.41 doublet of doublets (H-6a). Conversely, irradiation at δ 4.41 produced a 6% enhancement of the δ 3.39 singlet. It follows that the *N*-methyl group and H-6a must be *syn* to each other. Because the alkaloid is dextrorotary, it belongs to the C-6a *S* absolute configuration as indicated in expression **1** (1).

The remaining evidence that was gathered is in accord with the assignment of structure **1** to the alkaloid. The uv spectrum shows maxima at 218, 280, and 302 nm, with a strong bathochromic shift and a hyperchromic effect in base due to the presence of a phenolic group at C-9 (5). The mass spectrum exhibited a weak molecular ion *m/z* 357 with a base peak *m/z* 339 $(M-18)^+$.

Zinc in H_2SO_4 reduction of the *N*-oxide provided (+)-*N*-methyllaurotetanine which significantly is also present in the plant.

Molecular models indicate that the conformation of (+)-*N*-methyllaurotetanine-β-*N*-oxide approximates that represented in expression **1a**. The *N*-oxide oxygen is pseudo-axial and is *anti* to the pseudo-axial H-6a.

Known alkaloids that we found in the

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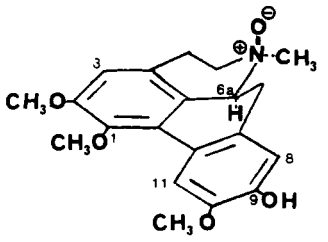

1a

plant, besides (+)-*N*-methyllaurotetanine, include the benzylisoquinolines (−)-*O*-methylnorarmepavine (6-8), (+)-orientaline, and (+)-reticuline; the proaporphines (+)-pronuciferine and (+)-stepharine; the aporphines (−)-asimilobine, (−)-tuduranine, (+)-lauro tetanine, (+)-norisodomesticine, (+)-isoboldine, (+)-nantenine, and (+)-isocorydine; the oxoaporphine liriodenine (1); and the morphinandienone (−)-flavinantine (9).

EXPERIMENTAL

PLANT COLLECTION AND EXTRACTION.—*G. brevipes* (5 kg, dry) was collected at Awi, Calabar, in Cross Rivers State, in February 1982. A sample is kept in the herbarium of the Forestry Research Institute of Nigeria, Eleiyele, Ibadan.

The powdered plant was extracted with cold EtOH, and the solvent was evaporated. The residue was taken up in 5% HCl, and the insoluble material was removed by filtration. The aqueous acidic solution was extracted with $CHCl_3$ and made basic with NH_4OH. The alkaloids were extracted with $CHCl_3$, and the organic layer was separated. Evaporation left an alkaloidal residue which was placed on a silica gel column. Elution was with $CHCl_3$ enriched with increasing amounts of MeOH. Further purification was achieved by means of tlc on silica gel plates.

The following alkaloids were isolated: (+)-nantenine (15 mg), (+)-isocorydine (6 mg), liriodenine (32 mg), (−)-*O*-methylnorarmepavine (24 mg), (+)-*N*-methyllaurotetanine (43 mg), (+)-*N*-methyllaurotetanine-β-*N*-oxide (1) (18mg), (+)-isoboldine (11 mg), (+)-pronuciferine (43 mg), (−)-asimilobine (57 mg), (+)-reticuline (39 mg), (+)-stepharine (18 mg), (−)-flavinantine (7 mg), (+)-orientaline (32 mg), (+)-norisodomesticine (32 mg), (+)-laurotetanine (33 mg), and (−)-tuduranine (12 mg).

(+)-*N*-METHYLLAUROTETANINE-β-*N*-OXIDE (**1**).—Amorphous, λ max (MeOH) 218, 280, 302 nm (log ε 4.55, 4.15, 4.10); λ max (MeOH-OH^-) 215, 323 nm (log ε 4.52, 4.20); *m/z* 357 (M^+) (0.6), 355 (0.6), 341 (20), 340 (43), 339 (100), 337 (20), 324 (80), 310 (14), 296 (25), 281 (20), 266 (14); $[\alpha]^{25}D$ +49° (c 0.15, MeOH).

REDUCTION OF **1**.—In a 10-ml flask equipped with a magnetic stirrer, **1** (2 mg) was placed, together with zinc (2 mg), $CHCl_3$ (5 ml), and H_2SO_4 (1 ml). The mixture was stirred and gently heated over a steam-bath for 1 h. Only one product could be isolated following work-up, namely (+)-*N*-methyllaurotetanine, $[\alpha]^{25}D$ +72° (c 0.16, MeOH), identical with authentic material (1) in terms of ^1H-nmr spectra, tlc Rf values, and specific rotations.

ACKNOWLEDGMENT

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