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# SRILANKINE: A 4-HYDROXYLATED APORPHINE

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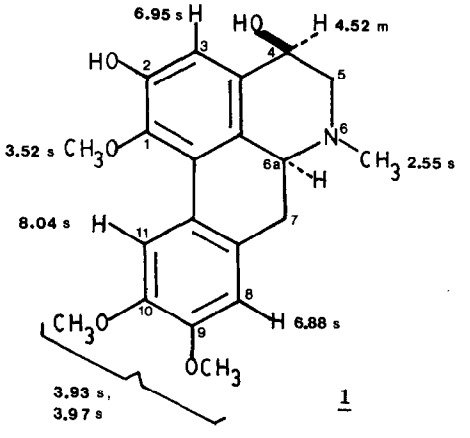
Physical methods of structural elucidation including pmr, $^{13}$Cmr, uv, and mass spectroscopy, have presently reached the stage where it is possible to assign a conclusive structure to a new and unusual aporphine alkaloid without the further assistance of chemical correlation with a known analog. Specifically, we wish to report the isolation and structure determination of srilankine (1), the only phenolic aporphine alkaloid to possess a C-4 alcoholic function known to date.

Extraction of Alseodaphne semicarpifolia Nees (Lauraceae) (9.5 kg), native to Sri Lanka,[2] with ethanol, followed by partition, and then column and thin layer chromatography, yielded 64 mg of colorless and amorphous srilankine (1), $C_{20}H_{23}NO_5$, $[\alpha]_D$ +122° (18 mg/10 ml MeOH). The uv spectrum of 1, $\lambda_{max}^{EtOH}$ 210, 277 and 301 nm (log ε 4.68, 4.35 and 4.22), indicative of a 1,2,9,10-tetrasubstituted aporphine,[3] undergoes a bathochromic shift upon addition of base ($\lambda_{max}^{EtOH-OH^-}$ 248, 279 and 300 nm; log ε 4.66, 4.58 and 4.46) similar to that shown by the C-2 phenolic aporphine base predicentrine (2).[3]

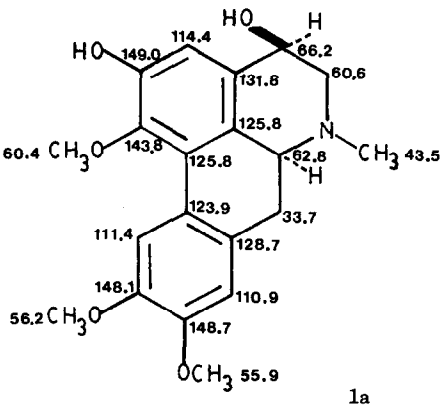
The mass spectrum of srilankine contains a molecular ion at m/e 357 (50), with a base peak at m/e 314 due to the loss of 43 mass units $(H_2C{=}N{-}CH_3)^+$ through a retro Diels-Alder cleavage. Other important ions were present at m/e 342 (18), 327 (11), 312 (15) and 254 (6). This fragmentation pattern indicates the presence in 1 of an N-methyl group, three aromatic methoxyls, one phenolic function and, additionally, one aliphatic hydroxyl group which must be located at either C-4 or C-7.

The pmr spectrum ($CDCl_3$) furnishes further support for these conclusions, and is summarized in expression 1. The two most salient features of the spectrum are the presence of a one-proton

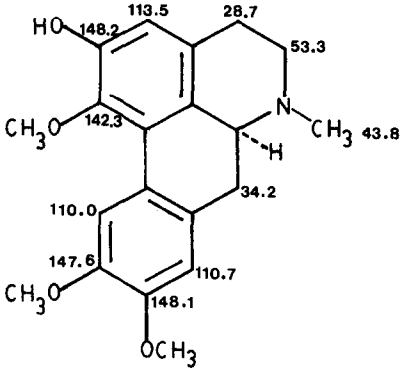
multiplet at δ4.52 (half-height width ≈ 6 Hz) assignable to a benzylic methine hydrogen gem to the alcohol function, and the unusually downfield position of the H-3 signal (δ6.95 in 1 versus δ6.65 in predicentrine (2)) possibly due to a peri relationship with an alcohol oxygen at C-4.[4]



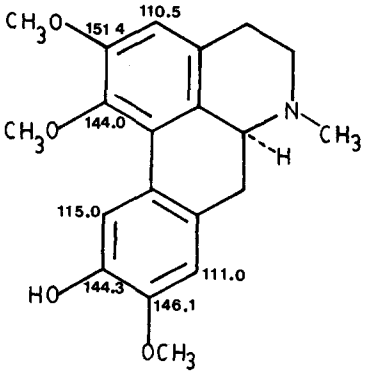

1




1a




2




3

Since unequivocally assigned $^{13}$Cmr spectra of several known aporphines have been reported,[5] this relatively new structural probe was employed in the characterization of the new aporphine alkaloid 1. Analysis of both the noise decoupled and off resonance decoupled $^{13}$Cmr spectra ($CDCl_3$) of srilankine revealed the expected signals downfield from TMS at δ33.7 (t) and 62.8 (d), for C-7 and C-6a, respectively, of an aporphine system as shown in expression 1a above. However, the usual triplet near δ29.0 was absent, so that the downfield doublet at δ66.2 corresponds to

C-4, which must bear the alcoholic function. Furthermore, the C-5 triplet is found appropriately downfield at δ60.6 due to the presence of the alcoholic function at C-4.[6,7]

While the location of a phenolic function at C-1 or C-9 of the aporphine skeleton can be easily ascertained,[3] the differentiation of a phenol at C-2 from one at C-10 is quite delicate. Through extensive model studies of aporphines,[5] the chemical shifts of both ipso-oxygenated and ipso-protonated carbons may be predicted with accuracy, thus providing a simple spectroscopic solution to this problem. In the case of predicentrine,[5] the chemical shifts for the critical ipso-oxygenated carbons C-1, C-2, C-9, and C-10, are shown in expression 2. Diagram 3, on the other hand, indicates our predicted $^{13}$Cmr chemical shifts for the rare alkaloid (+)-lirioferine,[8] which bears a phenolic function at C-10. Comparison of the experimentally determined shifts for C-1, C-2, C-9, and C-10, of srilankine (1a) with the corresponding values for predicentrine and for lirioferine (calculated) clearly supports the assignment of the phenolic function in srilankine to C-2.[9,10] This conclusion reinforces that drawn from the comparison of uv data in basic solution discussed above.

The pmr spectrum further allows an unambiguous assignment of the relative stereochemistry of 1, such that H-4 and H-6a must be in a cis relationship, since in the alternate trans arrangement H-4 is known to be located at or near δ4.93 as a doublet of doublets with $J$ = 10 Hz and $J'$ = 5.5 Hz.[4] Since srilankine is dextrorotatory, its absolute configuration is as indicated. This conclusion is consistent with the fact that all 1,2,9,10-tetrasubstituted aporphine alkaloids possess the identical chirality.

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## References


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9. The $^{13}C$ chemical shifts in ppm downfield from TMS for the aromatic carbons of srilankine have been assigned by analogy with model aporphines on which $T_1$ relaxation experiments were employed.[5]
10. As an internal check, our calculated $^{13}C$ chemical shifts for predicentrine were found to be within ± 0.2 ppm of the corresponding values determined experimentally.


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