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BHARATAMINE - A UNIQUE PROTOBERBERINE ALKALOID FROM ALANGIUM LAMARCKII THW., BIOGENETICALLY DERIVED FROM MONOTERPENOID PRECURSOR[1]

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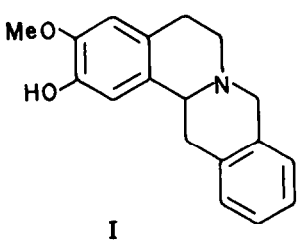
Summary: Bharatamine (I), mp 182-183°, a novel racemic protoberberine alkaloid unoxygenated at ring D and biogenetically derivable from loganin, a pathway hitherto unknown for this class of compounds, has been isolated from the seeds of Alangium lamarckii and structure established by an unequivocal synthesis.

We had earlier published the isolation and characterization[2,3] of a new class of benzo[a]pyrido[3,4-g]quinolizine bases from the seeds of Alangium lamarckii Thw.(Alangiaceae). From the same source, we now report a unique protoberberine alkaloid of immense biogenetic interest.

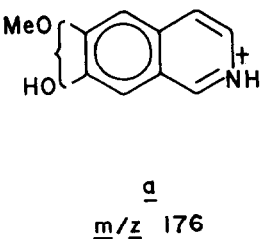
While repeating the isolation of benzopyridoquinolizines from the weakly basic fraction of the methanolic percolate of the seeds of A. lamarckii by chromatography over deactivated silica gel column, we obtained a new alkaloid in ca 0.00035% yield in the earlier fractions eluted with light petrol-chloroform (3:1). The compound, designated as bharatamine, mp 182-183°, $[\alpha]_D \pm 0°$, crystallised from light petrol-chloroform in granules. The IR (Nujol) band at 3160 (br) cm^{-1} and the UV absorptions [λ_{max}^{EtOH} (logϵ) 206 (5.08), 290 (2.77) nm; $\lambda_{max}^{0.01N\ NaOH}$ (logϵ) 208 (4.85), 295 (3.91), 310 (2.71) nm] indicated it to have a phenolic tetrahydroprotoberberine skeletal structure.

The ^1H NMR spectrum ($CDCl_3$, 100 MHz with TMS as internal standard) exhibited a three-proton singlet for one $ArOCH_3$ (δ 3.84), two one-proton singlets (δ 6.60, 6.84) for a tetrasubstituted benzene, a four-proton multiplet (δ 7.74) for a disubstituted benzene and a multiplet (δ 2.48-4.12) for nine aliphatic protons.

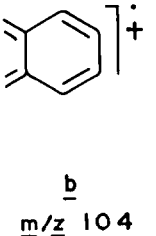
The mass spectrum (M^+ m/z 281, 86%) showed, besides the primary fragments at M-1 (100%) and M-CH_3 (15%), prominent and significant peaks at m/z 176 (46%) and 104 (60%) assignable to species a and b respectively conceivably arising by way of retro-Diels-Alder cleavage of ring C.



I



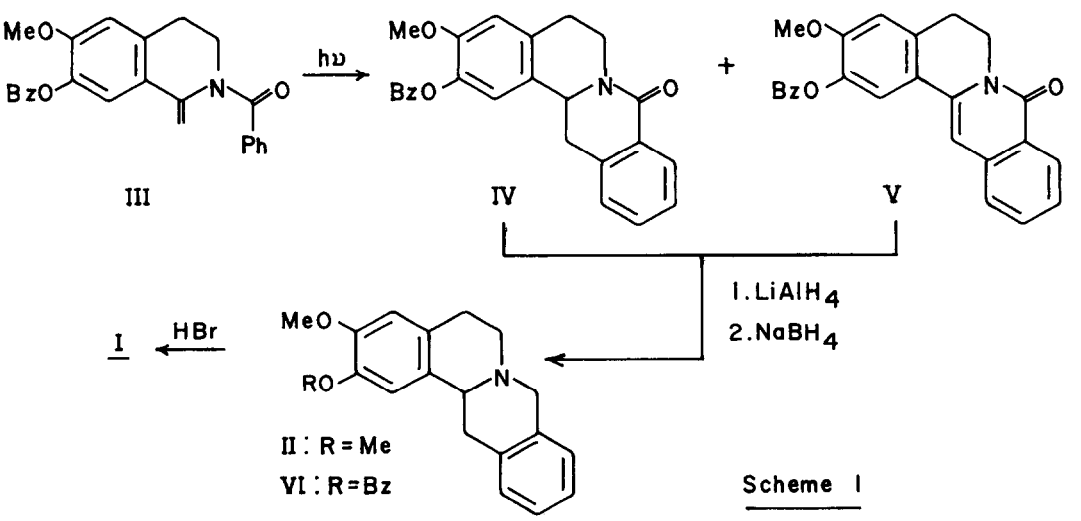
a
m/z 176



b
m/z 104

All the above data led to only two possible alternative structures, viz., 2-hydroxy-3-methoxy-5,8,13,13a-tetrahydro-6H-dibenzo[a,g]quinolizine (I) or its 2-methoxy-3-hydroxy isomer, for the compound.

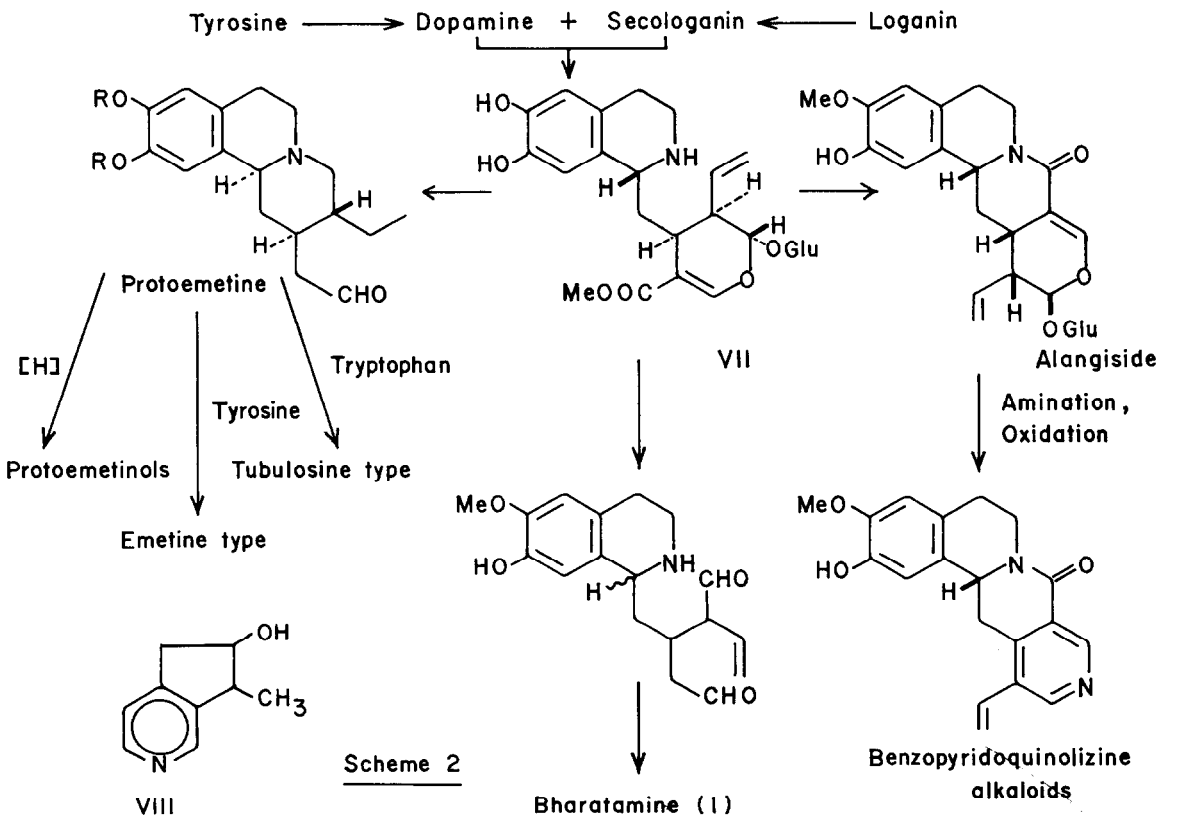
Bharatamine on treatment with diazomethane and purification through hydrochloride yielded a substance, mp 250° which proved to be exactly identical with an authentic specimen[4] of a synthetic 2,3-dimethoxyberbine (II) hydrochloride[5] by direct comparison (IR, mmp, TLC).



Scheme I

The positions of the ring A substituents could be finally established by the unequivocal synthesis (Scheme 1) of bharatamine following a known route[6-8].

To the best of our knowledge, bharatamine represents the first ring D unoxygenated member of more than a hundred protoberberine alkaloids so far known to occur in nature. Evidently, it could not have been arisen *via* the hitherto accepted biogenetic route for the protoberberines from benzylisoquinoline precursor derived from tyrosine or its equivalents[22a]. Its genesis could rather be conceived from desacetylipecoside (VII) or its equivalents, the common precursor for the cooccurring alangiside[9], benzopyridoquinolizines[2], the protoemetinols[1,10-13], emetine[14,15], psychotrine[15-18] and tubulosine[10,15,16,19-21] types, involving secologanin *via* loganin[22b] (Scheme 2). The isolation of venoterpene (VIII)[23], the rare monoterpene alkaloid hitherto encountered only in Apocynaceae species, from *A. lamarckii* is very significant. It is, however, too premature to conjecture whether protoberberines oxygenated at ring D could also be derived from monoterpenoid precursor and get oxidised at a later stage.



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REFERENCES AND NOTES

1. Part 71 of the series, 'Studies on Indian Medicinal Plants'. Part 70: E. Ali, R. K. Sinha, B. Achari, and S. C. Pakrashi, Heterocycles (communicated).
2. S. C. Pakrashi, B. Achari, E. Ali, P. P. Ghosh Dastidar, and R. K. Sinha, Tetrahedron Letters, 2667 (1980).
3. T. Naito, O. Miyata, I. Ninomiya, and S. C. Pakrashi, Heterocycles, 16, 725 (1981).
4. Kindly made available to us by Dr. Werner Meise[5].
5. W. Meise and F. Zymalkowski, Arch. Pharm., 304, 175 (1971).
6. I. Ninomiya, T. Naito, and H. Takasugi, J. Chem. Soc. Perkin I, 1720(1975).
7. G. R. Lenz, J. Org. Chem., 39, 2839 (1974).
8. Satisfactory spectroscopic data obtained for all the synthetic intermediates.
9. A. Shoeb, K. Raj, R. S. Kapil, and S. P. Popli, J. Chem. Soc. Perkin I, 1245 (1975).
10. A. R. Battersby, R. S. Kapil, D. S. Bhakuni, S. P. Popli, J. R. Merchant, and S. S. Salgar, Tetrahedron Letters, 4965 (1966).
11. J. D. Albright, J. C. Vanmeter, and L. Goldman, Lloydia, 28, 212 (1965).
12. B. Dasgupta, J. Pharm. Sci., 54, 481 (1965).
13. T. Fuji, M. Ohba, H. Suzuki, S. C. Pakrashi, and E. Ali, Heterocycles (communicated).
14. H. Budzikiewicz, S. C. Pakrashi, and H. Vorbrueggen, Tetrahedron, 20, 399 (1964); S. C. Pakrashi and P. P. Ghosh Dastidar, Indian J.Chem.,2,379(1964).
15. S. C. Pakrashi and B. Achari, Experientia, 26, 933 (1970) and refs. cited therein.
16. S. C. Pakrashi and E. Ali, Tetrahedron Letters, 2143 (1967).
17. T. Fujii, S. Yoshifuji, S. Minami, S. C. Pakrashi, and E. Ali, Heterocycles, 8, 175 (1977).
18. T. Fujii, M. Ohba, S. C. Pakrashi, and E. Ali, Tetrahedron Letters,4955(1979)
19. S. C. Pakrashi, Indian J. Chem., 2, 468 (1964).
20. A. Popelak, E. Haack, and H.Spingler, Tetrahedron Letters,1081, 5077(1966).
21. T. Fujii, M. Ohba, A. Popelak, S. C. Pakrashi, and E. Ali, Heterocycles, 14, 971 (1980).
22. M. Shamma, 'The Isoquinoline Alkaloids', Academic Press, New York, (a) p.300, (b) p.447, 1972.
23. B. Achari, E. Ali, P. P. Ghosh Dastidar, R. K. Sinha, and S. C. Pakrashi, Planta Med. (Suppl.), 5, (1980).

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