Tetrahedron Letters No. 8, pp 601 - 602, 1976. Pergamon Press. Printed in Great Britain.

SYNTHESIS OF CEPHARADIONE B [1]

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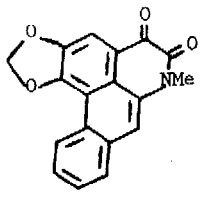
(Received in USA 17 December 1975; received in UK for publication 13 January 1976)

The recently described cepharadiones A and B (1 and 2, respectively)[2] are examples of a new sub-group of the aporphine alkaloids, namely the 4,5-dioxoaporphines. We now report a simple synthesis of cepharadione B (2) from dehydronuciferine (3).

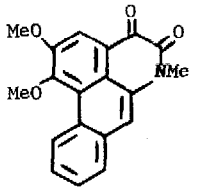
A stream of oxygen was passed through a dilute solution of dehydronuciferine in hexane, while irradiation was carried out using a Hanovia 450-watt lamp with a Vycor filter. After disappearance of the starting material, the products were divided into a basic and neutral fraction. The basic fraction afforded a 5% yield of lysicamine (4) and a 2% yield of the blue-green zwitterion 5, mp 275-277°, which is a simpler analog of corunnine (6);[3] as anticipated from corunnine chemistry, 5 is also formed in good yield (80%) by refluxing 4 with methyl iodide in acetone for one day. Silica separation (plc) of the neutral photooxidation fraction afforded (7 to 9%) cepharadione B (2) as orange needles (EtOH), mp 263-264° (lit.[2] mp 267-268). Its uv maxima (244, 273 sh, 303, 315, and 444 nm), ir carbonyl bands (5.95 and 6.05 in KBr) and the major peaks of its mass spectrum (m/e 321, 293, 278, 263, 250, 235, 207 and 179) are virtually identical to those previously reported.

The course of the photooxidation of 3 is critically dependent upon solvent polarity. In methanol solution, 3 gives much higher yields (ca. 35%) of lysicamine (4) as well as traces of zwitterion 5, but no detectible amount of cepharadione B (2). In a non-polar solvent, it would appear that oxygenation of the enamine system of 3 is sufficiently slowed down so that oxygen attack at the benzylic position of ring B becomes competitive. An analogous enzymatic oxidation of 3 to 2 is most likely involved in the biogenesis of natural 2.

Since 3 has been prepared synthetically,[4] its conversion into 2 constitutes the first formal total synthesis of a 4,5-dioxoaporphine alkaloid.



1



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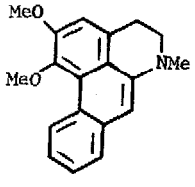

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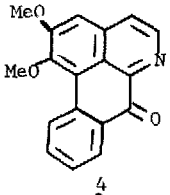

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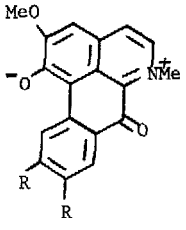

5, R = H

6, R = OMe

References

1. This work was supported by National Institutes of Health Grant CA-11445. One of us (J. M. Saá) also thanks the Fundación Juan March for a supporting fellowship.

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