

## Daphnine, a Unique Bisbenzylisoquinoline Alkaloid: X-Ray Crystal Structure of its Dihydroiodide

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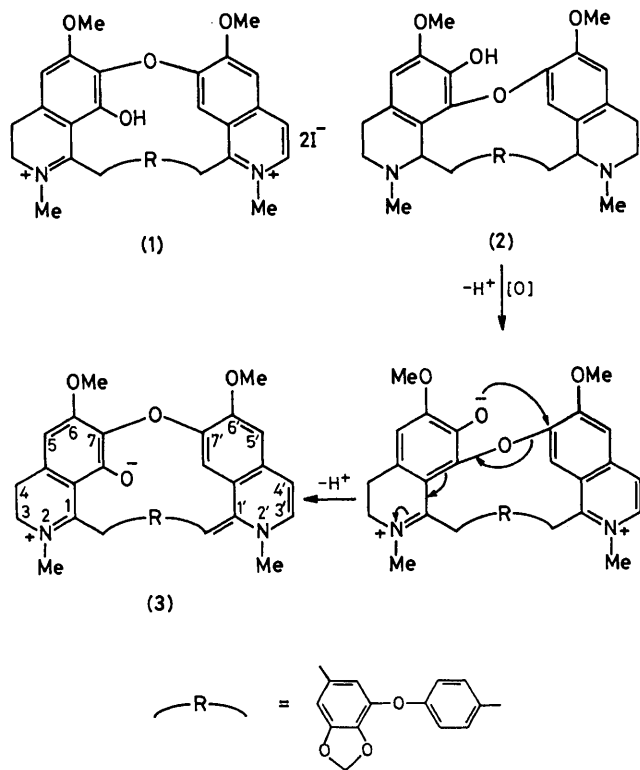
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**Summary** The structure of daphnine, a novel bisbenzylisoquinoline alkaloid with a 7-7' ether link, has been determined by X-ray crystallography of its dihydroiodide, and a possible route for its biosynthesis is proposed.

THE unique orange-yellow bisbenzylisoquinoline alkaloid daphnine (**3**) was isolated as its water-soluble dihydrochloride from bark and leaves of the north Queensland monimiacious tree *Daphnandra repandula*,<sup>1</sup> from which several other biscoclaurine alkaloids had previously been

reported.<sup>2</sup> Considerable difficulties have been encountered in the structural determination of daphnine by degradative and spectroscopic means; details of this work will be published elsewhere.



SCHEME.

Daphnine dihydroiodide (**1**), prepared from the dihydrochloride by ion exchange on an IR45(I) column, was crystallised from water, and a crystal suitable for *X*-ray analysis was sealed in a glass capillary to slow down solvent loss; fast decay was nevertheless observed in the *X*-ray flow.

*Crystal data*: monoclinic, space group  $P2_1/n$ ,  $a = 14.54(1)$ ,  $b = 13.92(1)$ ,  $c = 19.00(2)$  Å,  $\beta = 94.52(5)^\circ$ . The data were obtained from an automatic, graphite-monochromated four-circle diffractometer, using Mo- $K_\alpha$  radiation ( $\lambda = 0.7107$  Å). From 2807 measured data, only 1716 [with  $I \geq 3\sigma(I)$ ] were considered to be observed. The crystal structure was solved using the Patterson function, and refined by the full-matrix least-squares method, keeping all the atomic temperature factors isotropic except those of the iodide ions. Three water molecules and the hydroxy-hydrogen atom were located on Fourier-difference syntheses, but the methyl hydrogens could not be located. All calculable hydrogen atoms were included in the structure factors calculations, which gave a final  $R_w = \sum_w(F_o - F_c)^2/$

$\sum_w F_o^2$  of 0.095.† The molecule is depicted in the Figure, from which the central position of the hydroxy-function is evident. The crystal packing shows a complicated network of hydrogen bonds between the phenolic group, the water molecules, and the iodide ions.

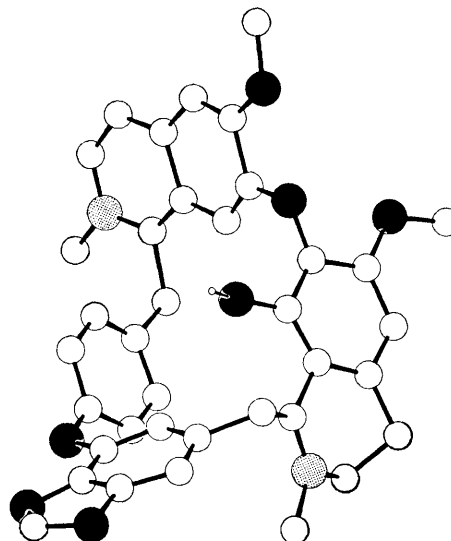


FIGURE. Perspective drawing of the daphnine dihydroiodide molecule. Black circles are oxygen atoms, shaded circles nitrogen atoms. The only hydrogen atom shown is that of the OH function.

The bisbenzylisoquinoline alkaloids so far reported number about 180,<sup>3</sup> and are considered to originate biosynthetically from two coclaurine-type units by phenolic oxidative coupling.<sup>4</sup> The wide variety of diphenyl, diphenyl ether, and benzyl phenyl ether linkages encountered in these bases is consistent with this assumption. Daphnine (**3**), however, with its unique 7-7' ether link between the two isoquinoline residues, does not fit into this simple scheme of formation from two units of coclaurine or some simple naturally occurring analogue of it. We suggest that it arises from nortenuipine<sup>2b</sup> (**2**), an alkaloid with the commonly occurring 8-8' type of diphenyl ether linkage. As outlined in the Scheme, nortenuipine could undergo dehydrogenation followed by a molecular rearrangement of the Smiles<sup>5</sup> type to give daphnine (**3**). Nortenuipine, which occurs along with daphnine in *D. repandula*, has also been postulated as the biosynthetic precursor of repanduline.<sup>2c</sup>

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† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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