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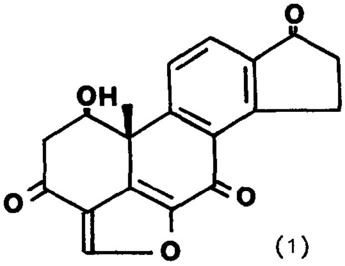
HINNULIQUINONE, A BIS-INDOLYL-2,5-DIHYDROXYBENZOQUINONE PIGMENT FROM <u>NODULISPORIUM</u> <u>HINNULEUM</u>

Margaret A.O'Leary and James R.Hanson,

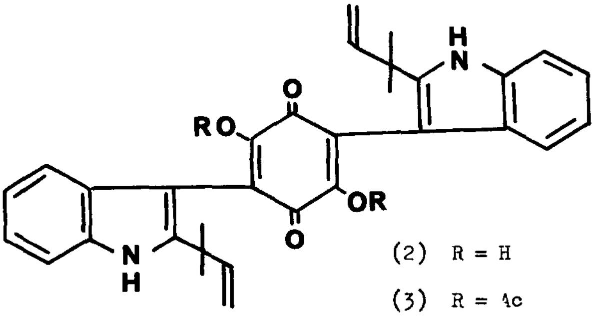
School of Molecular Sciences, University of Sussex, Brighton, Sussex, BN1 9QJ

Abstract: A pigment, hinnuliquinone, isolated from the fungus Nodulisporium hinnuleum, has been shown to be 2,5-bis-[2-(1,1-dimethyl-2-propenyl)1H-indol-3-yl-]-3,6-dihydroxy-2,5-cyclohexadiene-1,4-dione and to be biosynthesized from tryptophan and mevalonic acid.

The fungus, Nodulisporium hinnuleum (ACC 3199),produces the steroidal antibiotic demethoxyviridin (1)[1] when grown on a Raulin-Thom medium. In the course of biosynthetic studies[2] on this metabolite, we have isolated a new fungal pigment, hinnuliquinone (2). The initial vegetative mycelial growth of the fungus is white but it becomes black when sporulation occurs after approximately 10 days growth on surface culture. Extraction of the mycelium with chloroform after 20 days growth, afforded a dark-red pigment,$C_{32}H_{30}N_2O_4$, (2),m.p. 243°. The i.r. and u.v. spectra [$\nu_{max.}$ 3410,3300,1640 cm^{-1}, $\lambda_{max.}$ 280(logϵ 4.44), 288 (4.24),506(2.98)] established the hydroxy-quinonoid nature of the pigment. On reaction with acetic anhydride in pyridine, the pigment gave a diacetate (3) whilst on treatment with diazomethane it formed a dimethyl ether (4). These compounds retained N-H absorption ($\nu_{max.}$3380 cm^{-1}) in their i.r. spectra. Reductive acetylation of the dimethyl ether (4) with zinc and acetic acid gave a leuco-derivative (5) ($\lambda_{max.}$ 280 (3.32),288(3.29)).



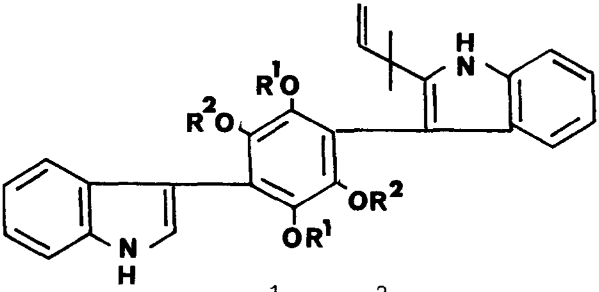
(1)



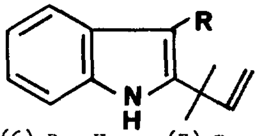
(2) R = H

(3) R = Ac

(4) R = Me



(5) R^1 = Ac, R^2 = Me.



(6) R = H, (7) R = CO_2H.

Addition of alkali to an ethanolic solution of the pigment caused the appearance of a strong band in the u.v. at 332 nm typical of a 2,5-dihydroxy-p-benzoquinone. In addition to aromatic signals (δ 7.03 - 7.42), the ^1H NMR spectrum (determined in $CDCl_3$) of the pigment and its derivatives contained singlet signals (δ 1.49) assigned to 4 -C-CH_3 groups and the ABX system typical of 2 vinyl groups (δ 5.02, 5.24 and 6.13, J 10 and 17 Hz). Oxidation of the pigment with alkaline hydrogen peroxide gave 2-(1,1-dimethylprop-2-enyl)-indole (6), identified by its ^1H NMR spectrum,[3] together with the corresponding C-3 carboxylic acid (7). The presence of a free β-indole position (δ 6.33) in (6) indicated the position of attatchment of the quinone ring. Indole-3-carboxylic acids are known to undergo ready decarboxylation.[4]

A plausible biogenesis of hinnuliquinone (2) involves transamination of tryptophan to form indolylpyruvic acid and self-condensation of two moles of the latter. This was supported in biosynthetic experiments by the incorporation of $[U-^3H]$-tryptophan (0.8%) and $[2-^{14}C]$mevalonate (0.2%) into the metabolite by N.hinnuleum. Hinnuliquinone thus joins a small group of prenylated bis-indolyl-2,5-dihydroxybenzoquinones which also includes asteriquinone[5] and cochliodinol.[6] A larger group of fungal benzoquinones are dimers of C_6 - C_3 precursors.

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