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NEW TRIHYDROXYLATED TETRAHYDROANTHRAQUINONES FROM FUNGI OF THE GENUS *DERMOCYBE*[1]

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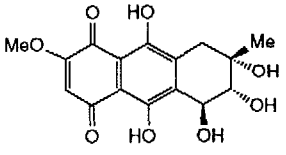
Summary - The pigments **6**, **7** and **8**, the first trihydroxylated tetrahydroanthraquinones from Basidiomycetes, have been isolated from an Australian toadstool belonging to *Dermocybe*; the absolute stereochemistry of each pigment is established by synthesis.

There is continuing interest in the synthesis and stereochemistry of tetrahydroanthraquinones such as bostrycin (**1**)[2] and the altersolanols A (**2**)[3] and B (**3**),[4] constituents of pathogenic microorganisms, and in the discovery of new members[5,6] of this small class of biologically potent[7] natural colouring matters. We earlier reported the occurrence in the toadstool *Dermocybe splendida* of the pigments **4** and **5**, which bear notable structural and stereochemical similarities with anthracyclinones of the feudomycinone class.[5] We report here the occurrence in a related toadstool of three new quinones to which structures **6**, **7** and **8** are assigned by spectroscopy and synthesis. These pigments, the only trihydroxylated tetrahydroanthraquinones to be found to date in Basidiomycetes, represent the first naturally occurring tricyclic analogues of anthracyclinones of the rhodomycinone-citromycinone group.[8]



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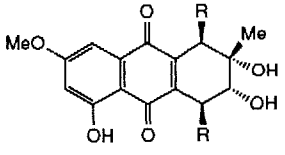
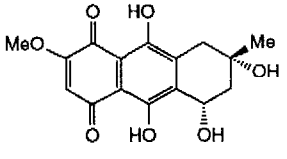


2 R=OH
3 R=H



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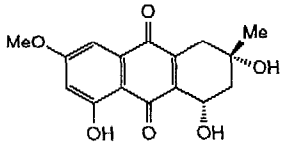

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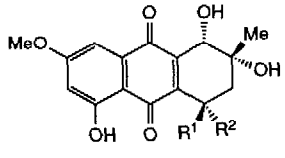
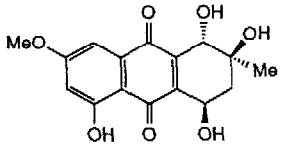


6 R^1=OH, R^2=H
7 R^1=H, R^2=OH



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Extraction of the fresh fungus[9] with ethanol followed by extensive chromatography separated three diastereoisomeric yellow pigments, $C_{16}H_{16}O_7$. The predominant isomer **6** (4.4 x 10^{-3}% fr.wt.), m.p. 72-75°C, $[\alpha]_D$ -323° (*c* 0.35, $CHCl_3$) was identified as a derivative of 5-hydroxy-1,4-naphthoquinone from the electronic spectrum (λ_{max}^{EtOH} 229, 269, 430 nm)[10] and from the appearance in the ^{1}H-n.m.r. spectrum of methoxyl and phenolic

hydroxyl singlets at δ 3.92 and 12.08, respectively, together with a pair of *meta*-coupled aromatic proton resonances at δ 6.65 and 7.19. Signals in the aliphatic proton region of the n.m.r. spectrum of **6** are summarised in Fig. 1a. The chemical shifts and couplings observed are entirely consistent with the structure, conformation, and relative stereochemistry shown.[11] Of particular note are (i) *trans*-diaxial coupling (J 9.2 Hz) between 1-H_{ax} and 2-H_{ax}, (ii) W coupling (J 1.8 Hz) between 2-H_{ax} and 3-OH (possible only if 3-OH is strongly hydrogen bonded to a *cis*-disposed hydroxyl at C-4), and (iii) the lack of W coupling between 2-H_{eq} and the methine proton at C-4.

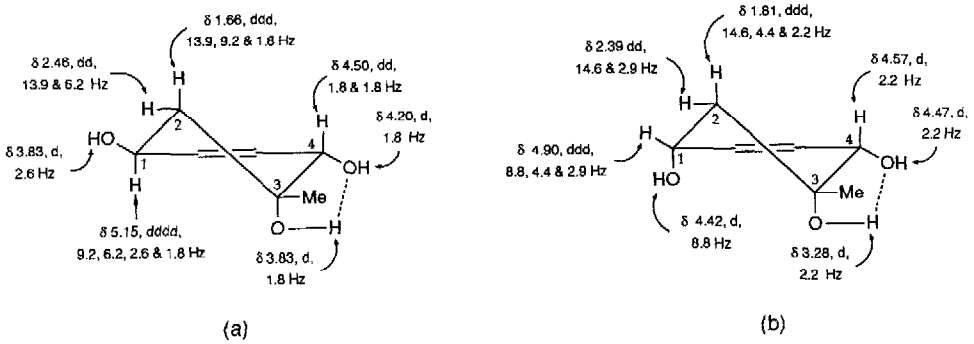
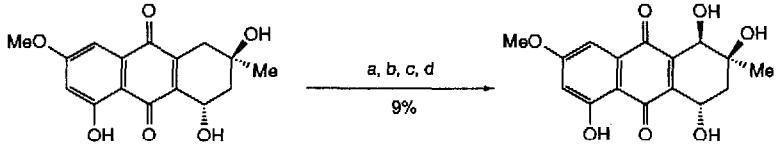


Figure 1. ^{1}H-n.m.r. data ($CDCl_3$) for aliphatic and hydroxylic protons, (a) in **6**, and (b) in **7**.

The absolute configuration of **6** was established by synthesis of its antipode **10** (Scheme 1) beginning from the natural product **9** of known structure and absolute stereochemistry.[1] The synthetic substance **10**, m.p. 72-76°C, is chromatographically and spectroscopically (*cf.* Fig. 1a) indistinguishable from the natural product **6**. Comparison of the specific rotation of **10** ($[\alpha]_D$ +330° (*c* 0.4, $CHCl_3$)) with the value cited above for **6** then establishes the 1*R*, 3*R*, 4*S* stereochemistry for the natural product.



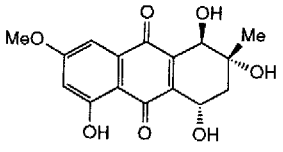
9 **10**

Scheme 1. Reagents: a. $(CF_3CO)_2O$, 0°C, 15 min; b. Br_2, hν, 45°C, 2h; c. CF_3CO_2Ag, DMSO, 30°C, 1h; d. 0.5M NaOH, 0°C, 30 min.

A second isomer **7** (2.7 x 10^{-3}% fr.wt.), m.p. 74-80°C, $[\alpha]_{365}$ +350° (*c* 0.6, $CHCl_3$) differs from **6** in the aliphatic proton region of the n.m.r. spectrum. In this case the observed couplings (Fig. 1b) define that half chair conformation shown in which the three hydroxyls in **7** occupy the same mean face of the tetrahydroaromatic ring. The absolute stereochemistry of **7** was established by synthesis from the natural product **5** of known

absolute configuration.[1] Thus, benzylic hydroxylation of 5 *via* a sequence of reactions analogous to those depicted in Scheme 1 gave a pair of tetrahydroanthraquinones, $C_{16}H_{16}O_7$, epimeric at C-4, which were separated by chromatography. One of these, m.p. 75-82°C, $[\alpha]_{365}$ +520° (*c* 0.4, $CHCl_3$) proved indistinguishable (*cf.* Fig. 1b) from the natural product **7**. Furthermore, the natural and synthetic materials possess a specific rotation of the same sign and of a similar order of magnitude[12] thus establishing 1*S*, 3*R*, 4*S* stereochemistry for the fungal metabolite.

The second tetrahydroanthraquinone **11**, m.p. 93-98°C, obtained upon hydroxylation of 5 exhibits identical spectroscopic properties with the third, and least abundant, pigment obtained from the toadstool extractives. That **11** represents the antipode of the natural product **8** (1.0 x 10^{-3}% fr. wt.), m.p. 93-98°C, was evident from comparison of the chiroptical properties ($[\alpha]_D^{CHCl_3}$ **8** -152°, **11** +157°) which establishes 1*R*, 3*S*, 4*S* stereochemistry for **8**.



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In view of the importance of anthraquinone and pre-anthraquinone pigments to the developing taxonomy of *Dermocybe* and its allies in the southern hemisphere[13] the isolation of these more highly hydroxylated analogues **6**, **7** and **8** of **5** and **9** will no doubt prove significant. Tests are currently underway to assay the biological activity of the compounds described herein and the results will be reported in a full paper.

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9. Fungi were collected during June, 1985 from native forest close to Marysville, Victoria. Voucher specimens of the fungi dicussed here are lodged in the herbarium of the Royal Botanic Garden, Edinburgh, under accession number WAT 21567.
10. R. H. Thomson, 'Naturally Occurring Quinones', 3rd Edition, Chapman and Hall, London, 1987.
11. All assignments are supported by proton decoupling and D_2O exchange experiments.
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