Tetrahedron Letters,Vol.26,No.21,pp 2593-2596,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain ©1985 Pergamon Press Ltd.

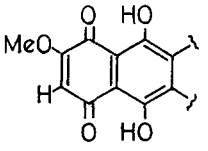
NEW TETRAHYDROANTHRAQUINONES FROM THE GENUS *CORTINARIUS*

Melvyn Gill* and Richard J. Strauch
Department of Organic Chemistry, University of Melbourne, Parkville,
Victoria 3052, Australia.

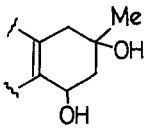
Summary - Austrocortirubin (1a) and austrocortilutein (2), the first hydroxylated tetrahydroanthraquinones from Basidiomycetes, have been isolated from an Australian toadstool belonging to the subgenus *Dermocybe* of *Cortinarius*.

Hydroxylated anthraquinones occur in great variety in toadstools of the genus *Cortinarius* where they are responsible for the bright yellow, red or green colours of fruit bodies.[1,2] Due to Steglich[3] many of these quinones have been identified[1-3] and now occupy an important position in the taxonomy of the group. Thus, studies of their distribution among British,[4] European,[5] N.[6] and S. American[7] *Cortinarius* have demonstrated the possibility of differentiating infrageneric taxa conveniently by monitoring pigment content and thus alleviating nomenclatural confusion which exists in *Dermocybe*.[4] In view of the importance of pigments to the systematics of *Cortinarius* and the lack of chemical knowledge of Australian members we examined the fruit bodies of a red *Cortinarius* toadstool* collected in Victoria, Australia, and report here the presence of two novel hydroxylated tetrahydroanthraquinones, 1a and 2. We also note our failure to detect any of the familiar *Cortinarius* anthraquinones[1-3] in this species.[8]

Extraction (EtOH) of the fresh fungus followed by chromatography gave two principal pigments.[9] A red metabolite, 1a (4.1 × 10^{-2}% fr.wt), $C_{16}H_{16}O_7$, m.p. 193-195°, $[\alpha]_D^{20}$ +109±20° (*c* 0.824, EtOH), here named austrocortirubin, was identified as a naphthazarin derivative from its electronic (λ_{max}^{EtOH} 302, 475 sh., 504 and 541 nm; *cf* bostrycin, 6,[10]) and infra red (ν_{max}^{KBr} 1600 cm^{-1}, C=O) spectra. Its ^1H n.m.r. spectrum ($CDCl_3$) showed, in addition to a MeO singlet at δ3.95 and singlets at δ6.21, 12.69 and 13.32 characteristic of the substructure I,[11] a singlet at δ1.48 due to a C-Me group and an aliphatic proton couplet (*Table*) corresponding to partial structure II. The vicinal coupling constants between 1-H and the two protons at C2 (*Table*) preclude any *trans*-axial relationship[12] and place the OH group at C1 in an axial configuration in the probable preferred conformation 3 (no configuration at C3 yet implied) of the cyclohexene ring of austrocortirubin.[13]



I



II

* This fungus is placed in the subgenus *Dermocybe* close to *C. puniceus* Orton and *C. sanguineus* (Wulf. ex. Fr.) Fr. (R. Watling, personal communication). Voucher specimens are held in the herbariums of the New South Wales Department of Agriculture, Rydalmere, N.S.W., and the Royal Botanic Gardens, Edinburgh.

The connectivity between substructures I and II followed treatment of the pigment with Ac_2O/H_2SO_4 whereupon the diacetate 4, m.p. 245-252° (lit.[14] 242-248°), of 1,4-dihydroxy-2-methoxy-7-methylanthraquinone[15] was obtained. Finally, with 2,2-dimethoxypropane (CH_2Cl_2, *p*-TSA, rt) austrocortirubin afforded an acetonide, $C_{19}H_{20}O_7$, m.p. 264-268°, $[\alpha]_D^{20}$ +205±10° (*c* 0.308, $CHCl_3$), which establishes the (relative) configuration of the stereocentres in this pigment as depicted in 1a.

Austrocortirubin might be expected to exist in solution as an equilibrium mixture of tautomers 1a and 1b. However, comparison of the chemical shifts in $CDCl_3$ of the H-7 resonance of 1 (δ6.21) with the shifts of analogous protons located in benzenoid (typically δ6.6-6.7) and in quinonoid (typically δ6.1-6.2) rings in a range of 2-alkoxynaphthazarins[16] strongly suggests that austrocortirubin exists predominantly as the tautomer 1a. Notably, in d_6-DMSO the H-7 resonance of 1a moves to δ6.45, precisely the shift of the corresponding proton in the spectrum of bostrycin (6).[16,17]

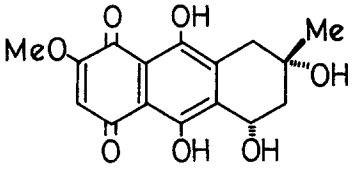
A yellow pigment (2.2 × 10^{-2}%), $C_{16}H_{16}O_6$, m.p. 183-185°, $[\alpha]_D^{20}$ +62±10° (*c* 0.546, EtOH), austrocortilutein, exhibits an electronic spectrum (λ_{max}^{EtOH} 269, 275 sh., and 428 nm) indicative of a 5-hydroxy-1,4-naphthoquinone chromophore while in the ^1H n.m.r. spectrum a pair of *meta*-coupled aromatic resonances (δ6.62 and 7.14, *J*=1.9 Hz) and a single low field signal (δ12.14) replace the quinonoid proton singlet and the two OH resonances, respectively, in the spectrum of 1a. The aliphatic proton region (*Table*) reveals the same substructure II as occurs in austrocortirubin and this, together with the isolation of the monoacetate 5, m.p. 175-178° (lit.[18] 171-173°) on exposure to Ac_2O/H_2SO_4 and the smooth formation of an acetonide, $C_{19}H_{20}O_6$, m.p. 192-195°, establishes structure 2 for the yellow pigment.

Only five hydroxylated tetrahydroanthraquinones have been isolated previously and, hitherto, these have been restricted in distribution to a group of predacious, ascomycetous conidial fungi.[1] The pigments 1a and 2 represent therefore the first examples of this group of potent[19] quinones to be isolated from higher fungi and are the only ones which possess the *cis*-1,3 arrangement of OH groups in the hydroaromatic ring. Thus, they differ in relative stereochemistry from bostrycin (6) and from altersolanol-A (7),[20] the two known tetrahydroanthraquinones with an OH group both at C1 and C3, and correspond more closely to the anthracyclinone class, *eg.* feudomycin-C (8).[21]

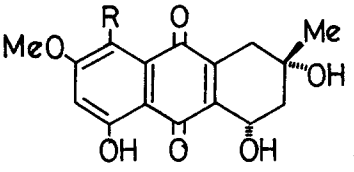
Our isolation of 1a and 2 from *Cortinarius* and the absence of otherwise widespread anthraquinones suggest a new branch in those biosynthetic pathways leading from octaketide precursors to pigments in this, and perhaps other, Australian cortinares. It is feasible that atrochrysone (9), a metabolite of *C. atrovirens*[2] and the precursor of all anthraquinones of the emodin group isolated from *Cortinarius*,[1,2] could be the common intermediate after which the 'old' and 'new' pathways diverge.

	1-H	2-H_α	2-H_β	4-H_α	4-H_β
1a	5.20 (m)	2.35 (ddd, 14.7, 1.8, 1.8)	1.88 (dd, 14.7, 4.8)	3.19 (dd, 19.1, 1.8)	2.59 (d, 19.1)
2	4.87 (m)	2.29 (ddd, 14.7, 1.8, 1.8)	1.79 (dd, 14.7, 4.8)	3.01 (dd, 19.8, 1.8)	2.37 (dd, 19.8, 1.1)

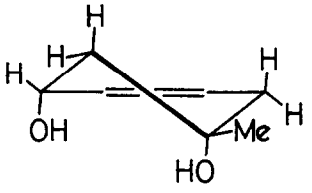
Table Chemical Shifts (δ), multiplicities and coupling constants (*J*, Hz) of protons in hydroaromatic rings of quinones 1a and 2.



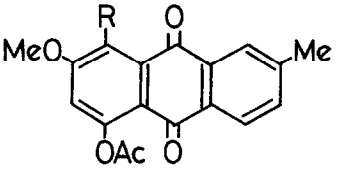
1a†



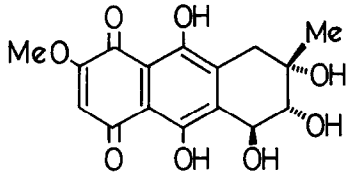
1b R = OH
2† R = H



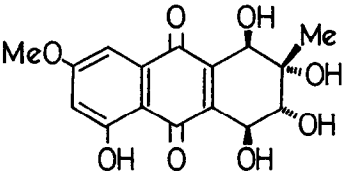
3



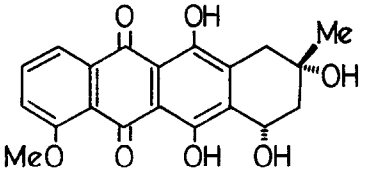
4 R = OAc
5 R = H



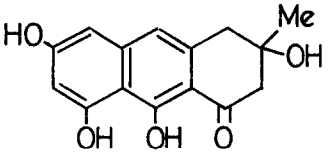
6[17]



7



8



9

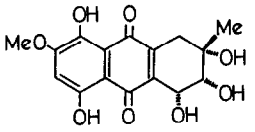
† The absolute configurations of 1a and 2 are not known; the (1*S*, 3*S*) enantiomer is depicted here for comparison with quinones 6, 7 and 8.

Studies on the absolute configuration of 1a and 2, and on their synthesis and biological activity are continuing and will be reported in due course.

Acknowledgements We thank Drs R. Watling (Edinburgh) and J. Walker (Rydalmere) for their efforts towards classification, and the Australian Research Grants Scheme for financial support.

References and Footnotes

1. W.B. Turner and D.C. Aldridge, 'Fungal Metabolites II', 1983, pp.140-156. Academic Press, London.
2. W. Steglich in 'Pigments in Plants', F.-C. Ezygan (ed.), 2nd. Ed., 1980, pp.394-395. Gustav Fischer, Stuttgart.
3. See for example: W. Steglich *et al.*, *Tetrahedron Lett.*, 1966, 3077; *Chem. Ber.*, 1972, *105*, 2928; *ibid.*, 1972, *105*, 2922; *Z. Naturforsh.*, 1972, *27b*, 1009; *ibid.*, 1978, *33c*, 294; *Phytochem.*, 1972, *11*, 3299.
4. C.B.M. Kidd, B. Caddy, J. Robertson, I.R. Tebbett and R. Watling, *Trans. Brit. Mycol. Soc.*, in press.
5. I. Gruber, *Z. Pilzk.*, 1970, *36*, 95; and G. Keller, *Sydowia*, 1982, *35*, 110.
6. G. Keller and J.F. Ammirati, *Mycotaxon*, 1983, *18*, 357.
7. I. Gruber, *Beihefte zur Nova Hedwigia*, 1975, *52*, 524.
8. M.A. Archard, M. Gill and R. J. Strauch, *Phytochem.*, submitted.
9. All compounds gave satisfactory combustion analysis.
10. T. Noda, T. Take, T. Watanabe and J. Abe, *Tetrahedron*, 1970, *26*, 1339.
11. R.E. Moore and P.J. Scheuer, *J. Org. Chem.*, 1966, *31*, 3272.
12. L.M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry', 2nd. Ed., 1969, pp.280-304, Pergamon Press, Oxford.
13. A.M. Becker, R.W. Rickards, K.J. Schmalzl, and H.C. Yick, *J. Antibiotics*, 1978, *31*, 324.
14. T.R. Kelly, *Tetrahedron Lett.*, 1978, 1387.
15. We are grateful to Professor T.R. Kelly for a sample of this quinone.
16. T.R. Kelly, J.K. Saha and R.R. Whittle, *J. Org. Chem.*, in press. We thank Professor Kelly for this paper prior to publication.
17. The original structure (i) for bostrycin (ref. 10) has been revised (ref. 16).
18. A. Stoessl, *Can. J. Chem.*, 1969, *47*, 777. We thank Dr Stoessl for authentic materials.
19. Members exhibit antibacterial and phytotoxic properties (R. Charudattan and K.V. Rao, *Appl. and Environ. Microbiol.*, 1982, *43*, 846) and are antiprotazoal and cytotoxic (ref. 13).
20. A. Stoessl, *Can. J. Chem.*, 1969, *47*, 767.
21. O. Toshikazu, Y. Marsuzawa, K. Koyoshima, A. Yoshimoto, H. Naganawa, T. Takeuchi, and H. Umezawa, *J. Antibiotics*, 1981, *34*, 783.



i

(Received in UK 15 March 1985)