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THE STRUCTURE OF BOSTRYCOIDIN, A β-AZA-ANTHRAQUINONE FROM *Fusarium solani* D_2 PURPLE*

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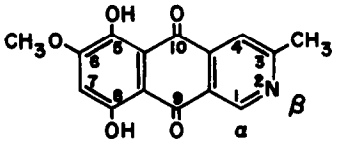
The chemistry (1) and antibiotic properties (2) of bostrycoidin were investigated by Cajori, Hamilton and co-workers who isolated this pigment from *Fusarium bostrycoides*. They suggested the molecular formula $C_{18}H_{14}O_7$ and concluded bostrycoidin was a substituted napthazarin with one methoxyl and one methyl group. We isolated 60 mg. of the pigment from *F. solani* D_2 purple (3) and found the molecular formula to be $C_{15}H_{11}NO_5$ (4). We propose structure I for bostrycoidin on the basis of its



I

ultraviolet, visible, infrared and proton magnetic resonance spectra, and biogenetic considerations.

Bostrycoidin is easily decolorized by sodium dithionite

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* Fungal Metabolites - II. For paper I in this series see G. P. Arsenault, Can. J. Chem. 43, in press (1965). Presented in part at the 48th Canadian Chemical Conference, Montreal, Quebec, May 31-June 2, 1965.

and the reduced product is readily oxidized by air, suggesting that the metabolite is a quinone. The visible spectrum of bostrycoidin is similar to that of substituted naphthazarins (1) and quinizarins. The infrared evidence supports the presence of the elements of naphthazarin in bostrycoidin. The spectrum of the metabolite (KBr pellet) showed carbonyl absorption at 1615 cm.$^{-1}$ and no hydroxyl absorption above 3100 cm.$^{-1}$. By contrast, bostrycoidin diacetate ($CHCl_3$) showed $\nu_{C=O}$ (phenolic acetate) at 1775 cm.$^{-1}$ and $\nu_{C=O}$ (quinone) at 1682 and 1667 cm.$^{-1}$. Thus each quinone carbonyl is intramolecularly hydrogen bonded to a phenolic hydroxyl. No N-H stretching vibration was present in the infrared spectra of bostrycoidin and its diacetate.

A comparison of the proton magnetic resonance spectra (Table I) of bostrycoidin and its diacetate with model compounds indicates bostrycoidin is a β-aza-anthraquinone substituted with the following groups: one methyl, one methoxyl and two strongly hydrogen-bonded hydroxyls. The chemical shift and width of the singlets at τ 0.53 and τ 2.09 show that they are due to the resonance of 1,4-related protons in the heteroaromatic ring. The upfield shift of these singlets upon acetylation (0.17 and 0.15 p.p.m., respectively) supports this assignment. The model compounds (Table I) show that aromatic protons in the same ring as the 5,8-dihydroxy substituents are shifted downfield upon acetylation while those in the opposite ring are shifted upfield. Furthermore, the shift upfield is less than 0.10 p.p.m. if the aromatic protons are β and 0.15 p.p.m. or more if they are α. The similarity

of the ultraviolet and visible spectra of bostrycoidin and 5,8-dihydroxy-2-aza-9,10-anthraquinone provides strong support for our structural assignment. The chemical shift (Table I) of the methyl group suggests that it be placed in position 3 rather than 6 or 7.

The above evidence allows us to place the methoxyl group in either position 6 or 7. However, we isolated javanicin (5), fusarubin (6) and solaniol (7), as well as bostrycoidin, from F. solani D_2 purple. Since the first three compounds have well-established structures in which the methoxyl substituent on the naphthazarin ring is in a position equivalent to position 6 in a 2-aza-anthraquinone, we use this circumstantial evidence to assign the methoxyl group to position 6 and propose structure I for bostrycoidin. Javanicin was shown to be derived by the acetate-malonate pathway and the methyl group directly attached to the naphthazarin ring to be derived by reduction of a carboxyl group (8). This implies the formation of an intermediate aldehyde (8) which, after introduction of nitrogen, ring formation and aromatization, could lead to bostrycoidin.

Bostrycoidin takes a place alongside phomazarin (9) in the rather select group of aza-anthraquinones and is the first known naturally-occurring 2-aza-anthraquinone.

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TABLE I

PMR Data - Bostrycoidin and Related Compounds[a]

	Compound	Chemical Shift (τ) of Substituents on Carbon No. 1	2	3	4	5[b]	6	7	8[b]
I	Bostrycoidin	0.53s[c]	---	7.22s	2.09s[c]	-3.38s	6.00s	3.30s	-3.10s
II	Diacetate of I	0.70s[c]	---	7.27s[d]	2.24s[c]	7.53s	6.05s	3.02s	7.53s
III	5,8-Dihydroxy-6-methoxy-9,10-anthraquinone[e]	1.64q[f]	2.20q[f]	2.20q[f]	1.64q[f]	-3.52s	5.98s	3.28s	-3.42s
IV	Diacetate of III	1.83q[f]	2.30q[f]	2.30q[f]	1.83q[f]	7.53s	6.07s	3.07s	7.55s
V	5,8-Dihydroxy-2-aza-9,10-anthraquinone[g]	0.37s[c]	---	0.87d[h]	1.89d[h]	-2.73s	2.65s	2.65s	-2.60s
VI	Diacetate of V	0.60s[c]	---	0.97d[h]	2.11d[h]	7.57s	2.57s	2.57s	7.57s
VII	5,8-Dihydroxy-1-aza-9,10-anthraquinone[g]	---	0.92q[i]	2.27q[j]	1.36q[k]	-2.77s	2.65s	2.65s	-2.55s
VIII	Diacetate of VII	---	0.95q[i]	2.33q[j]	1.51q[k]	7.50s	2.53s	2.53s	7.55s

[a] The spectra were taken at room temperature (acetates) and 60° (compounds with free hydroxyls) in $CDCl_3$ solution on a Varian A-60 spectrometer; the observed intensity of signals is in agreement with the assignments which were made using first order rules; s=singlet, d=doublet, q=quartet.

[b] PMR assignments to substituents on carbons 5 and 8 may be reversed. [c] Broad peak.

[d] Methyl signal of 3-methyl-*iso*-quinoline at τ 7.32.

[e] C. Graebe and H. Bernhard, Liebigs Ann. 349, 222 (1906). [f] J ≃ 3 and 6 c.p.s.

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[h] J ≃ 5 c.p.s. [i] J ≃ 2 and 5 c.p.s. [j] J ≃ 5 and 8 c.p.s. [k] J ≃ 2 and 8 c.p.s.

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