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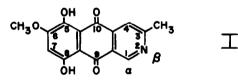
## THE STRUCTURE OF BOSTRYCOIDIN,

## A B-AZA-ANTHRAQUINONE FROM <u>Fusarium</u> solani D<sub>2</sub> 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 <u>Fusarium</u> <u>bostrycoides</u>. 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 <u>F. solani</u> D<sub>2</sub> 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



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

Bostrycoidin is easily decolorized by sodium dithionite

<sup>\*</sup> Fungal Metabolites - II. For paper I in this series see G. P. Arsenault, <u>Can. J. Chem. 43</u>, 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.<sup>-1</sup> and no hydroxyl absorption above 3100 cm.<sup>-1</sup>. By contrast, bostrycoidin diacetate (CHCl<sub>3</sub>) showed  $v_{c=0}$  (phenolic acetate) at 1775 cm.<sup>-1</sup> and  $v_{c=0}$  (quinone) at 1682 and 1667 cm.<sup>-1</sup>. 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  $\beta$ -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  $\tau$  0.53 and  $\tau$  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  $\beta$  and 0.15 p.p.m. or more if they are  $\alpha$ . 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 <u>F. solani</u>  $D_2$  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.

<u>Acknowledgments</u>: My thanks are due to Prof. F. A. Cajori for a sample of bostrycoidin, to Dr. D. Brewer for culturing <u>F. solani</u> D<sub>2</sub> purple, and to Dr. L. C. Vining for stimulating discussions.

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I III III VV VVIII VVIII VVIII P P M P M C V V V V V V V V V V V V V V V V V V	compound Bostrycoidin Diacetate of I 5,8-Dihydroxy-6-met 9,10-anthraquinone <sup>6</sup> Diacetate of III 5,8-Dihydroxy-2-aza anthraquinoneg Diacetate of VII 5,8-Dihydroxy-1-aza anthraquinoneg Diacetate of VII Spectra were taken cDC13 solution on a eement with the assi uartet. Ayl signal of 3-meth Graebe and H. Bernha Niementowski, J. Ftd 7 (1928). 5 c.p.s. i J	a - Bost 1 1. 0.53sc 0.70sc 0.70sc 1.64qf 1.83qf 1.83qf 0.60sc 0.60sc 0.60sc ampera * on car juinolin d R. Jo 5 c.p.s	TABLE I TABLE I TYCOIDIN and Chemical Shi 7.2 7.2 2.30 $q^f$ 2.3 2.30 $q^f$ 2.3 2.32 2.32 2.32 2.32 2.32 2.32 2.32	PMR Data - Bostrycoidin and Related Compounds <sup>a</sup> $I_{a} = Bostrycoidin and Related Compoundsa = Chemical Shift (r) of Substituents on Carbon No.b I_{a} = Chemical Shift (r) of Substituents on Carbon No.b 0.53sc 7.22s 2.09sc -3.38s 6.00s 3.30s -3.10s 0.70sc 7.22sd 2.24sc 7.53s 6.05s 3.02s 7.55s -9.10- 1.64qf 2.20qf 1.64qf -3.52s 5.98s 3.28s -3.42s 1.83qf 2.30qf 1.83qf 7.53s 6.07s 3.07s 7.55s -9.10- 0.37sc 0.87dh 1.89dh -2.73s 2.65s 2.65s -2.60s 0.60sc 0.97dh 2.11dh 7.57s 2.57s 2.55s 7.55s -9.10- 0.60sc 0.97dh 2.11dh 7.57s 2.57s 2.55s 2.55s -9.10- 0.56qf 2.23qf 1.54qk 2.77s 2.55s 2.55s 2.55s -9.10 0.95qf 2.33qf 1.51qk 7.50s 2.53s 2.55s 7.55s at room temperature (acetates) and 60° (compounds with free hydroxy Varian A-60 spectrometer; the observed intensity of signals is in guments which were made using first order rules; s=singlet, d=doub. tituents on carbons 5 and 8 may be reversed. C Broad pea v1-ieobigs Ann: 349, 222 (1906). f J = 3 and 6 c.p.s hing and R. Joszt, Boczniki Chem 2, 218 (1927); Chem Abstr. 2, * 2 and 5 c.p.s. J J = 5 and 8 c.p.s. k J = 2 and 8 c.p.s.$	I and Related Com 3 $4$ $47.22s 2.09s^{C}7.27s^{d} 2.24s^{C}7.27s^{d} 2.24s^{C}2.30q^{f} 1.89q^{h}0.97d^{h} 1.89d^{h}0.97d^{h} 2.11d^{h}0.97d^{h} 2.11d^{h}1.51q^{k}2.33q^{j} 1.51q^{k}2.33q^{j} 2.196^{0}32.$ $32.$ $32.$ $32.$ $32.$ $32.$ $33.$ $32$	and Related Compounds <sup>a</sup> Shift (r) of Substituents on Carbon No. ${}_{3}^{b}$ 7.22s 2.09s <sup>C</sup> -3.38s 6.00s 3.30s -3.10s 7.27s <sup>d</sup> 2.24s <sup>C</sup> 7.53s 6.05s 3.02s 7.53s 2.20q <sup>f</sup> 1.64q <sup>f</sup> -3.52s 5.98s 3.28s -3.42s 2.30q <sup>f</sup> 1.83q <sup>f</sup> 7.53s 6.07s 3.07s 7.55s 0.97d <sup>h</sup> 1.89d <sup>h</sup> -2.73s 2.65s 2.65s -2.60s 0.97d <sup>h</sup> 2.11d <sup>h</sup> 7.57s 2.57s 2.55s -2.55s 2.33q <sup>j</sup> 1.36q <sup>k</sup> -2.77s 2.557 2.55s -2.55s 2.33q <sup>j</sup> 1.51q <sup>k</sup> 7.50s 2.553 2.55s -2.55s 2.33q <sup>j</sup> 1.51q <sup>k</sup> 7.50s 2.53s 2.65s -2.55s 2.33q <sup>j</sup> 1.51q <sup>k</sup> 7.50s 2.53s 2.55s -2.55s 2.33q <sup>j</sup> 2.1160 <sup>k</sup> -2.77s 2.553 2.55s -2.55s 2.33q <sup>j</sup> 2.510 <sup>k</sup> -2.77s 2.553 2.55s -2.55s 2.33q <sup>j</sup> 2.510 <sup>k</sup> -2.77s 2.553 2.555 -2.555 2.33q <sup>j</sup> 2.510 <sup>k</sup> -2.77s 2.553 2.555 -2.555 2.100 <sup>k</sup> -2.77s 2.553 2.553 2.555 2.100 <sup>k</sup> -2.755 -2.53 2.553 2.555 2.100 <sup>k</sup> -2.755 -2.53 2.553 2.555 2.100 <sup>k</sup> -2.755 -2.553 2.555 2.100 <sup>k</sup> -2.755 -2.553 2.553 2.555 2.100 <sup>k</sup> -2.755 -2.755 2.100 <sup>k</sup> -2.755 -2.553 2.553 2.555 2.100 <sup>k</sup> -2.755 -2.553 2.555 2.100 <sup>k</sup> -2.755 -2.555 2.100 <sup>k</sup> -2.755 -2.555 2.257 -2.555 2.27 <sup>k</sup> -2.755 2.100 <sup>k</sup> -2.755 -2.555 2.200 <sup>k</sup> -2.755 2.100 <sup>k</sup> -2.755 2.200 <sup>k</sup> -2.755 2.200 <sup>k</sup> -2.755 2.200 <sup>k</sup> -2.755 2.200 <sup>k</sup> -2.555 2.200 <sup>k</sup> -2.755 2.200 <sup>k</sup> -2.555 2.200 <sup>k</sup> -2.555 2.200 <sup>k</sup> -2.555 2.200 <sup>k</sup> -2.555 2.200 <sup>k</sup> -2.555	<pre>bunds<sup>a</sup> stituents on C 5,51 3.538 6.008 7.538 6.078 7.538 6.078 7.578 2.658 7.578 2.658 7.508 2.538 compounds with itensity of sig t d i (1927); <u>f J ~ i</u> sed. </pre>	arbon Nc / 3.30s - 3.02s - 3.02s - 3.07s - 2.55s - 3 ad 6 2 and 7 2 and 7 3 and 7 3 and 7 3 and 7 3 and 7 3 and 7 3 and 6 3 and 6 3 and 7 3 an	<pre>s on Carbon No. 6 7 8 8 6.00s 3.30s -3.10s 6.05s 3.02s 7.53s 5.98s 3.28s -3.42s 6.07s 3.07s 7.55s 6.07s 3.07s 7.55s 2.65s 2.65s -2.60s 2.65s 2.65s -2.56s 2.53s 7.55s 2.53s 2.53s 7.55s 2.53s 2.53s 7.55s seinglet, d=doublet, of signals is in s=singlet, d=doublet, f J = 3 and 6 c.p.s. f J = 2 and 8 c.p.s.</pre>
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	PMR Dat	a - Bost	rycoidin	and Rel	ated Com	pounds <sup>a</sup>			
	Compound	- <b>- -</b>	Chemical Z	Shift ( 3	τ) of Su	bstituen 5b	ts on C 6	arbon N	o. <sub>8</sub> ک
г	Bostrycoidin	0.53s <sup>c</sup>	1	7.22s		-3,385	6.00s	3.30s	-3.10s
II	Diacetate of I	0.70s <sup>c</sup>	1	7.27s <sup>d</sup>		7.538	6.05s		
III	5,8-Dihydroxy-6-methoxy- 9,10-anthraquinone <sup>e</sup>	1.64g <sup>f</sup>	2.20g <sup>f</sup>	2.209 <sup>f</sup>	1.64g <sup>f</sup>	-3.52s	5 <b>.</b> 98s		-3.42s
ΛI	Diacetate of III	1.83g <sup>f</sup>	$2.30q^{f}$	2.30g <sup>f</sup>	1.83q <sup>f</sup>	7.53s	6.07s		
٨	5, 8-Dihydroxy-2-aza-9,10- anthraquinone <sup>g</sup>	0.37s <sup>c</sup>		0.87d <sup>h</sup>	1.89d <sup>h</sup>	-2.73s	2.65s	2.65s	-2.60s
ΙΛ	Diacetate of V	0.60s <sup>c</sup>		0.97d <sup>h</sup>	2.11d <sup>h</sup>		2.57s		
IIV	5,8-Dihydroxy-1-aza-9,10- anthraquinone <sup>g</sup>		0.92g <sup>1</sup>	2.27g <sup>j</sup>	1.36g <sup>k</sup>	-2.77s	2.655	2.65s	-2.558
VIII			0.95g <sup>1</sup>	2.33q <sup>j</sup>	$1.51q^{k}$	7.50s	2.53s	2.53s	7.55s
	<pre>spectra were taken at room CDCl<sub>3</sub> solution on a Varian reement with the assignments juartet.</pre>	tempera A-60 spe which w	ture (ac ctromete ere made	etates) r; the o using f	and 60° bserved irst ord	(compoun intensit er rules	ds with y of si ; s=sin	free h gnals i glet, d	ıydroxyls) s in =doublet,
iMg d	R assignments to substituent	s on car	oons 5 a	nd 8 may	be reve	rsed.		c Bro	ad peak.
d Met	thyl signal of 3-methyl- <u>iso</u> -	guinolin,	e at r 7	.32.					
	Graebe and H. Bernhard, Lie	oigs Ann	. 349, 2	22 (1906			њ С ≈	3 and 6	c.p.s.
	Niementowski, J. Frühling a. 57 (1928)	d R. Jo	szt, <u>Roc</u>	zniki Ch	em. 2, 2	18 (1927	); Chem	· Abstr	. 22,
h h h		5 c.p.s		j5 5 ≃ 5	and 8 c.	p.s.	ъ Ч	≃ 2 and	l 8 c.p.s.
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TABLE I

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