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STRUCTURE OF BOSTRYCIN

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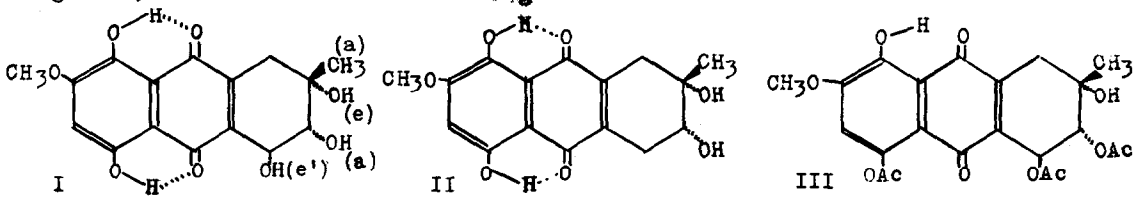
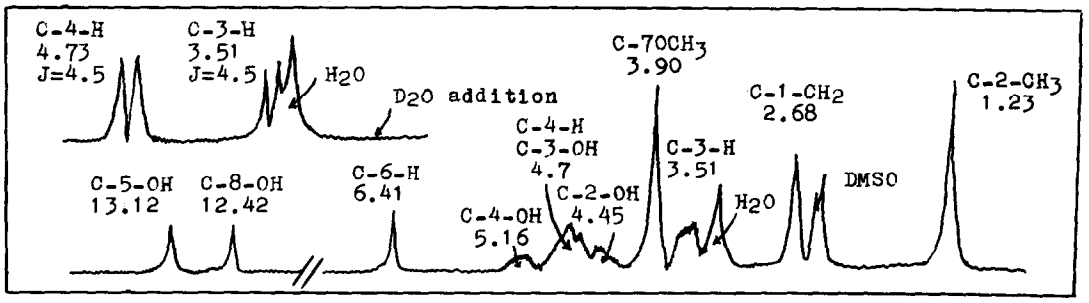
Bostrycin (I), a new red pigment antibiotic which is effective against mainly gram positive bacteria, was extracteble with chloroform from the broth culture of Bostrychonema alpestre.

After purification by recrystallization (pyridine-water), it melted at 222-224° dec. and was poorly soluble in all common solvents. On the basis of the following data, the constitution of the pigment has been established as I[1].



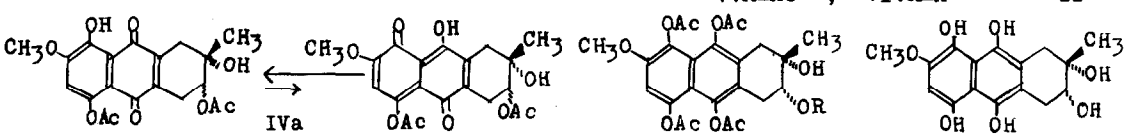
Bostrycin (I), $C_{16}H_{16}O_8$, has the following physical properties. M^+ion m/e336; ν_{max}^{KBr} 3510, 3480, 3360, 1595 cm^{-1}; λ_{max}^{EtOH} 228, 303, 472, 505, 542 mμ. The NMR chart is shown in Fig-1. Bostrycin I consumed about two moles of hydrogen (10% pd-C in pyridine) to give a greenish brown compound which was immediately oxidized by air into red desoxybostrycin (II), in which the benzylic hydroxyl group in I was eliminated by hydrogenolysis; $C_{16}H_{16}O_7$, m.p. 228-230° dec. M^+ion m/e320. The IR and UV spectra are similar to those of bostrycin I. In the NMR

Fig-1 The NMR Chart of Bostrycin in DMSO-6d.



spectrum of II, the four methylene protons at the C-1 and C-4 are observed at 2.62-2.80 ppm as broad peaks, and the C-4 hydroxyl proton disappears.

Bostrycin I was treated with acetic anhydride in pyridine to give triacetate (III); $C_{22}H_{22}O_{11}$, m.p. 255.5-260.5°, ν_{max}^{KBr} 3400, 1772(sh.), 1743, 1722(sh.), 1637(free quinone carbonyl), 1602(hydrogen bonded quinone carbonyl); λ_{max}^{EtOH} 220, 256, 291, 430 mμ; δ_{ppm}^{DMSO} 1.29(3H,s., C-2-CH_3), 2.01(6H,s., C-3-OAc, C-4-OAc), 2.18(3H,s., C-5-OAc), 4.95(1H, C-2-OH), 5.02(1H,d., J=6 cps, C-3-H), 5.93(1H,d., J=6 cps, C-4-H), 12.39(1H,s., C-8-H). Hydrogenation of III in chloroform with Pd-C (10%) yielded the diacetate (IV); $C_{20}H_{20}O_9$, m.p. 206-209°, ν_{max}^{KBr} 3460, 1764, 1740, 1712, 1638, 1608; $\nu_{max}^{CHCl_3}$ 3670, 3580-3400, 1765, 1737, 1720(sh.), 1640, 1610 cm^{-1}; $\delta_{ppm}^{CDCl_3}$ 1.33(3H,s., C-2-CH_3), 2.06(1H, C-2-OH), 2.12(3H,s., C-3-OAc), 2.41(3H,s., C-5-OAc), 2.72-3.10(4H, C-1-CH_2, C-4-CH_2), 3.89(3.96)* (3H, C-7-OCH_3) 5.05(1H,t., J=6.0 cps, C-3-H), 5.98(6.68)* (1H, C-6-H), 12.59(12.96)* (1H, C-8-OH). The loss of the C-4 acetoxyl group (of III) through catalytic hydrogenation was also confirmed to obtain the diacetate IV by acetylation of desoxybostrycin II. In the IR spectra of IV the absorptions at 3460 and 1712 cm^{-1} in KBr disk are shown at 3670, 3580-3400 and 1720(sh.) cm^{-1} in the chloroform solution. From these observations, the compound IV is inferred to have a hydroxyl group intramolecularly hydrogen bonded with an acetoxyl group. The two peaks of the OCH_3 (δ3.89, 3.96), C-6 proton (δ5.98, 6.68) and C-8 proton (δ12.59, 12.96) seemed to be in the tautomerism as follows (IVa)[2].



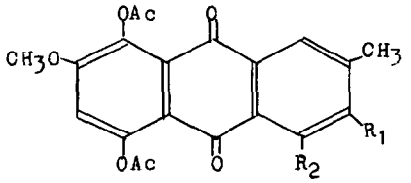
As indicated above, on hydrogenation over Pd-C in pyridine, bostricin I gave a greenish brown compound which was labile to air. This unstable material was acetylated with acetic anhydride in the absence of air to give leuco-penta-acetate (V) (amorphous): $C_{26}H_{28}O_{12}$, ν_{max}^{KBr} -3480, 1767, 1745 cm^{-1}; λ_{max}^{EtOH} 233, 282.5, 295.5, 303, 335, 347 mμ; $\delta_{ppm}^{CDCl_3}$ 2.05(3H,s., C-3-OAc), 2.24(1H,s., C-2-OH), 2.36 (12H, C-5, C-8, C-9, C-10-OAc), 5.03(1H,t., J=6.0 cps, C-3-H); and a small amount of crystalline product (VI): $C_{24}H_{26}O_{11}$, m.p. 205-207; ν_{max}^{KBr} 3300(broad), 1760 cm^{-1}; δ_{ppm}^{DMSO} 3.61(1H,m., C-3-H), 4.43(1H, C-2-OH), 4.77(1H,d., J=5 cps, C-3-OH).

* The intensities of the peaks in parentheses are about ten percent.

From the above observation, the labile product was appeared to have the structure (IIa). Bostrycin was easily dehydrated by refluxing it in formic acid to yield the anthraquinone derivatives which were acetylated to give three acetates: triacetate (VII) (main product); $C_{22}H_{18}O_9$, m.p. 232-240°, ν_{max}^{KBr} 1780, 1765, 1670, 1660, 1590, 1580 cm^{-1}; diacetate (VIII); $C_{20}H_{16}O_7$, m.p. 238-243°, ν_{max}^{KBr} 1770, 1675, 1597 cm^{-1}; and tetra-acetate (IX) (minor product); $C_{24}H_{20}O_{11}$, m.p. 220.5-221°, ν_{max}^{KBr} 1780, 1675, 1595 cm^{-1}. The NMR spectra of the above three acetates are listed in Table-1. The relative positions of the C-2 methyl and the C-7

Table-1 NMR Spectra of Anthraquinone Derivatives

	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8
VII	8.08	2.30	2.34	7.81	2.46	6.92	3.39	2.46
VIII	7.94,d., J=2.0	2.47	7.94,q., J=7.6, 2.0	8.05,d., J=7.6	2.47	6.91	3.93	2.47
IX	7.98	2.31	2.34	2.45	2.40	6.89	3.90	2.40

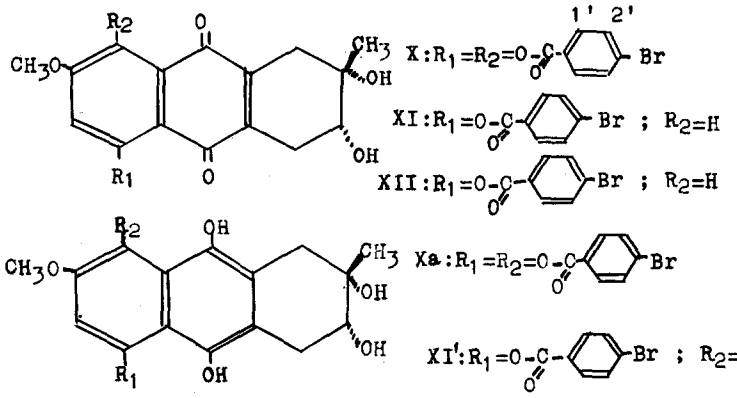


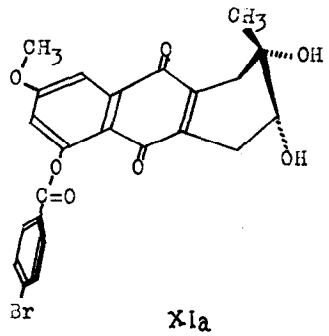
VII : R_1=OAc ; R_2=H

VIII : R_1=R_2=H

IX : R_1=R_2=OAc

methoxyl group can be seen in many naturally occurring anthraquinones[3]. When bostrycin was treated with p-bromobenzoyl-chloride in pyridine, it did not give any crystalline product, but IIa, which had very activated hydroxyl groups, gave an amorphous unstable compound (X) and a yellow material (XI). Futher hydrogenation of X over 10% Pd-C in pyridine, the mono-benzoate XI was also obtained. From the above observation, it seems that IIa was benzoylated to give Xa and oxidized by air to X. When Xa was further hydrogenated to XI', XI was obtained by air oxidation. XI was crystallized from ethanol as fine needles; $C_{23}H_{19}O_7Br$, m.p. 193-196°; ν_{max}^{KBr} 3400, 1755, 1655, 1600 cm^{-1}; λ_{max}^{EtOH} 267, 278, 376 mμ; δ_{ppm}^{DMSO} 1.18 (3H,s., C-2-CH_3), 2.4-2.7(4H, C-1-CH_2, C-4-CH_2), 3.6(1H, C-3-H), 3.95(3H,s., C-7-OCH_3), 4.49(1H,s., C-2-OH), 4.80(1H,d., J=4.5 cps, C-3-OH), 7.30(1H,d., J=3 cps, C-6-H), 7.45(1H,d., J=3 cps, C-8-H), 7.85(2H,d., J=9 cps, C-1'-H), 8.13(2H,d., J=9 cps, C-2'-H). By adsorption upon silica gel, the unstable compound X decomposed to a light yellow compound (XII) which was crystallized as needles from methanol; $C_{23}H_{19}O_8Br$, m.p. 238-241°, ν_{max}^{KBr} 3600-3200, 1740, 1640, 1580 cm^{-1}; λ_{max}^{EtOH} 253.5, 260, 385 mμ. When compound XI was crystallized from dimethyl formamide (DMF), it





XIa

grew into single crystals containing one mole of DMF. The molecular structure of XI is found to be represented as XIa[4] from a three dimensional X-ray diffraction study. The chemical shifts of the C-2 methyl (1.23 ppm for I) is not affected by the C-4 acetoxyl group (1.29 ppm for III). This show that the C-4 hydroxyl group was a pseudo equatorial configuration in I.

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1) Symbols a,e, and e' denote the axial, equatorial and pseudo equatorial configurations of the bonds in quenstion.

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