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N_1-PYRROMYCINONE, A NEW TETRACENEQUINONE (ANTHRACYCLINONE) FROM STREPTOMYCES SP. I-8

Jane R. Hegyi and Nancy N. Gerber

Institute of Microbiology, Rutgers, The State University,

New Brunswick, New Jersey 08903

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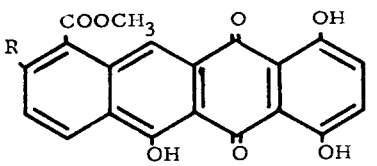
Streptomyces sp. I-8 (1), growing at 28° in a well-aerated soybean meal-peptone-glucose (2) liquid medium, produced mainly one orange pigment extractable with chloroform (yield: 2-6 mg/l. of whole broth, found mainly in the cell mass). After purification by column chromatography on silica and recrystallization (benzene-hexane or dioxane-water) it melted at 290-292° and was poorly soluble in all common solvents.

The pigment belonged to the anthracyclinone group (3) as shown by its electronic absorption spectra, $\lambda_{max}^{cyclohexane}$ 526, 515, 504, 492, 482, 275, 252 mμ, $\lambda_{max}^{H_2SO_4}$ 631, 580, 315, 281 mμ which were identical with those of n-pyrromycinone (3, 4) (I) and by the spectrum of its zinc dust distillation product, $\lambda_{max}^{chloroform}$ 475, 445, 418, 397, 295, 280 mμ which was identical to that of tetracene (5). However, high resolution mass spectroscopy indicated a molecular formula of $C_{21}H_{14}O_7$; the nmr spectrum in $CDCl_3$ (60 MHz, time-averaged, 25 and 100 scans) showed singlet peaks at 2.55 δ (3H, aromatic methyl), 4.08



I R = CH_2-CH_3

II R = CH_3

(3H, O-methyl), 12.20, 13.00 and 13.75 δ (each 1 H, hydrogen-bonded OH); the infra-red spectrum exhibited a carbonyl band at 5.9 μ and no free O-H band.

These observations suggested structure II for the pigment, now named n_1-pyrromycinone (6) which was verified in the following ways. The yellow acetate derivative λ_{max} 400, 301, 250 mμ, mp 224-226°, had a molecular weight of 504 (mass spec) corresponding to a triacetate and gave strong mass peaks corresponding to the loss of one, two and three acetyl fragments. It showed nmr singlet peaks at 2.45, 2.50, 2.55, 2.58 δ (each 3H, 3 acetyl methyls and 1 aromatic methyl) and 4.10 δ (O-methyl). Hydrolysis of II in concentrated sulfuric acid on the steam bath for 2 hours gave the corresponding acid, mp 328-330° (yellow acetate derivative mp 197-8°), whose electronic absorption spectra were identical with those of II and its acetate.

Decarboxylation of the acid with copper powder in diphenyl ether furnished a substance which lacked the acid carbonyl band in the infra-red but in the visible region was identical with II, $\lambda_{max}^{cyclohexane}$ 525, 515, 505, 490, 480 mμ. If two fully aromatic anthracyclinones, which differ only in the presence or absence of a carbomethoxy group at C-10, have identical absorption maxima in cyclohexane then they have no hydroxy group at C-11 (peri to the carbomethoxy group) (3). Further evidence that the three hydroxyl groups were located as in I came from the reaction of II with manganese dioxide in sulfuric acid. As for I (4), this produced a pink-purple pigment whose spectra, $\lambda_{max}^{cyclohexane}$ 565, 553, 540, 525, 514, 490, 482 mμ $\lambda_{max}^{H_2SO_4}$ 616, 570, 310 mμ were very similar to those of 1,4,6,11-tetrahydroxy-8-ethyltetracene quinone (7).

Most anthracyclinones have an ethyl side chain (8) which arises biosynthetically from propionic acid (3). Apparently, only β_1-rhodomycinone (9) and isoquinocycline A (10) have been shown previously to bear a methyl group in this position.

On agar media, n_1-pyrromycinone did not inhibit the growth of a variety of microorganisms (11) at a concentration of 8 μg/ml.

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Footnotes and References

1. Isolated from orchid greenhouse soil, Somerville, N. J.

2. SBM/J medium, see N. N. Gerber, Biochemistry 5, 3824 (1966).

3. H. Brockmann, Prog. Org. Chem. Nat. Prod. 21, 121 (1963).

4. H. Brockmann and W. Lenk, Chem. Ber. 92, 1880 (1959).

5. R. A. Friedel and M. Orchin, Ultraviolet Spectra of Aromatic Compounds, No. 532, Wiley, New York, 1951.

6. In accord with ref. 3. The Chemical Abstracts' systematic name would be 2-methyl-6, 11-dihydro-5, 7, 10-trihydroxy-6, 11-dioxo-1-naphthacenecarboxylic acid, methyl ester, however by the system used in ref. 3, 10-carbomethoxy-9-methyl-1, 4, 6-trihydroxy-tetracenequinone.

7. H. Brockmann and E. Wimmer, Chem. Ber. 96, 2399 (1963).

8. However see references in K. Eckardt, Chem. Ber. 100, 2561 (1967).

9. H. Brockmann, J. Niemeyer, H. Brockmann Jr., and H. Budzikiewicz, Chem. Ber. 98, 3785 (1965).

10. A. Tulinsky, J. Amer. Chem. Soc. 86, 5368 (1964).

11. Similar to those used for testing in N. N. Gerber and M. P. Lechevalier, Biochemistry 4, 176 (1965).