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A REVISED STRUCTURE FOR CYCLOPRODIGIOSIN

Hartmut Laatsch and Ronald H. Thomson

Department of Chemistry, University of Aberdeen,

Meston Walk, Old Aberdeen AB9 2UE, Scotland

Abstract: The structure of cycloprodigiosin has been revised from 2 to 4 in which the side chain is cyclised to form a six-membered ring.

Cultures of the aerobic marine bacterium *Alteromonas rubra*[1] produce red pigments[2] with indicator properties, and a compound(s) showing antibiotic activity[3] against a variety of bacterial species.

During trials to isolate the active water-soluble component(s) the red pigments were extracted into ethyl acetate and separated by repeated PLC on acetate-buffered silica gel in chloroform-hexane-ethyl acetate (5:9:1). The main component, $C_{20}H_{25}N_3O$, prodigiosin (1) was easily recognised by its characteristic electronic spectrum with a sharp maximum at 541 nm (1 hydrochloride in $CHC\ell_3$). On repeated chromatography on acetate-buffered silica gel (6% NaOAc; chloroform-hexane-ethyl acetate, 5:9:1) it was possible to separate a slower moving component, $C_{20}H_{23}N_3O$,[4] $\lambda_{max.}$($CHC\ell_3$) 544 nm (log ε 5.03) (for the hydrochloride) which was clearly another prodigiosin. Its ^{1}H-NMR spectrum is similar to that of 1, and according to the literature[2] this pigment should be cycloprodigiosin 2 but there is a significant difference in the ^{1}H-NMR spectrum. We reinterpret the spectrum (200 MHz FT) as follows.

The hydrochloride shows three coupled 1H-multiplets at δ 7.25, 6.94 and 6.36 which are broadened by N-quadrupole coupling. Their chemical shifts and coupling constants agree well with those reported for 2-substituted pyrroles such as 3 and derive from H-10, H-8 and H-9, respectively, in ring A. The doublet at δ 6.11 which collapses to a singlet on irradiation of the NH-resonance, originates from H-7 and hence the sharp singlet at 7.04 arises from H-5.[5]

The cyclisation of 1 results in the disappearance of the H-4 signal at δ 6.70 in the spectrum of 1.HCℓ. However, instead of the triplet reported[2] for the terminal methyl group in the ethyl side chain of 2 our pigment clearly shows a doublet at δ 1.29 (J 7 Hz) (see Fig. 1) which collapses to a singlet on irradiation of the multiplet at δ 3.14.

It follows that this minor pigment is an isomer of 2 and has structure 4. Direct comparison with an authentic specimen[6] previously regarded as 2 established their identity. The structure of cycloprodigiosin is therefore 4.

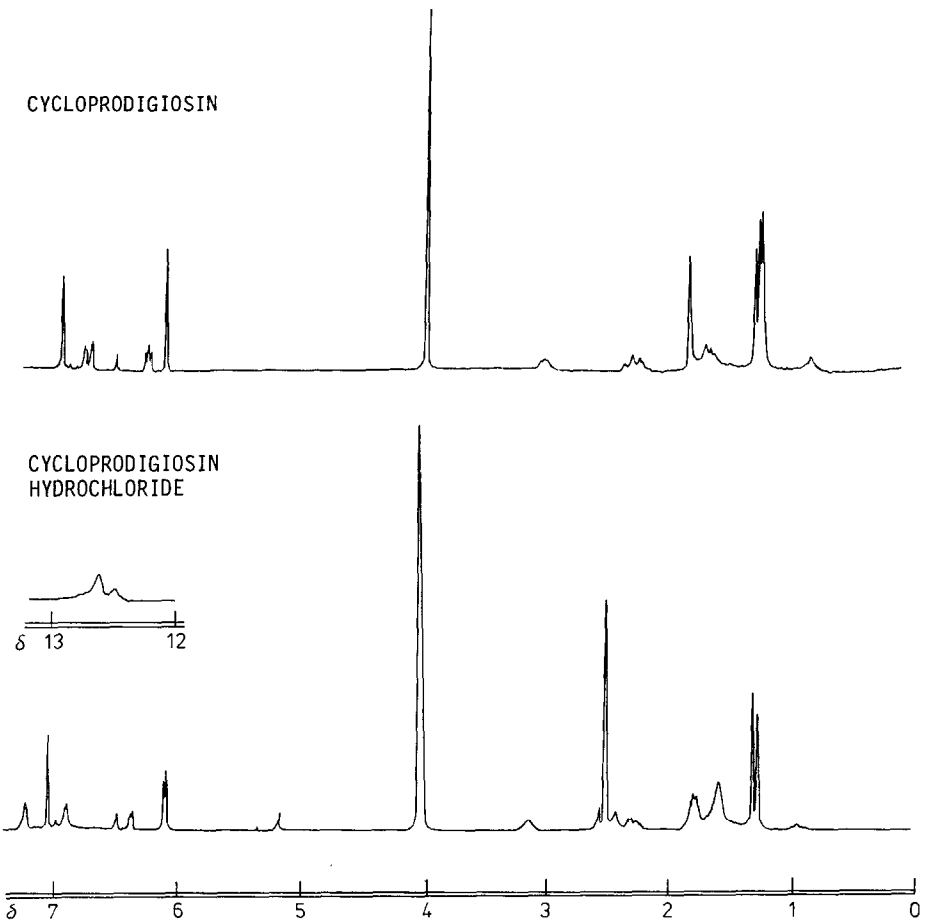
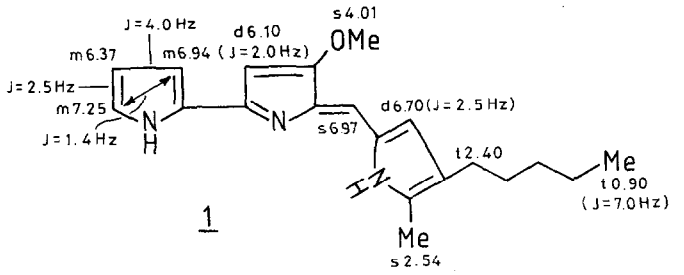


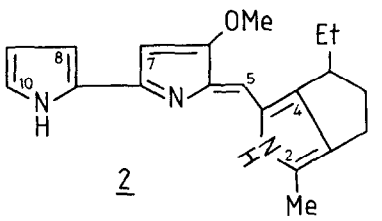
Fig. 1 ^{1}H-NMR (200 MHz FT) Spectra in $CDC\ell_3$



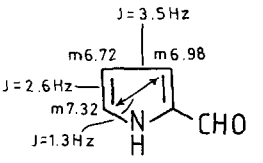
1

NH=12.68(2H), 12.53(1H), s, broad

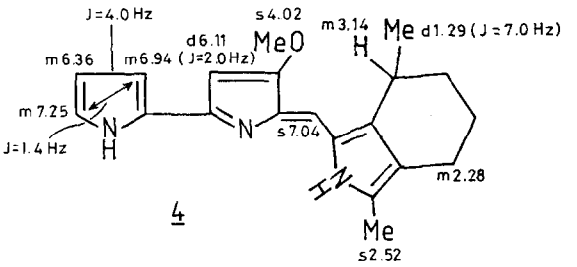
(NMR data refer to the hydrochloride in $CDCl_3$)



2



3



4

NH= 12.63(2H), 12.52(1H), s, broad

(NMR data refer to the hydrochloride in $CDCl_3$)

Misinterpretation of the previous spectrum[2] evidently arose from the presence of an aliphatic impurity with a long alkyl chain responsible for a triplet at δ 0.95.[7] Our sample of the free base was similarly contaminated and the spectrum (Fig. 1) included an extra singlet at δ 1.25 showing an apparent triplet.

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3 M. Ballester, J.M. Ballester and J.P. Belaich, *Microbiol. Ecol.*, 1977, *3*, 289.

4 MS(70 eV); m/e (%) 321(100, M^+), 306(54), 290(13), 266(16), 198(12), 175(11), 160(19), 135(19).

5 B.S. Deal, J.R. Alden, J.L. Still, A.V. Robertson and J. Winkler, *Aust. J. Chem.*, 1974, *27*, 2657.

6 For which we thank Dr. N.N. Gerber.

7 The signal previously reported at δ 2.0 and attributed to the methyl at C-2 in cycloprodigiosin was probably due to the presence of prodigiosin as an impurity.

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