

The Structure and Synthesis of Undecylprodigiosin. A Prodigiosin Analogue from *Streptomyces*

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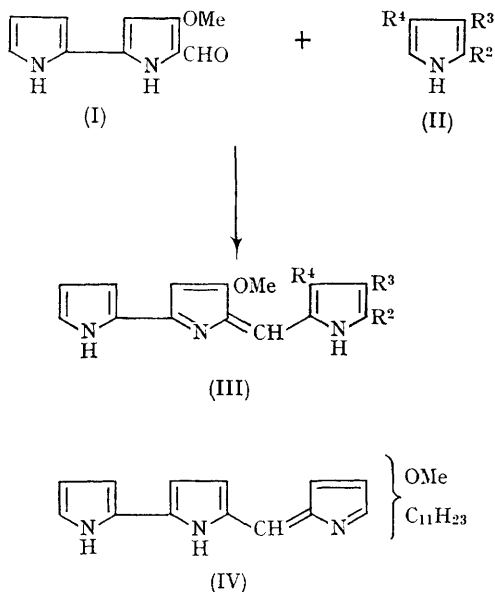
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IN recent years several groups of workers have reported the isolation of C_{25} prodigiosin analogues from various actinomycetes.¹ While the relationship of these metabolites to methylpentylprodigiosin (III; $R^2=Me$; $R^3=n-C_6H_{11}$; $R^4=H$) has been shown by spectral comparison,^{1a,1b,1b} and by partial synthesis^{1d} from the bipyrrrole aldehyde (I), there has, as yet, been no complete structure proof for any naturally occurring analogue of prodigiosin. We now report evidence establishing (III; $R^2=n-C_{11}H_{23}$; $R^3=R^4=H$) as the structure of one of the C_{25} pigments produced by a *Streptomyces* strain.

Streptomyces longisporus ruber, strain M-3,² was grown on a soymeal-mannitol medium in shake culture for 1–3 weeks. Methylene chloride extraction of the lyophilized cells followed by acid

and base washing and chromatography on basic alumina yielded a base, convertible into a hydrochloride, m.p. 176–180°. This hydrochloride consisted of two major components, one of which, $C_{25}H_{35}N_3O \cdot HCl$, m.p. 106–107°, could be separated in pure form by successive recrystallization from carbon tetrachloride and then heptane.³ This product was shown to be identical with prodigiosin-25C recently isolated and assigned partial structure (IV) by Harashima and co-workers.^{1b,4}

The general spectroscopic properties of this pigment clearly show it to be a member of the prodigiosin series. More particularly, the mass spectrum contains a parent peak at m/e 393 and a strong peak at m/e 252 (loss of $C_{10}H_{21}$) suggesting the presence of an undecyl side chain on the



alkylpyrrole fragment. Pyrolysis of the crude pigment over soda-lime yielded a mixture of pyrroles separable by v.p.c. containing a $C_{15}H_{27}N$ base as one of the main fractions. The mass spectrum of this base (peaks at m/e 221 and m/e 80) as well as the n.m.r. spectrum [τ 3.6 (1H), 3.59 (1H), 4.02 (1H), 4.20 (1H), 7.6 (2H), 8.65 (18H), and 9.1 (3H)] are in accord with a 2-undecylpyrrole structure. This assignment was confirmed by comparison with an authentic sample of (II); $R^2 = n-C_{11}H_{23}$, $R^3 = R^4 = H$) prepared from the reaction of pyrrole Grignard with undecanoyl chloride followed by lithium aluminium hydride reduction.⁵

Condensation of 2-undecylpyrrole with the bipyrrrole aldehyde (I)^{6,7} in ethanol containing HCl yielded undecylprodigiosin (III; $R^2 = n-C_{11}H_{23}$, $R^3 = R^4 = H$) identical in all respects with the natural pigment. Since (I) has been previously synthesized,⁷ the structure determination and synthesis of the C_{25} pigment is thus complete.

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¹ (a) E. Dietzel, *Naturwiss.*, 1948, **35**, 345; (b) E. Dietzel, *Z. physiol. Chem.*, 1949, **284**, 262; (c) R. A. Nicolaus, R. Nicoletti, and F. Arcamone, *Ricerca sci.*, 1958, **28**, 2314; (d) H. H. Wasserman, J. Keggi, F. Bohlmann, and W. Luders, *Angew. Chem.*, 1960, **72**, 779; (e) H. H. Wasserman, L. L. Williams, and J. Keggi, *Angew. Chem.*, 1961, **73**, 467; (f) J. J. Perry, *Nature*, 1961, **191**, 77; (g) I. M. Khokhlova, A. V. Puchina, and O. I. Artamonova, *Biokhimiya*, 1964, **29**, 841; (h) K. Harashima, N. Tsuchida, and J. Nagatsu, *Agric. and Biol. Chem. (Japan)*, 1966, **30**, 309.

² The strains of *Streptomyces longisporus ruber* used in this work were kindly provided by Dr. K. Haider, Institut für Biochemie des Bodens, Braunschweig, Germany.

³ Structural and synthetic investigations on the other prodigiosin-like component of this mixture, $C_{25}H_{33}N_3O$, m.p. 201–202° (hydrochloride), will be reported separately.

⁴ We thank Dr. Harashima for sending us a sample of his C_{25} pigment for mixed melting-point and infrared-spectral comparison.

⁵ Satisfactory elemental analyses were obtained for all new compounds.

⁶ H. H. Wasserman, J. E. McKeon, L. Smith, and P. Forgione, *J. Amer. Chem. Soc.*, 1960, **82**, 506; *Tetrahedron*, Supplement No. 8, in the press.

⁷ H. Rapoport and K. G. Holden, *J. Amer. Chem. Soc.*, 1962, **84**, 635.