

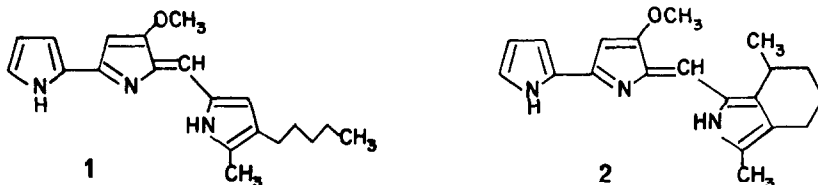
### THE SYNTHESIS OF (+)-CYCLOPRODIGIOSIN

Harry H. Wasserman\* and James M. Fukuyama

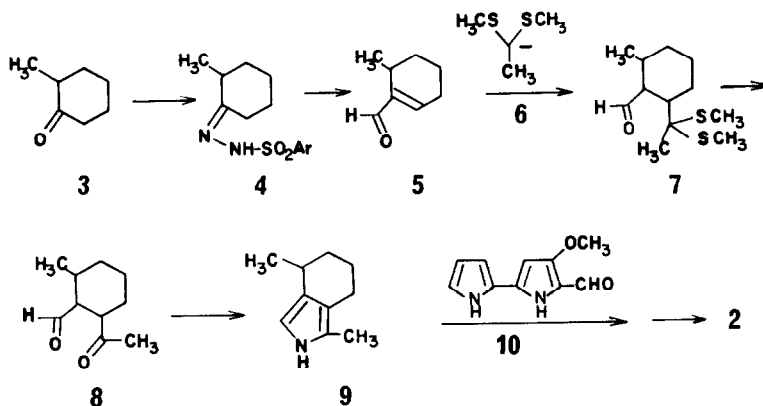
Department of Chemistry, Yale University, New Haven, CT 06511

**Abstract:** The cycloprodigiosin isolated from the marine bacteria, *Beneckea gazogenes* and *Alteromonas rubra* has been synthesized from the fused ring pyrrole (9) and the methoxy formyl bipyrrole (10).

Recent reports have described the production of pigments related to prodigiosin by marine bacteria.<sup>1,2,3</sup> Along with the parent tripyrrole species (1), a novel C-20 pigment, named cycloprodigiosin has been isolated from cultures of *Alteromonas rubra* and *Beneckea gazogenes*.<sup>2,3</sup> An earlier assignment of structure to this pigment<sup>12</sup> was later corrected in favor of the formulation (2), containing a six-membered ring fused to the alkylpyrrole.<sup>2,4</sup> We now report a synthesis of cycloprodigiosin (2) which serves to corroborate the new structural assignment.



The key intermediate in the synthesis of 2 is the dicarbonyl component (8) convertible to pyrrole (9) by standard methods. 2-Methylcyclohexanone (3) was condensed with 2,4,6-triisopropylbenzenesulfonyl hydrazide to form the hydrazone (4) (95%). Treatment of 4 with *sec*-butyllithium (2 equiv.) generated the vinyl anion which could be trapped with DMF to form the  $\alpha,\beta$ -unsaturated aldehyde (5) (60%).<sup>5</sup> This product was then allowed to react with the anion (6) in THF/HMPA at  $-78^\circ$  (1 equiv. *n*-butyllithium) to produce the addition product (7) (37%).<sup>6</sup> Compound 7 was then treated with  $\text{HgCl}_2$  and  $\text{CaCO}_3$  in  $\text{CH}_3\text{CN}/\text{H}_2\text{O}$  (4:1) yielding the aldehyde ketone (8) (85%).<sup>7</sup> The pyrrole derivative (9) could then be formed by warming 8 with ammonium carbonate to  $110^\circ\text{C}$  in  $\text{DMF}/\text{H}_2\text{O}$  (4:1) (63%).<sup>8</sup>



Completion of the synthesis of **2** was accomplished by coupling the pyrrole (**9**) with the known 2-formyl-3-methoxy- $\alpha,\alpha'$ -bipyrrole (**10**)<sup>9,10,11</sup> in the presence of ethanolic HCl. The resulting pyrrolyl dipyrromethene hydrochloride was shown to be identical with samples of the natural product derived both from *Beneckeia gazogenes* and *Alteromonas rubra*. The 500 MHz NMR spectra of natural and synthetic materials were superimposable in all respects except for minor peaks in the spectra of the natural material associated with small amounts of lipid impurity. 4,12

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12. Early structural work on this cyclic prodigiosin was complicated by the presence of an aliphatic impurity with a long alkyl chain. Thus, the initial assignment of structure (**11**) to this pigment reflected the presence of a spurious triplet in the NMR spectrum.

