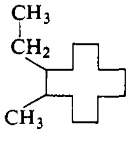
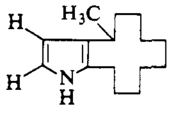
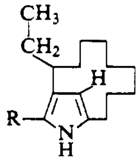
$C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.48; H, 9.97; N, 5.64. The nmr spectrum of the formyl derivative shows the presence of a single β-ring hydrogen, the chemical shift of which (τ 4.00) is not significantly altered from that observed for the β proton in the parent pyrrole (τ 4.18).



III



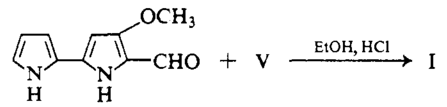
IV



V, R=H
VI, R=CHO

Studies of model systems[6] show that a formyl group at the 2 position of a pyrrole ring has a pronounced deshielding effect on the adjacent hydrogen at the 3 position, causing a downfield shift of about 0.8 ppm. On the other hand, the corresponding effect of a 2-formyl group on a β hydrogen at the 4 position is very slight (0.1–0.2 ppm). The formyl derivative, therefore, clearly has structure VI, and the C-15 dialkylpyrrole must accordingly have structure V.[12]

As a member of the prodigiosin series, metacycloprodigiosin would be expected to incorporate residues corresponding to pyrrole (V) and the methoxybipyrrole aldehyde (VII) as shown in structure I.[14–16] The validity of this assignment was established when the parent pigment was reconstituted by the HCl-catalyzed condensation of the alkylpyrrole V, with the C-10 prodigiosin precursor (VII) obtained from a mutant strain of *Serratia*.[17] This reaction yielded metacycloprodigiosin hydrochloride identical (nmr and infrared absorption spectra, mass spectrum) with the natural material.



VII

Acknowledgments. We wish to acknowledge support of this work by National Institutes of Health Grant A1-04798. We also wish to thank Dr. W. McMurray for the mass spectrometric analyses.

Harry H. Wasserman, George C. Rodgers,[18] Dennis D. Keith[19]
Department of Chemistry, Yale University
New Haven, Connecticut 06520

Received November 27, 1968

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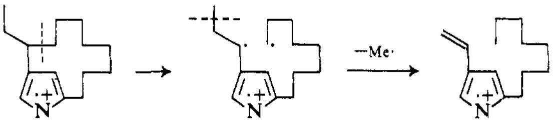
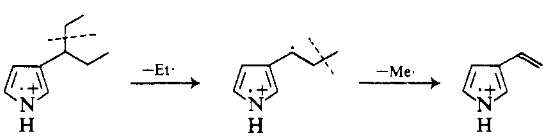
[12] The mass spectrum of V exhibits peaks at *m/e* 204 (loss of methyl) and 190 (loss of ethyl). Although the $M^+ - 15$ peak seems on first consideration to be exceptional, it is readily explained in terms of the sequence



As would be expected from the above, we have observed that the mass spectrum of 3-(3-pentyl)pyrrole (i)[13] exhibits peaks at *m/e* 137, 108, and 93.



i

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[18] National Science Foundation Cooperative Graduate Fellow, 1962–1963; National Science Foundation Predoctoral Fellow, 1963–1965.

[19] National Institutes of Health Predoctoral Fellow, 1966–1968.

The Synthesis of Metacycloprodigiosin

Sir:

In the accompanying communication[1] we have reported the isolation and structure determination of metacycloprodigiosin (**1**), a tripyrrole pigment from *Streptomyces*. We now describe the synthesis of the racemic form of this pigment which confirms the structural assignment.

Cyclododecanone (**2**) was converted by sodamide in glyme followed by ethyl bromide to the 2-ethyl derivative **3** (45%): bp 80° (0.1 mm); $\nu_{\max}^{\text{liquid film}}$ 1706 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 7.38–7.83 (m, 3 H), 9.18 (t, 3 H).[2] Treatment of **3** with ethylene glycol-*p*-toluenesulfonic acid monohydrate in benzene afforded the ketal **4**[3] (70%): bp 114° (0.5 mm); $\tau_{\mathrm{CCl_4}}$ 6.20 (s, 4 H, OCH_2CH_2O). Treatment of **4** with pyridine hydrobromide perbromide[4] in dry THF yielded 2-bromo-12-ethylcyclododecanone ethylene ketal **5**[3] (~100): mp 59.5–60.5°. The location of bromine at the less substituted position[5] was shown by the nmr spectrum exhibiting five protons (two multiplets) in the region τ 5.6–5.9, associated with the groups $-OCH_2CH_2O-$ and $-CHBr-$. Dehydrobromination of **5** with 1,5-diazabicylo[4.3.0]non-5-ene[6] at 110° for 72 hr furnished the α,β-unsaturated ethylene ketal **6**[3] (90%): bp 84–85° (0.03 mm); $\nu_{\max}^{\mathrm{CCl_4}}$ 1667, 992 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 4.5 (m, 1 H), 4.80 (d, 1 H), 6.37 (s, 4 H). Acid hydrolysis of **6** gave 12-ethyl-2-cyclododecenone (**7**)[3] (95%): bp 98–101° (0.2 mm); semicarbazone mp 157–159°; $\lambda_{\max}^{\mathrm{EtOH}}$ 230 mμ (ν 10,200); $\nu_{\max}^{\mathrm{CCl_4}}$ 1692, 1666, 1625, 990 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 3.31 (m, 1 H), 3.72 (d, 1 H), 7.7 (m, 3 H).

When **7** was treated with H_2O_2 and NaOH in MeOH at 5°[7] the α,β-epoxy ketone **8**[3] was obtained (94%); bp 115–117° (0.1 mm); $\nu_{\max}^{\mathrm{CCl_4}}$ 1717 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 6.73 (d, 1 H, $J = 2$ Hz), 7.2 (m, 2 H). Gas chromatographic analysis (SE 30 column, 200°) indicated that the product was a mixture of two diastereomers. It was possible to obtain one isomer as a crystalline solid[3] from MeOH, mp 67.5–

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[2] L. I. Zakharin, and V. V. Korneva, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2102 (1964).

[3] Satisfactory elemental analyses were obtained for all new compounds.

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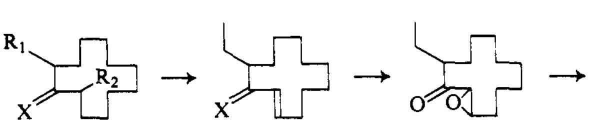
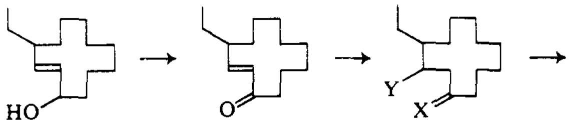
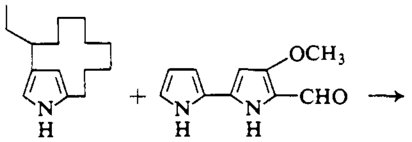


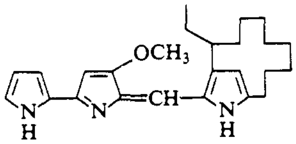
2, X = O; R$_1$ = R$_2$ = H
3, X = O; R$_1$ = Et; R$_2$ = H
4, X = (OCH$_2$CH$_2$O); R$_1$ = Et; R$_2$ = H
5, X = (OCH$_2$CH$_2$O); R$_1$ = Et; R$_2$ = Br
6, X = (OCH$_2$CH$_2$O)
7, X = O
8



9
10
11, X = O; Y = CN
12, X = (OCH$_2$CH$_2$O); Y = CN
13, X = (OCH$_2$CH$_2$O); Y = CHO
14, X = O; Y = CHO



15
16



1

60°. The α,β-epoxy ketone mixture **8**, upon treatment with 85% aqueous hydrazine hydrate and a catalytic amount of HOAC in EtOH for 12 hr at 25°,[8] yielded 4-ethyl-2-cyclododecenol (**9**)[3] (33%): bp 97–100° (0.1 mm); $\nu_{\max}^{\mathrm{CCl_4}}$ 3636, 3490, 1695, 980 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 4.73 (m, 2 H, –C*H*=C*H*–), 6.08 (broad absorption, 1 H, C*H*OH), 8.23 (s, 1 H, O*H*).[9] Oxidation[11] of the allylic alcohol **9** (sodium dichromate in sulfuric acid) produced 4-ethyl-2-cyclododecenone (**10**)[3] (92%); $\lambda_{\max}^{\mathrm{EtOH}}$ 231 mμ (ε 11,200); $\lambda_{\max}^{\mathrm{CCl_4}}$ 1694, 1664, 1625, 994 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 3.7 (m, 2 H).

Reaction of **10** with KCN-NH$_4$Cl in 1:10 H$_2$O-DMF at 105° for 18 hr[12] yielded 3-cyano-4-ethylcyclododecanone (**11**) (42%): bp 113–116° (0.5 mm); $\nu_{\max}^{\mathrm{CCl_4}}$ 2240 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 6.5–8.0 (m, 5 H). Ketalization of **11** (ethylene glycol) gave the cyano ketal **12**[3] (95%): $\nu_{\max}^{\mathrm{CCl_4}}$ 2240 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 6.07 (m, 4 H), 7.3 (m, 1 H). The nitrile **12** was reduced with diisobutylaluminum hydride[13] yielding the ketal aldehyde **13**[3] (95%): $\nu_{\max}^{\mathrm{CCl_4}}$ 2820, 2712, 1723 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 0.40 (m, 1 H), 6.20 (m, 4 H), 7.5 (m, 1 H). Hydrolysis of **13** followed by reaction of the resultant keto aldehyde **14** [$\nu_{\max}^{\mathrm{CCl_4}}$ 2830, 2722, 1724, 1710 cm^{-1}; $\tau_{\mathrm{CCl_4}}$ 0.23 (m, 1 H), 6.9 (m, 1 H), 7.35 (m, 2 H), 7.68 (m, 2 H)] with (NH$_4$)$_2$CO$_3$ in 1:6 H$_2$O-DMF[14] yielded the C-15 *dl*-metacyclopyrrole **15** (58%): bp 109–111° (0.2 mm); mp 59–61°. The synthetic pyrrole has ir, nmr, and mass spectra identical with those of the pyrrole obtained by pyrolysis of natural metacycloprodigiosin.[1]

Condensation of **15** with the known C-10 methoxybipyrrole precursor **16**[15-17] in ethanolic HCl at 25° for 24 hr afforded, after chromatography on basic alumina, *dl*-metacycloprodigiosin (**1**) (90%), mp 219–221°. The brilliant red pigment has uv, visible, ir, nmr, and mass spectra identical with those of the natural prodigiosin.[1]

Acknowledgments. We are indebted to Dr. Eugene Gosselink and Mr. Richard Sykes for their participation in valuable exploratory studies on the synthesis of *meta*-bridged pyrroles. Mass spectrometric analyses were determined by Dr. W. McMurray. We also thank Mr. Stuart Rosenfeld for technical assistance. Financial support was provided by National Institutes of Health Grant AI 04798.

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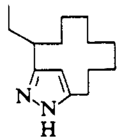
(9) The major product from this reaction was the pyrazole i.[10]



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(18) National Institutes of Health Predoctoral Fellow, 1966–1968.

Harry H. Wasserman, Dennis D. Keith,[18] Jeffrey Nadelson
Department of Chemistry, Yale University
New Haven, Connecticut 06520

Received November 27, 1968

The Mechanism of Direct *cis–trans* Photoisomerization of the Stilbenes. The Nature of the Azulene Effect

Sir:

The conclusion that intersystem crossing does not lie in the path leading to *cis–trans* photoisomerization of the stilbenes depends on the assumption that the azulene effect on the direct photoisomerization is due entirely to radiationless transfer of excitation from *trans*-stilbene singlets, ^1t, to azulene (eq 1).[1] The much larger azulene effect obtained under triplet (sensitized) excitation conditions

$$^1t + {}^0\mathrm{Az} \xrightarrow{k_1} {}^0t + {}^1\mathrm{Az} \qquad (1)$$

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