oxide structure. Such is the case. Reactions readily occur with boron trichloride just above the melting point of the solid, with oxygen on heating at 170° and with methyl iodide at room temperature.

The main product of the boron trichloride reaction is a clear liquid having a vapor pressure of less than 1 mm. at 30°, soluble in benzene and reacts violently with water. Elemental analysis yielded the composition $P_2N_3(CH_3)_3B_2Cl_3$. The vacuum line reaction corresponded to 4.2 moles of boron trichloride reacting per mole of imide. In addition small amounts of PCl_3 are produced as well as a solid product (presently being characterized). The latter solid must contain a low chlorine to boron ratio since the main product formed (in over 60% yield) contains a boron to chlorine ratio of 1:4.

Experimentally, the reaction proceeds rapidly on melting the crystalline imide in an excess of boron trichloride; the pressure drops abruptly and a clear liquid forms. On heating at 140° in an oven the liquid becomes yellowish and a solid product forms. What may be occurring is an addition of boron trichloride to the phosphorus atoms of the imide followed by a chlorination process. Investigation of the latter substance is currently under way.

The oxygen reaction is complex, yielding a white solid at 170° and some glassy looking material. Preliminary analysis indicates a formulation $P_2N_3(CH_3)_3O_2$ for the white product, that expected for the formation of a phosphorus pentoxide type structure.

The methyl iodide product has been established as $P_4N_6(CH_3)_7I$, a simple 1:1 reaction which proceeds readily at room temperature.

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RECEIVED AUGUST 15, 1960

THE SYNTHESIS OF PRODIGIOSIN

Sir:

We wish to report the synthesis, and concomitant proof of structure, of prodigiosin, the red pigment of *Serratia marcesens*. This pigment has been of much interest since first it provided the excuse for religious excesses.[1] It also has considerable antibiotic activity, although high toxicity precludes the use of prodigiosin itself.[2]

The first degradative work reported[3] on prodigiosin, $C_{20}H_{25}ON_3$, established its gross features; *viz.*, the presence of three pyrrole nuclei (pyrrole, 3-methoxypyrrole and 2-methyl-3-amylpyrrole) joined in some manner with the aid of a single bridging carbon. On the basis of this work Wrede, in 1933,[3b] proposed structures I and III for prodigiosin, later favoring III without any further experimental data. A pyrryldipyrrylmethene structure did not appear again in the literature until very recently.[4,5]

Of paramount importance to the structure elucidation of prodigiosin is the structure of a substance $C_{10}H_{10}O_2N_2$, isolated[6] from a mutant strain and shown by biosynthetic experiments[6] and condensation with 2-methyl-3-amylpyrrole[5] to be a precursor of prodigiosin. If the tripyrrylmethene structure III for prodigiosin were correct, this precursor would be a methoxy-2,2′-dipyrryl ketone, while a pyrryldipyrrylmethene structure, I or II, would require the precursor to be a methoxy-2,2′-bipyrrole aldehyde. It was found, by synthesis of 4-methoxy-2,2′-dipyrryl ketone,[7] that the ultraviolet absorption of this type compound is sufficiently different from that reported[5,6] for prodigiosin precursor to rule out a dipyrryl ketone structure. This in turn eliminates a tripyrrylmethene structure for prodigiosin. Isolation of pyrrole-2-carboxamide from oxidation of prodigiosin and the precursor[5] provided strong evidence for 2,2′-linked pyrrole rings, and coupled with n.m.r. data led to the proposal[5] of structures I and IV for prodigiosin, with I being favored.

We considered either of the pyrryldipyrrylmethenes I and II as most likely for prodigiosin. The precursor should then be a methoxy-2,2′-bipyrrole aldehyde. No existing methods for synthesizing bipyrroles appeared applicable to such a compound. However, condensation of Δ^1-pyrroline with pyrrole to give 2-(2′-pyrrolidinyl)-pyrrole has been reported recently,[8] and dehydrogenation of this compound readily gave 2,2′-bipyrrole (V), m.p. 187° (found: C, 72.5; H, 6.1 N, 21.4; mol. wt., 128). To apply this method to the preparation of the 2,2′-bipyrrole VI, we require the unknown ethyl 3-methoxypyrrole-2-carboxylate. Condensation of the sodium salt of ethyl N-ethoxycarbonylglycinate with diethyl ethoxymethylenemalonate gave diethyl 3-hydroxypyrrole-2,4-dicarboxylate, m.p. 121° (found: C, 52.9; H, 5.7; N, 6.0; OC_2H_5, 39.3) which with diazomethane formed diethyl 3-methoxypyrrole-2,4-dicarboxylate, m.p. 83° (found: C, 55.0; H, 6.3; N, 5.9; OR, 3.03/241). Hydrolysis of the diester with concd. sulfuric acid gave 2-ethoxycarbonyl-3-methoxypyrrole-4-carboxylic acid, m.p. 178° dec. (found: C, 50.9; H, 5.2; equiv. wt., 214) which on heating above its melting point, decarboxylated to ethyl 3-methoxypyrrole-2-carboxylate, m.p. 94° (found: C, 56.7; H, 6.8). This selective hydrolysis of the β-ester is common in the pyrrole series[9] and was verified by alkaline hydrolysis of the diester to 4-ethoxycarbonyl-3-

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(5) H. H. Wasserman, J. E. McKeon, L. Smith and P. Forgione, THIS JOURNAL, **82**, 506 (1960).

(6) U. V. Santer and H. J. Vogel, *Federation Proc.*, **15**, 1131 (1956); *Biochim. Biophys. Acta*, **19**, 578 (1956).

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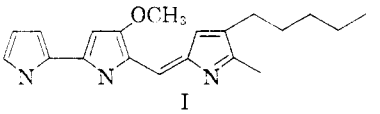
(8) D. W. Fuhlhage and C. A. VanderWerf, THIS JOURNAL, **80**, 6249 (1958).

(9) H. Fischer and H. Orth, "Die Chemie des Pyrrols," Band I, Akademische Verlagsgesellschaft, Leipzig, 1934.



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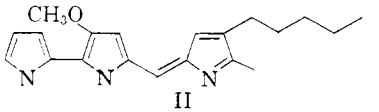

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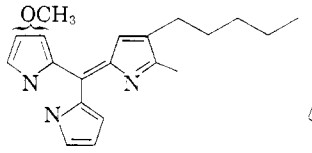

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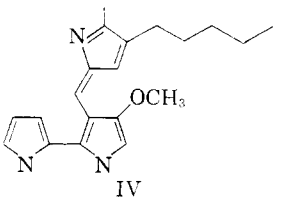

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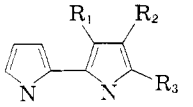

	R_1	R_2	R_3
V	H	H	H
VI	H	OCH_3	$COOC_2H_5$
VII	H	OCH_3	CHO
VIII	OCH_3	H	$COOCH_3$
IX	OCH_3	H	CHO

methoxypyrrole-2-carboxylic acid, which was decarboxylated to ethyl 4-methoxypyrrole-3-carboxylate (m.p. 107–109°), identical with material prepared from ethyl 1-ethoxycarbonyl-4-methoxy-Δ^3-pyrroline-3-carboxylate.[7]

Condensation of Δ^1-pyrroline with ethyl 3-methoxypyrrole-2-carboxylate gave ethyl 3-methoxy-5-(2′-pyrrolidinyl)-pyrrole-2-carboxylate which was dehydrogenated to ethyl 4-methoxy-2,2′-bipyrrole-5-carboxylate (VI), m.p. 214° (found: C, 61.2; H, 6.2). With hydrazine, VI formed a hydrazide, whose tosylate was heated with sodium carbonate to give 4-methoxy-2,2′-bipyrrole-5-carboxaldehyde (VII), m.p. 265° dec. (found: C, 63.5; H, 5.6); λ_{max}^{MeOH} 251 mμ (ε 14,700), 361 (40,300). This compound appears identical with the natural prodigiosin precursor, reported[6] m.p. > 250°; λ_{max}^{EtOH} 254 mμ (ε 13,000), 363 (35,000). 2-Methyl-3-amylpyrrole[3d] and VII in methanolic hydrochloric acid[5] produce a deep red solution of the hydrochloride of I. Chromatography of the free base (I) on alumina gave a pure sample of synthetic prodigiosin whose infrared as well as ultraviolet and visible spectra under both acidic and alkaline conditions were identical with those of natural prodigiosin.[10,11]

Synthesis of the isomeric prodigiosin II proceeded in a similar sequence from methyl 4-methoxypyrrole-2-carboxylate,[7] m.p. 86° (found: C, 54.2; H, 6.0; OCH_3, 39.9). Condensation with Δ^1-pyrroline gave methyl 4-methoxy-5-(2′-pyrrolidinyl)-pyrrole-2-carboxylate which was dehydrogenated to methyl 3-methoxy-2,2′-bipyrrole-5-carboxylate (VIII), m.p. 178° (found: C, 60.2; H, 5.5; N, 12.8; OCH_3, 28.0). This was converted to the isomer of the prodigiosin precursor, 3-methoxy-2,2′-bipyrrole-5-carboxaldehyde (IX), m.p. 186°[5] (found: C, 63.3; H, 5.5); λ_{max}^{MeOH} 236 mμ (ε 12,400), 386 (26,800). Condensation of IX with 2-methyl-3-amylpyrrole gave II. In acid solution prodigiosin (I) absorbs at 535 mμ while the isomer II has its maximum at 585 mμ.

(10) We are indebted to Dr. M. C. Bachman of the Commercial Solvents Corporation for a sample of natural prodigiosin.

(11) The demonstration of a pyrryldipyrrylmethene nucleus for prodigiosin eliminates the one postulated, natural occurrence of a tripyrrylmethene and thus removes any support such an occurrence might give to the intermediacy of a tripyrrylmethene in porphyrin biosynthesis [D. Shemin, C. S. Russel, and T. Abramsky, *J. Biol. Chem.*, **215**, 613 (1955)]. However, prodigiosin now becomes the second natural substance containing a 2,2′-dipyrrole skeleton, vitamin B_{12} being the other [R. Bonnett, J. R. Cannon, V. M. Clark, A. W. Johnson, L. F. J. Parker, E. L. Smith and A. Todd, *J. Chem. Soc.*, 1158 (1957)].

(12) Public Health Service Predoctoral Research Fellow of the National Heart Institute.

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RECEIVED JULY 20, 1960

ALTERNATING COPOLYMERS OF DIMETHYLKETENE WITH KETONES

Sir:

High polymers in which the monomeric units are, at least in part, originated by the opening of the carbonyl bond of a ketone were not known up to now.

During our work on the polymerization of cumulative double bonds, we have found that by direct polymerization of mixtures of dimethylketene and acetone in the presence of lithium alkyls it is possible to obtain in good yields macromolecular products containing both monomers.

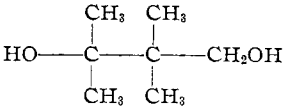
By adding, at −60°, 1.4 millimoles of butyllithium to a solution of dimethylketene (8 g.) and acetone (8 g.) in toluene (20 ml.), rapid polymerization takes place. After precipitation with methyl alcohol, 8 g. of a white solid polymer (I) is isolated. This product shows an intrinsic viscosity in chloroform at 30° of approximately 0.4, is soluble in boiling benzene and dioxane, and proves to be highly crystalline on X-ray examination. This result indicates that the polymer possesses a high regularity of structure.

The analysis of (I) demonstrates that dimethylketene and acetone are present in a molar ratio of 1:1.

Anal. Calcd. for $C_4H_6OC_3H_6O$: C, 65.60; H, 9.44. Found: C, 65.98; H, 9.55.

After reduction of the polymer, dissolved in tetrahydrofuran, with $LiAlH_4$, we have isolated in good yields (78%) a product (II) having m.p. 138–140°.

Composition analysis and molecular weight of (II) agree with the formula



Anal. Calcd. for $C_7H_{16}O_2$: C, 63.51; H, 12.18; mol. wt., 132. Found: C, 63.51; H, 12.12; mol. wt., 138.

The structure of this glycol also has been confirmed by comparison with the product obtained