4. Two alternative schemes of consecutive reactions are proposed to account for the self-oxidation reaction.

5. The ring-bound halogen of 2,4-dimethyl-3-carbethoxy-5-bromopyrrole is shown to have the oxidizing properties of a "positive halogen" atom.

6. A tripyrrylmethane is synthesized which can cleave to give two different dipyrrylmethenes, depending upon the condition of the reaction.

7. A dipyrrylmethene is converted into another dipyrrylmethene in a new type of "displacement reaction."

8. Further evidence is given to establish the structure of 3,5,4'-trimethyl-4,3'-dicarbethoxy-5'-bromo dipyrrylmethene.

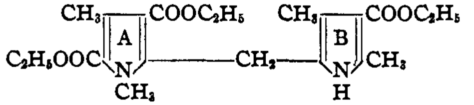
BALTIMORE, MD. RECEIVED MARCH 29, 1944

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

An Anomalous Reaction of Dipyrrylmethanes Leading to a New Class of Heterocyclic Compounds[1,2]

BY ALSOPH H. CORWIN AND RUDOLPH C. ELLINGSON[3]

In an investigation of the methylation of dipyrrylmethanes, Corwin, Bailey and Viohl[4] noted the development of a deep blue fluorescence upon treating 1,4,3',5'-tetramethyl-3,5,4'-tricarbethoxy dipyrrylmethane (I) with sodium. Corwin and Ellingson[5a] reported the isolation and analysis of the compound responsible for this effect and found that it could result from the elimination of the elements of ethanol from the dipyrrylmethane. Similar compounds are also reported by Corwin and Buc,[6] who develop additional methods for their investigation in the accompanying paper.



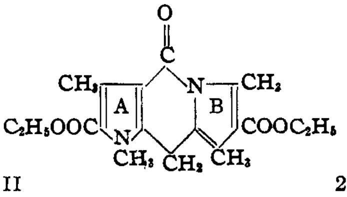
I

Compounds of this new class have aroused interest in the laboratory because their color and fluorescence in organic solvents markedly resemble those of crude oil. Since decomposition products of chlorophyll might conceivably be responsible for the fluorescence of crude oils and might also be related to these synthetic products, the possibility exists that analogs of these synthetic products occur in nature. Both for this reason and to clarify the mechanisms of the reactions involved, we deemed it worth while to investigate the structure of these substances.

It was found that the condensation reaction could be carried out conveniently in dioxane with sodium triphenylmethyl as a catalyst but that it failed in benzene in which the sodium salt of the dipyrrylmethane is insoluble. The reaction also fails if the 1-position is unmethylated or if a methyl group is in the 1'-position. The condensation is distinctly an anomalous reaction of dipyrrylmethanes since it is absent in the great majority of these substances studied.

The condensation product failed to react with phenylhydrazine, hydroxylamine and semicarbazide. This indicates that a true keto group is not present in the molecule. There are, however, ketones such as dipyrryl ketones and hindered aliphatic and aromatic ketones which fail to show the usual ketonic reactions.

The compound was titrated with sodium triphenylmethyl to determine the number of active hydrogen atoms present.[5c] A color indicative of an end-point was obtained as soon as the solvent blank had been passed in the titration, but this color is much deeper than that of sodium triphenylmethyl, itself. This same deep violet-red color appears during the formation of these compounds when sodium triphenylmethyl is the condensation catalyst. We attribute this color to the formation of a carbanion from the condensation product by the action of sodium triphenylmethyl and hence to the absence of an active N-H linkage and the presence of an active C-H linkage. These facts suggest that the observed elimination of ethanol involves the hydrogen atom originally present on Ring B of dipyrrylmethane I and strongly suggest that the compound has the structure of formula II. This conclusion is supported by the fact that methylation of the nitrogen on Ring B of dipyrrylmethane I blocks the reaction.



II 204°

The ring system postulated in structure II is new.

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[1] Studies in the Pyrrole Series, XIII; Paper XII, Corwin and Viohl, THIS JOURNAL, 66, 1137 (1944).

[2] This paper is from the doctoral dissertation of Rudolph C. Ellingson, The Johns Hopkins University, 1938, and was presented in part at the Boston Meeting of the American Chemical Society, September, 1939.

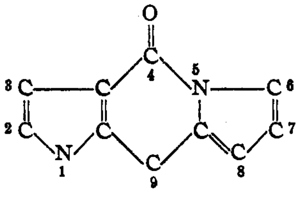
[3] Present address, Research Laboratory, Mead Johnson and Company, Evansville, Ind.

[4] Corwin, Bailey and Viohl, THIS JOURNAL, 64, 1271 (1942).

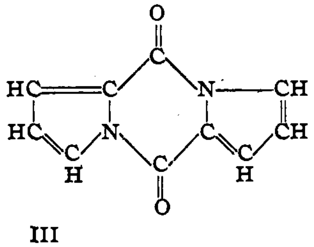
[5] Corwin and Ellingson, *ibid.*, (a) 2106, (b) 2101, (c) 2098 (1942).

[6] Corwin and Buc, *ibid.*, 66, 1151 (1944).

Dr. A. M. Patterson in a private communication has very kindly informed us that compound II, according to the nomenclature of *Chemical Abstracts*, should be called 1,3,6,8-tetramethyl-2,7-dicarbethoxy-dipyrrolo-(1,2-*a*,2′,3′-*d*)pyridine-4(9)-one. For convenience we may refer to it as a dipyrrolopyridine.



The nearest analog to the dipyrrolopyridone system is the pyrokoll ring[7] (III). The pyro-

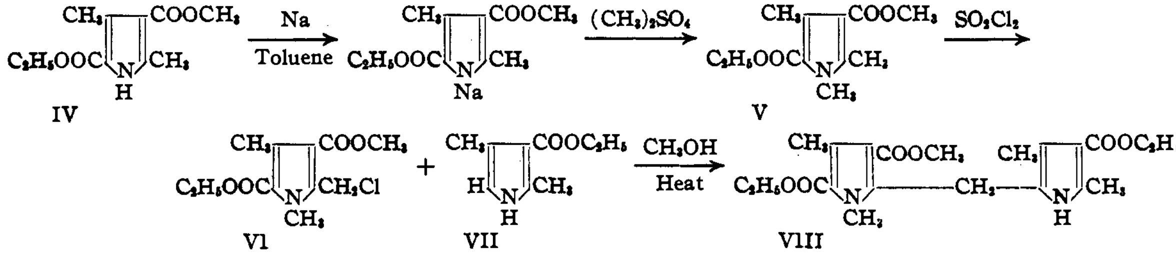


III

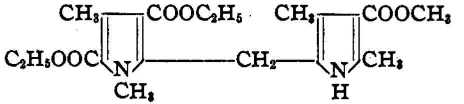
kolls are yellow crystalline materials which according to Ciamician[8] are surprisingly stable to fuming nitric acid. The new product is also stable to acid. It has been refluxed with alcohol, saturated with dry hydrogen chloride and no change took place. With sulfuric acid in water and acetic acid, a slight hydrolysis of a carbethoxy group occurred but most of the starting material was recovered unchanged.

To determine definitely which carbethoxy group is involved in the condensation, each carbethoxy group in the dipyrrylmethane was replaced in turn by a carbomethoxy group and the three isomeric dipyrrylmethanes were subjected to the condensation reaction. The first dipyrrylmethane prepared was 1,4,3′,5′-tetramethyl-3-carbomethoxy-4,5′-dicarbethoxydipyrrylmethane. This was synthesized as shown in Chart I.

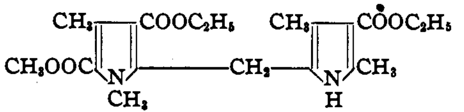
CHART I



This dipyrrylmethane (VIII) melts at 139°. When treated with sodium triphenylmethyl in dioxane, it undergoes the same color changes observed for 1,4,3′,5′-tetramethyl-3,5,4′-tricarbethoxy dipyrrylmethane (I). Analysis shows that the condensation product is derived from dipyrrylmethane VIII by the loss of the elements of methanol. By analogy, this establishes that the 3-carbethoxy group of compound I is the one involved in the condensation. The proof lacks decision in only one feature: the condensation product derived from compound VIII melts at 189–190° while that from compound I melts at 204°. There is no depression of the mixed melting point. The crystals appear identical under the microscope but repeated recrystallization fails to raise the melting point of the lower melting product. Hence the condensation products of the remaining isomers of compound VIII were prepared from dipyrrylmethanes IX and X.

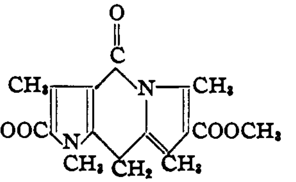


IX



X

The course of the preparations was similar to that sketched in Chart I. Dipyrrylmethane IX melts at 135°. On treatment with sodium triphenylmethyl in dioxane it undergoes the condensation reaction to yield a substance melting at 194°. We shall designate this as compound XI.



XI 194°

Analysis of this compound shows that one molecule of ethanol has been lost in the condensation, yet the substance undergoes no depression with its homolog melting at 204°. This shows that in this particular case the method of mixed melting points is not reliable as a means of demonstrating the difference between the compounds.

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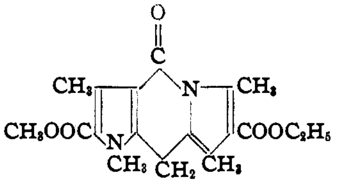
[7] Weidel and Ciamician, *Monatsh.*, **1**, 279 (1880).

[8] Ciamician, *Ber.*, **18**, 1456 (1885).

Dipyrrylmethane X melts at 130–131°. Its condensation product melts at 188° and, although the analysis is beyond the usual experimental error, it agrees best with the loss of the elements of ethanol. In spite of this, it shows no depression with its homolog melting at 204°.

This unsatisfactory state of affairs was finally cleared up by a more minute examination of the course of the reaction. Because of the known sensitivity to alkali of ester groups in the α-position of the pyrrole ring it was postulated that an alcohol interchange might have occurred in the course of the condensation in those cases in which the alcohol liberated by the condensation differed from that esterified in the α-position. Such a homolog could be present to the extent of 10% without throwing the analytical values for carbon and hydrogen beyond the experimental error. Experiment also showed that the extreme basicity of sodium triphenylmethyl was unnecessary for the reaction, sodium alkoxides being sufficiently basic to catalyze it. Therefore, the two dipyrrylmethanes I and VIII were treated with sodium methoxide and both gave a yellow compound melting at 210–211°, designated as compound XII.



XII 210–211°

On treatment of the same dipyrrylmethanes with sodium ethoxide, compound II melting at 204° was obtained. It was then discovered that compounds XII and II give a decisive depression on mixing, the mixed melt being 180–190°.

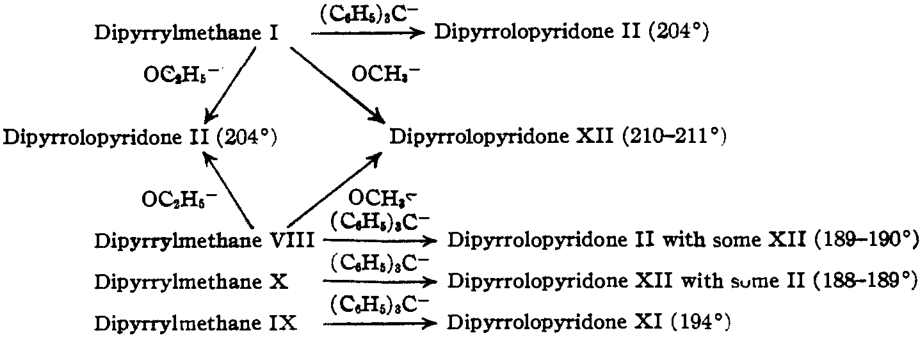
The fact that partial alcohol exchange takes place offers a plausible explanation for the paradox of low melting points and apparently correct analyses. Dipyrrylmethane VIII on condensation liberates methanol which can exchange with the carbethoxy group in the α-position giving rise to compound II with some XII as an impurity. This product melts at 189–190°. Condensation of dipyrrylmethane X liberates ethanol which exchanges with the carbomethoxy group in the α-position, yielding compound XII with some II as an impurity. The melting point of the mixture from VIII may be raised by shaking with sodium ethoxide. By this treatment the impurity XII is converted in part at least to compound II. Likewise the melting point of the mixture from X can be raised by shaking with sodium methoxide to eliminate the impurity II. These relationships are sketched in Chart II.

The fact that the analyses after the reaction with sodium triphenylmethyl agree best with those expected while the melting points are low shows that while the reactions of condensation and alcohol exchange proceed with comparable velocities, that of condensation must be somewhat more favored under the conditions of the experiment. If this were not true, equimolar mixtures of II and XII would result from the condensations of both VIII and X. Following this lead, the reaction with VIII was terminated by the addition of water after thirty-five seconds resulting in a product melting at 197–199° instead of 188–189° for the previous condensation of VIII and 204° for pure II. Dipyrrylmethane X similarly treated gave a product melting at 199–200° instead of 187–189° for the previous condensation product of X and 210–211° for the pure product. The product obtained in this manner gives a marked depression when mixed with compound II.

We thus feel that we are justified in concluding that the condensation reaction involves the ester group in the 3-position of Ring A. This conclusion is based primarily upon the analytical data. We conclude, further, that the clarity of the melting point data is vitiated by a rapid alcohol interchange during the condensation reaction and by a steeply descending melting point *vs.* composition curve of mixtures of II and XII. Mixed melting points are completely useless in contrasting II and XI, which give no depression.

The structural conditions for the formation of dipyrrolopyridones are that a dipyrrylmethane shall have an ester group in the 3-position and a free hydrogen in the 1′-position. Chemically, it is apparent that still a further factor may influence the formation of these compounds, namely,

CHART II



the relative acidities of the hydrogens on Rings A and B. The function of the base is to attack the hydrogen in Ring B with the formation of a sodium salt. If mono-sodium salt formation on Ring A takes place to the exclusion of that on Ring B, the striking power of the ester carbonyl group is reduced and the condensation fails to take place. This is illustrated in the failure, under our experimental conditions, of the reaction with 3,5,4′-tricarbethoxy-4,3′,5′-trimethyldipyrrylmethane, which differs from compound I only by the absence of the N–CH_3 on Ring A. The greater acidity of the N–H linkage on this ring was shown by Corwin and Ellingson.[5b]

Experimental Part

Properties of 1,3,6,8-Tetramethyl-2,7-dicarbethoxy-dipyrrolopyridone-4 (II).—The substance was prepared by the method of Corwin and Ellingson[5] who reported its analysis and molecular weight.

(A) **Attempted Hydrolyses.**—When compound II is dissolved in concentrated sulfuric acid, it gives a deep blue solution with a grass-green fluorescence. Addition of water precipitates the compound unchanged.

Ninety milligrams of II was suspended in 10 cc. of absolute ethanol and the suspension saturated with dry hydrogen chloride at 0°. The compound dissolved and the solution lost its fluorescence. After several hours a portion was diluted with water, precipitating the compound unchanged. The other portion was refluxed for several hours and then diluted with water. It also gave the starting compound unchanged.

A few milligrams was refluxed with a mixture of acetic acid, sulfuric acid and water. Hydrolysis of a carbethoxy group apparently took place to a slight extent but most of the material was recovered unchanged.

On warming the substance with a dry alcoholic solution of sodium ethoxide, water soluble materials were formed. It is possible that sufficient moisture entered this mixture to permit the saponification of the ester groups.

(B) **Active Hydrogen Determination.**—Fifty-nine milligrams of compound II was dissolved in 5 cc. of benzene and titrated by the method of Corwin and Ellingson.[5] The first drop of sodium triphenylmethyl solution caused the appearance of the characteristic violet color which deepened as more reagent was added. The depth of color of the solution was so great that it obscured the orange-yellow end-point color of sodium triphenylmethyl. An equimolar quantity of the reagent was added and the solution hydrolyzed and worked up as usual. The starting compound was recovered. We conclude that there is no imino-nitrogen present since this would give a colorless sodium salt. The colored salt is attributed to the presence of a CH linkage more acidic than triphenylmethane.

(C) **Attempted Ketone Reactions.**—Solutions of compound II were treated with the hydrochlorides of phenylhydrazine, hydroxylamine and semicarbazide. Only starting material could be recovered.

2,4-Dimethyl-3-carbomethoxy-5-carbethoxypyrrole[9] (IV).—Seventy-three grams of methyl acetoacetate and 325 cc. of glacial acetic acid were placed in a one-liter three-neck flask fitted with a stirrer, thermometer, dropping funnel and gas outlet. The temperature of the solution was brought to 80° and 164 g. of sodium acetate and 137 g. of zinc dust were added. The temperature was raised to 90° and a solution of 100 g. of isonitroso ethyl acetoacetate in 168 cc. of glacial acetic acid and 71 cc. of water was added in small portions over a period of one hour, the temperature being held between 100° and 108°. The reaction mixture was heated at 110° for two hours after which it was poured into 3 liters of ice water. The crude pyrrole was collected and crystallized from ethanol; yield, 96 g. or 68%; m. p. 130–131°.

1,2,4 - Trimethyl - 3 - carbomethoxy - 5 - carbethoxypyrrole (V).—In a one-liter flask fitted with a stirrer, thermometer, condenser and dropping funnel were placed 50 g. of 2,4-dimethyl-3-carbomethoxy-5-carbethoxypyrrole and 500 cc. of dry toluene. The solution was warmed to 98° and 6.0 g. of sodium metal was added in small pieces over a period of forty-five minutes, the temperature being held at 105–110°. The reaction mixture was kept at about 110° for ninety minutes, cooled to 90° and then 23 cc. of freshly distilled dimethyl sulfate was added dropwise over a period of thirty minutes. The reaction mixture was refluxed for one hour, filtered while hot to remove the sodium methyl sulfate and the filtrate was replaced in the flask and treated with one gram of sodium metal at 110° to precipitate unmethylated pyrrole as sodium salt. The solution was filtered from the unreacted sodium and steam distilled to remove the toluene. The oil remaining with the aqueous part solidified on cooling. The compound was purified by crystallization from methanol and water; yield 40 g. or 76%; m. p. 78–80°. For analysis the material was crystallized again from methanol and water and three times from hexane; m. p. 82°.

Anal. Calcd. for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16. Found: C, 60.38; H, 7.21.

1,3 - Dimethyl - 2 - carbethoxy - 4 - carbomethoxy - 5-chloromethylpyrrole (VI).—In a 500-cc. flask fitted with a stirrer, thermometer and dropping funnel were placed 30 g. of 1,2,4-trimethyl-3-carbomethoxy-5-carbethoxypyrrole and 200 cc. of glacial acetic acid. The solution was cooled to 10° and 12 cc. of sulfuryl chloride in 25 cc. of glacial acid was added over a period of ten minutes, the temperature being held between 10 and 20°. The temperature was raised to 70° and held there for forty-five minutes, then lowered to room temperature and chipped ice added to the reaction mixture. After the chloropyrrole had started to crystallize, water was added to the capacity of the flask. The crude product weighed 15 g. after drying. It crystallized from petroleum ether in soft fluffy fibers; m. p. 69–71°. The aqueous filtrate was diluted with water and allowed to stand for a day and then filtered. Eight grams of material was recovered; m. p. 85–87°. This by-product was neither purified nor identified.

Anal. Calcd. for $C_{12}H_{16}O_4NCl$: C, 52.65; H, 5.89. Found: C, 52.72; H, 5.98.

1,4,3′,5′ - Tetramethyl - 3 - carbomethoxy - 5,4′ - dicarbethoxy-dipyrrylmethane (VIII).—Four and twenty-six hundredths grams of 1,3-dimethyl-2-carbethoxy-4-carbomethoxy-5-chloromethylpyrrole and 2.50 g. of 2,4-dimethyl-3-carbethoxypyrrole were each dissolved in 7 cc. of methanol. The two solutions were combined and refluxed for three and one-half hours. After cooling, the solid was collected and washed with cold ethanol. The dipyrrylmethane crystallized in long colorless needles; yield, 5.19 g. or 82%; m. p. 137–138°. For analysis it was recrystallized three times from ethanol and water; m. p. 139°.

Anal. Calcd. for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98. Found: C, 62.26; H, 6.94.

Condensation of Compound VIII to a Substance Melting at 189–190°.—Five hundred milligrams (0.00124 mole) of 1,4,3′,5′-tetramethyl-3-carbomethoxy-5,4′-dicarbethoxy dipyrrylmethane in 10 cc. of dioxane was treated with 0.00123 mole of sodium triphenylmethyl solution in addition to that necessary for the blank on the dioxane. The same fluorescence and deep violet color appeared as for the higher homolog under the same conditions. The solution was treated in the same manner for the isolation of the condensation product; yield, 380 mg. of yellow powder which melted at 184–188° after one crystallization from ethanol. After three recrystallizations from alcohol and one from benzene and hexane, the substance melted at 189–190°. Mixed melting points with compound II melting at 204° were between the two melting points, showing no depression.

Anal. Calcd. for $C_{20}H_{24}N_2O_5$ (loss of methanol): C,

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(9) Küster, Weber, Maurer, Schlack, Niemann, Willig and Sclbayerbach, *Z. physiol. Chem.*, **121**, 135–163 (1922).

64.50; H, 6.49. Calcd. for $C_{19}H_{22}N_2O_5$ (loss of ethanol): C, 63.68; H, 6.19. Found: C, 64.51; H, 6.40.

1,4,3',5'-Tetramethyl-3,5-dicarbethoxy-4'-carbomethoxy-dipyrrylmethane (IX).—Four and twenty-eight hundredths grams of 1,3-dimethyl-2,4-dicarbethoxy-5-chloromethylpyrrole and 2.28 g. of 2,4-dimethyl-3-carbomethoxypyrrole[9] were each dissolved in 7 cc. of methanol and the two solutions combined and refluxed for three and one-half hours. After cooling, the solid was collected and washed with cold alcohol; yield, 5.07 g. or 84%; m. p., 134°. The material was crystallized four times from ethanol and water for analysis.

Anal. Calcd. for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98. Found: C, 62.45; H, 7.02.

1,3,6,8-Tetramethyl-2-carbethoxy-7-carbomethoxy-dipyrrolopyridone-4 (XI).—Three hundred milligrams (0.000744 mole) of 1,4,3',5'-tetramethyl-3,5-dicarbethoxy-4'-carbomethoxy-dipyrrylmethane dissolved in 10 cc. of dioxane was treated with 0.00075 mole of sodium triphenylmethyl solution beyond the blank of the solvent. The typical fluorescence and deep violet color appeared. The material was isolated as described previously; 160 mg. of a yellow powder melting at 181–185° was obtained. After three recrystallizations from absolute ethanol the melting point was 194°. The yellow compound shows no depression on mixed melt with its higher homolog, compound II, yet analysis shows it to have one carbon and two hydrogen atoms less than II.

Anal. Calcd. for $C_{19}H_{22}N_2O_5$: C, 63.68; H, 6.19. Found: C, 63.59; H, 6.29.

Isonitroso Methyl Acetoacetate.—One hundred sixteen grams of methyl acetoacetate, 200 cc. of glacial acetic acid and 1 kg. of crushed ice were placed in a flask and stirred; 75 g. of sodium nitrite in 180 cc. of water was added to the cold mixture and the stirring continued for three hours. After the ice had melted, enough sodium hydroxide solution was added to leave the solution slightly on the acid side. The solution was extracted several times with ether, the extracts totalling about 700 cc. The ether extracts were dried over sodium sulfate, filtered and the ether was removed at the water pump with slight warming. The thick, orange oil was crystallized by adding a few cubic centimeters of carbon tetrachloride and shaking. The solid was collected, washed twice with carbon tetrachloride, once with hexane and finally crystallized from carbon tetrachloride; yield, 80 g. of a straw-colored solid. The compound is quite hygroscopic.

2,4-Dimethyl-3-carbethoxy-5-carbomethoxypyrrole.[9]—Seventy-two grams of ethyl acetoacetate and 285 cc. of glacial acetic acid were placed in a one-liter, three-neck flask fitted with a stirrer, thermometer, condenser and dropping funnel. The temperature was raised to 80° and 144 g. of sodium acetate and 120 g. of zinc dust were added. The temperature was then raised to 90° and a solution of 80 g. of isonitroso methyl acetoacetate in 147 cc. of glacial acetic acid and 62 cc. of water was added in small portions so that the temperature remained between 100 and 106°. The solution was refluxed at 110° for two hours, poured into 3 l. of ice water and filtered. The pyrrole was crystallized from 800 cc. of ethanol, coming out in long colorless needles; yield, 67 g. or 54%; m. p. 164°.

1,2,4-Trimethyl-3-carbethoxy-5-carbomethoxypyrrole.—Forty-one grams of 2,4-dimethyl-3-carbethoxy-5-carbomethoxypyrrole was dissolved in 500 cc. of toluene and warmed to 100°; 5 g. of metallic sodium was added in small pieces over a period of thirty minutes and the reaction mixture was warmed and stirred an additional eighty minutes. Twenty cubic centimeters of freshly distilled dimethyl sulfate was added over a period of thirty minutes and the reaction mixture held at 110° for ninety minutes. The hot toluene solution was filtered from the sodium methyl sulfate and steam distilled to remove the toluene. The oil left in the flask solidified on cooling. The product was crystallized from alcohol and water, coming out as colorless needles; yield, 32 g. or 74%; m. p. 86–87°.

Anal. Calcd. for $C_{12}H_{17}O_4N$: C, 60.24; H, 7.16. Found: C, 60.19; H, 7.23.

1,3-Dimethyl-2-carbomethoxy-4-carbethoxy-5-chloromethylpyrrole.—Thirty-two grams of 1,2,4-trimethyl-3-carbethoxy-5-carbomethoxypyrrole was dissolved in 225 cc. of glacial acetic acid and cooled to 10°. Twelve cubic centimeters of sulfuryl chloride was added over a period of twelve minutes, the temperature being kept at 10–15°. After about two-thirds of the sulfuryl chloride had been added, the pyrrole crystallized, filling the solution completely. The temperature was raised to permit addition of the remaining reagent and then was taken to 70° and held there for thirty minutes. The reaction mixture was next cooled to room temperature and the flask filled with cold water. The solid was collected and air-dried; yield, 30 g. or 82%; m. p. 99–100°.

Anal. Calcd. for $C_{12}H_{16}O_4NCl$: C, 52.65; H, 5.89. Found: C, 52.68; H, 5.94.

1,4,3',5'-Tetramethyl-3,4'-dicarbethoxy-5-carbomethoxy-dipyrrylmethane (X).—Ten grams of 1,3-dimethyl-2-carbomethoxy-4-carbethoxy-5-chloromethylpyrrole was dissolved in 30 cc. of methanol and 6.1 g. of 2,4-dimethyl-3-carbethoxypyrrole was dissolved in 15 cc. of methanol. The two solutions were combined and refluxed for three and one-half hours. The solution was cooled and the solid collected and washed with cold alcohol. It was crystallized from ethanol and water; yield, 8.5 g. or 58%; m. p. 129–130°. For analysis, a sample was crystallized twice again from ethanol and water; m. p. 130–131°.

Anal. Calcd. for $C_{21}H_{28}N_2O_6$: C, 62.36; H, 6.98. Found: C, 62.34; H, 6.95.

Condensation of Compound X to a Substance Melting at 188–189°.—Three hundred fifty milligrams (0.000868 mole) of 1,4,3',5'-tetramethyl-3,4'-dicarbethoxy-5-carbomethoxy-dipyrrylmethane in 10 cc. of dioxane was treated with 0.00087 mole of sodium triphenylmethyl solution beyond the solvent blank. The typical fluorescence and violet color appeared. The solutions from three such experiments were combined, poured into water, heated to remove the benzene and ether and cooled. The solid was collected and washed with hexane to remove the triphenylmethane. 0.66 g. of yellow powder was obtained; m. p. 180–186°. After one crystallization from ethanol the compound melted at 188°. A sample for analysis was obtained by crystallizing the compound again from ethanol and then from a benzene–hexane mixture; m. p. 188–189°.

Anal. Calcd. for $C_{19}H_{22}N_2O_5$: C, 63.68; H, 6.19. Calcd. for $C_{20}H_{24}N_2O_5$: C, 64.50; H, 6.49. Found: C, 63.94; H, 6.35.

It will be noted that this analysis is beyond the usual error of the analytical method, ±0.10% for C and H.

Formation of 1,3,6,8-Tetramethyl-2,7-dicarbethoxy-dipyrrolopyridone-4 (II) with Sodium Ethoxide. A.—Five hundred seventy milligrams of 1,4,3',5'-tetramethyl-3,5,4'-tricarbethoxy-dipyrrylmethane (I) was shaken with 15 cc. of absolute ethanol in which a small piece of sodium metal had been dissolved. The methane slowly dissolved and the solution turned yellow with a green fluorescence. After four hours the yellow crystalline material was collected and dried; yield, 0.27 g.; m. p. 201°. This sample showed no depression with the compound melting at 204° obtained with sodium triphenylmethyl as the catalyst.

B.—Five hundred eighty milligrams of 1,4,3',5'-tetramethyl-3-carbomethoxy-5,4'-dicarbethoxy-dipyrrylmethane (VIII) was treated exactly as in A. The 385 mg. of crude yellow powder obtained was crystallized from ethanol; m. p. 202°. There was no depression on mixed melt with the compound melting at 204°. The compound was crystallized twice for analysis.

Anal. Calcd. for $C_{20}H_{24}N_2O_5$: C, 64.50; H, 6.49. Found: C, 64.36; H 6.40.

Formation of 1,3,6,8-Tetramethyl-2-carbomethoxy-7-carbethoxy-dipyrrolopyridone-4 (XII) with Sodium Meth-

oxide. **A.**—Four hundred milligrams of compound I was treated as in A above except that absolute methanol was used as the solvent; yield, 300 mg.; m. p., 209–210°.

B.—Four hundred milligrams of compound VIII was treated as in B above except that absolute methanol was used as the solvent; yield, 300 mg., m. p. 207°; crystallized again for analysis, m. p. 210–211°; mixed m. p. with compound II, 180–190°.

Anal. Calcd. for $C_{19}H_{22}N_2O_6$: C, 63.68; H, 6.19. Found: C, 63.55; H, 6.24.

Purification of the Mixed Dipyrrolopyridones by Alcohol Exchange, A.—A sample of the mixed dipyrrolopyridones obtained by the condensation of compound VIII with sodium triphenylmethyl and melting at 188–190° was shaken with sodium ethoxide. The melting point was raised to 195–196° by a single treatment. A pure sample of compound II melts at 204°.

B.—A sample of the mixed dipyrrolopyridones obtained by the condensation of compound X with sodium triphenylmethyl and melting at 187–189° was shaken with sodium methoxide. The melting point was raised to 206–207°.. A pure sample of compound XII melts at 210–211°.

Rapid Condensation of Compound VIII with Sodium Triphenylmethyl.—One hundred seventy-seven milligrams (0.00044 mole) of dipyrrylmethane VIII in 5 cc. of dioxane was treated with 0.00045 mole of sodium triphenylmethyl solution and thirty-five seconds later was worked up in the usual manner. 130 mg. of the yellow material was obtained. After one crystallization from ethanol the melting point was 195–197°. Two additional recrystallizations raised the melting point to 197–199°. The compound showed no depression on mixed melt with the sample of compound II melting at 204° obtained by the condensation of compound I.

Rapid Condensation of Compound X with Sodium Triphenylmethyl.—One hundred eighty milligrams (0.000446 mole) of dipyrrylmethane X in 5 cc. of dioxane was treated with 0.00046 mole of sodium triphenylmethyl and sixty seconds later 10 cc. of water was added and the solution was worked up in the usual manner. 85 mg. of the yellow powder was obtained. After one crystallization this melted at 195–197°. Another crystallization raised the melting point to 199–200°. Mixed melting point with compound II melting at 204° obtained by condensation of compound I depresses to 189–190°.

Anal. Calcd. for $C_{19}H_{22}N_2O_6$: C, 63.68; H, 6.19. Found: C, 63.60; H, 6.15.

Summary

1. The structure of the pyrrole derivatives earlier observed to fluoresce like lubricating oil has been investigated.

2. These substances belong to a new heterocyclic system and are called dipyrrolopyridones. A typical compound is 1,3,6,8-tetramethyl-2,7-dicarbethoxydipyrrolo-(1,2-*a*,2',3'-*d*)pyridine-4(9)-one, formed by the condensation of 1,4,3',5'-tetramethyl-3,5,4'-tricarbethoxy-dipyrrylmethane with basic catalysts.

3. By progressive "tagging" of the ester groups with methanol it was shown that the ester group in the 3 position is involved in the condensation and that the others are not.

4. The structural determination was complicated by alcohol exchange in the ester group on the alpha position.

5. Two of the homologs in this series fail to give a depression by the mixed point determination.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

The Formation of Dipyrrolopyridones in the Course of a Proposed Porphyrin Synthesis[1,2]

BY ALSOPH H. CORWIN AND SAUL R. BUC[3]

The stepwise condensation of pyrrole derivatives to give linear tetrapyrryl compounds capable of producing porphyrins would provide the most simple and logically satisfying method for the preparation of rings in which the sequence of substituents on all of the positions capable of substitution in the porphyrin ring would be rigorously established. Such a synthesis has not been achieved. Because of the desirability of accomplishing this, we undertook the preparation of suitable tetrapyrryl compounds from the most readily available pyrrole with suitable substituents, 2,4-dimethyl-3,5-dicarbethoxypyrrole. This proposed synthesis was blocked by the intervention of an unexpected reaction whose investigation now permits us to delimit the conditions under which such a synthesis might succeed.

The point of departure was 3,5,3',5'-tetracarbethoxy-4,4'-dipyrrylmethane (I, Chart I) which is the most readily available dipyrrylmethane.[4] It was found possible to saponify a single carbethoxy group in this compound yielding the mono-basic acid II in surprisingly good yields. This substance was then readily decarboxylated to give the dipyrrylmethane III which was condensed with formaldehyde to yield the tetrapyrryl compound IV. The projected saponification of this substance failed for reasons which were not rigorously established but which are strongly suggested by the studies recorded below. The successful reactions involved are sketched in Chart I.

Since we were unable to saponify compound IV, we attempted to saponify compound III instead with the objective of condensing the carboxylic acid to a tetrapyrryl compound and

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(1) Studies in the Pyrrole Series XIV; Paper XIII, Corwin and Ellingson, THIS JOURNAL, **66**, 1146 (1944).

(2) This paper is from the doctoral dissertation of Saul R. Buc, The Johns Hopkins University, 1938. The major portion of it was presented at the Baltimore meeting of the American Chemical Society, April, 1939.

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(4) Corwin, Bailey and Viohl, THIS JOURNAL, **64**, 1267 (1942).