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 $C_{19}H_{22}N_2O_5$: 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 $C_{19}H_{22}N_2O_5$: 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.

BALTIMORE, MD. RECEIVED MARCH 2, 1944

[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

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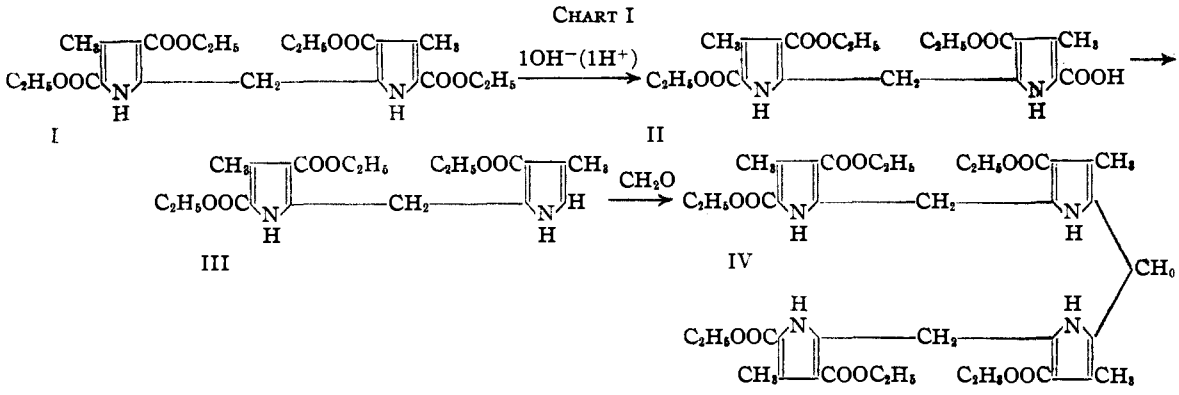
(4) Corwin, Bailey and Viohl, THIS JOURNAL, **64**, 1267 (1942).

CHART I



then decarboxylating the resulting substance. When the reaction was attempted it became apparent immediately that it was not following a normal course. Upon addition of alkali to a boiling alcoholic solution of compound III a brilliant display of color takes place. A light yellow color develops and darkens rapidly through orange to deep orange-red. This then becomes lighter very slowly as the reaction proceeds, so that the final liquor is light amber. If one mole of alkali is used, there are two products obtained. The minor product, comprising about 8% of the weight of the starting material, is a water insoluble, beautifully crystalline, yellow compound. Its structure has not been determined. The principal product is a sodium salt which may be recrystallized from a very small amount of water or better from 50% ethanol. It is easily demonstrated that this is not the sodium salt of the expected acid. Upon preparation of the acid from its salt and subsequent decarboxylation, a compound is obtained which is not identical with the known di-α-free methane which would be expected from compound III. Also, on esterification of a small sample of the free acid with diazomethane, a compound was obtained which did not melt up to 250° and therefore could not be the starting compound since this melts at 186–187°. We have not investigated this substance further. We conclude that a rapid, base-catalyzed reaction other than saponification is occurring simultaneously with the saponification. This conclusion is justified by the behavior of compound III in the presence of very dilute alkali using only 5% of the amount used in the attempted saponifications. Under these conditions a similar display of color occurs and a product is precipitated from the mother liquor at the boiling point within fifteen minutes after the reaction is begun. This new product may be crystallized from dioxane or acetic acid, yielding a bright yellow micro-crystalline precipitate from the former and orange crystals from the latter. Its analysis shows that it is formed from the original molecule by the loss of one molecule of ethanol. A molecular weight determination eliminates the possibility of a bimolecular condensation. We are therefore forced to formulate an internal condensation. By analogy with the reaction discussed in the preceding paper[1] we formulate the condensation as proceeding to a dipyrrolopyridone (Chart II).

CHART II

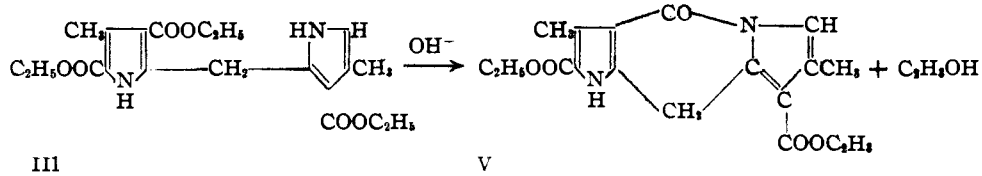


CHART III

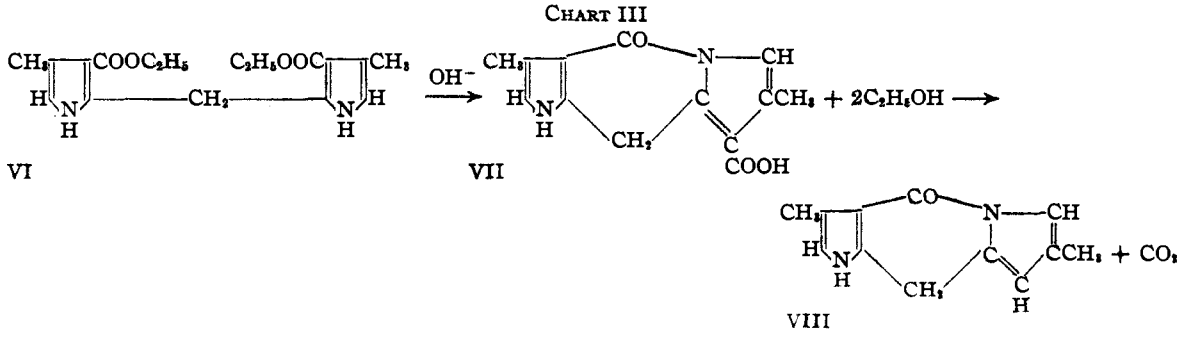
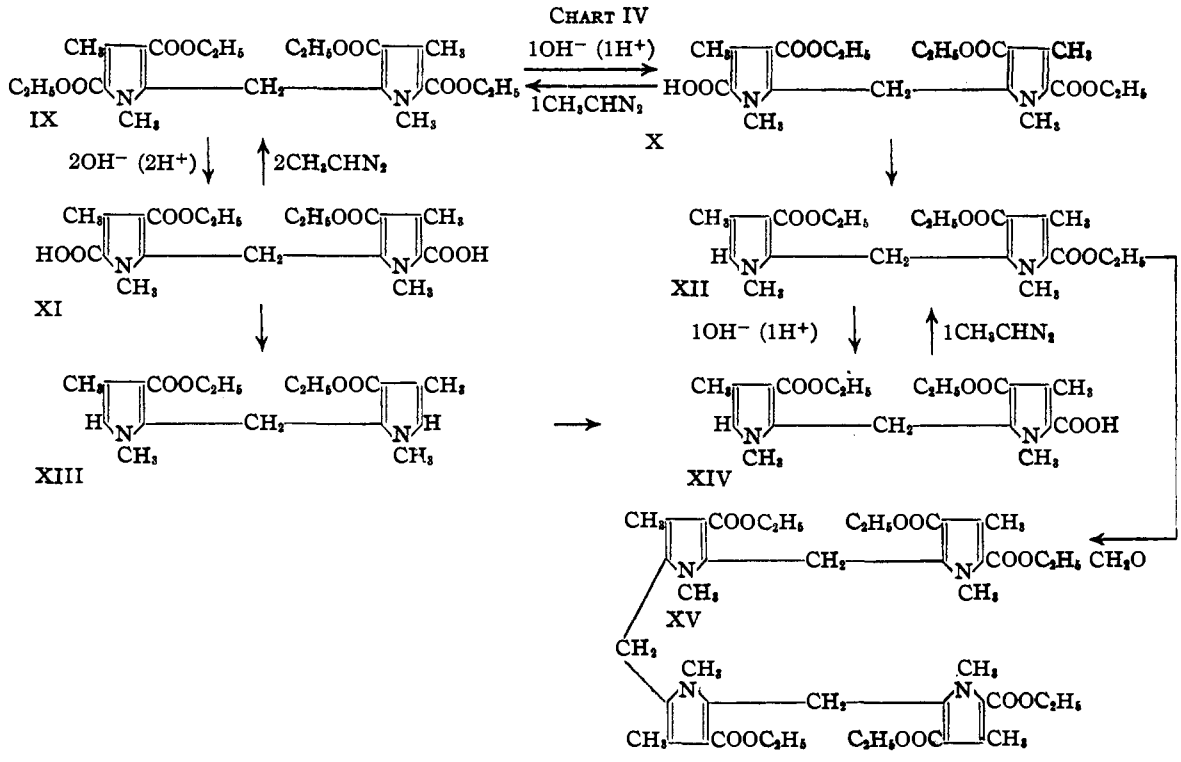


CHART IV



Compound V is indistinguishable to the eye in color or fluorescence from the dipyrrolopyridones reported by Corwin and Ellingson. In the present instance the formulation of a condensation by the β-carbethoxy group is strengthened by an analogous reaction in the same series (Chart III).

When the di-α-free methane VI is saponified with one mole of alkali and the product acidified, an acid is obtained which, if our reasoning is valid, should have the structure VII. This product was decarboxylated and analyzed, giving results in excellent agreement with the structure of formula VIII. Conceding the analogy between the reactions of Charts II and III on the basis of the similarity in structure and fluorescence, we have demonstrated that it is a β- and not the α-carbethoxy group which is involved, for we now have obtained a condensation with loss of ethanol in the absence of any α-carbethoxy group.

In the condensation of Chart II, we must still choose between the two β-carbethoxy groups in the formulation of the product. We formulate the loss of the ethoxyl group from the carbethoxy of Ring A without rigid proof but on the basis of analogy. Compound VI (Chart III) undergoes the condensation while compound I (Chart I) does not. We interpret this as indication that an α-carbethoxy group prevents condensation on the nitrogen adjacent to it. On this basis, ring A of compound III should condense to give compound V.

As would be predicted, blocking of the imino nitrogens with methyl groups blocks the condensation and permits normal saponification to proceed. The reactions which have been performed with N-methylated methanes are given in Chart IV.

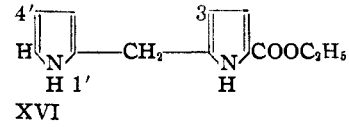
The normal course followed by the saponification of compound XII confirms the involvement of an imino hydrogen in the condensation of compound III.

It is conceivable that a tetra-N-methyl leuco porphyrin might be obtained by the saponification, decarboxylation and condensation of compound XV, since such a compound would not necessarily be planar and the four N-methyl groups need not interfere with each other. The porphyrin ring itself, however, is planar so in the oxidized form the four methyl groups would have to occupy the space ordinarily filled by the metallic atom in metallo-porphyrin complexes. It is conceivable that accommodation might take place by bending of bonds as in the case of the di-N-methyl dipyrrylmethenes[5] but the accommodation forces would be so much greater in the present instance that we are inclined to doubt the possibility of the existence of this compound. We concede, however, that accommodation may take place with the elimination of methyl groups to give a less highly methylated porphyrin.

Because of the peculiarities of the saponification of the compounds studied above, we are prepared to delimit the conditions under which a stepwise porphyrin synthesis of the type proposed above might succeed. These are: (1)

(5) Brunings and Corwin, THIS JOURNAL, 64, 593 (1942); 66, 337 (1944).

Carbalkoxy groups must be absent from positions 3 and 4′ of the dipyrrylmethane molecule (XVI) or (2) if carbalkoxy groups are present in these positions, position 1′ must be alkylated or otherwise blocked during the saponification.



XVI

It is necessary to specify that no ester group shall be in the 4′ position because of the possibility of a condensation of the type found above taking place in the tetrapyrryl compound after condensation, during saponification. If saponification took place in the dipyrrylmethane stage and were followed by condensation, this condition could be relaxed.

Experimental Part

Saponification of 3,5,3′,5′-Tetracarbethoxy-4,4′-dimethyl-dipyrrylmethane.[6]—The saponification is carried out in ethanol using sodium hydroxide. If one mole of the alkali is used, the mono-sodium salt will be the predominant product. If two moles are used, the di-sodium salt will predominate. In either case both will be present as will unchanged starting compound. The separation of the two sodium salts is readily effected by taking advantage of their differing solubilities in water and in solutions of sodium chloride.

The mono-sodium salt is soluble to the extent of 5 g. per liter in water at room temperature and obeys the laws of the solubility product. The solubility of the di-sodium salt was determined roughly at several concentrations of sodium chloride and was found to be as follows

% Saturation of NaCl	Solubility of di-Na salt, g./l.
0	125
10	84
20	72
45	9
75	1
100	Negligible

Both salts have very large temperature coefficients of solubility.

The preparative procedure for the mono-acid will be described. The procedure for the di-acid is essentially the same except for the amount of alkali used and the amounts of the products.

Two hundred grams of dipyrrylmethane I is dissolved in one liter of boiling ethanol in a 2-liter round-bottom flask fitted with a reflux condenser; 17 g. of sodium hydroxide dissolved in 100 cc. of water is dropped in over a period of seven hours, the solution being maintained at the boiling point throughout. Boiling is continued for an hour after all the alkali is added; 20 g. of charcoal is then added and boiling continued for twenty minutes. The solution is then filtered and evaporated to dryness, leaving a light brown soapy mass. This is extracted three times with boiling water, heating on steam the first time to bring the solid cake into solution; 900 cc. is used for the first extraction, 450 cc. for the next two. In each extraction, the mixture is filtered hot and the filtrate brought to 10% saturation with sodium chloride by the addition of saturated sodium chloride solution. This requires 100 cc. of solution for the first extract, 50 cc. for the second and third. Upon cooling, a large amount of mono-sodium salt precipitates from the first extraction liquor, less from the second and very little from the third. The second precipitate is now recrystallized from the third mother liquor, and the first from the second and then from the third. The combined precipitates are then recrystallized once from 15% saturated sodium chloride by dissolving in 1275 cc. of hot water and adding 225 cc. of saturated sodium chloride solution.

The solid residue from the three aqueous extractions is recrystallized from ethanol and the precipitate, which is recovered starting compound, is filtered off. The ethanol is then heated to boiling and an equal volume of boiling water added. On cooling, a second crop of recovered starting compound is obtained. The total recovery is 57 g.

The combined mono-sodium salt fractions are dissolved in hot ethanol and an equal volume of hot water is added, together with the liquor from the recrystallization of the recovered starting compound. Dilute hydrochloric acid is added with vigorous stirring until the congo red end-point is reached. A heavy precipitate of mono-acid (II) results. This is filtered off and washed three times with hot ethanol. The oven-dried product weighs 72 g. The mother liquor and combined washings yield 5 g. additional on standing; total yield of mono-acid, 77 g. or 58%.

The mother liquors from which the mono-sodium salt was precipitated are saturated with sodium chloride, yielding the di-sodium salt which they contain. This is recrystallized twice from 75% saturated sodium chloride, taken up in boiling ethanol and the di-acid precipitated by addition of hydrochloric acid to the congo red end-point. The product is filtered, washed with hot water, dried and weighed; yield, 14 g. or 12%.

The mono-acid may be recrystallized from ethanol or acetic acid, although the product obtained by the procedure given is pure enough for subsequent reactions. Beautiful crystals may be obtained by dissolving a gram of the acid in 200 cc. of boiling acetic acid, adding boiling water to incipient crystallization and allowing to cool.

Anal. Calcd. for $C_{21}H_{26}N_2O_8$: C, 58.05; H, 6.04. Found: C, 58.12; H, 6.07.

Re-esterification with Diazo-ethane.—The technique of the esterification will be described in detail for the di-acid and will not be repeated for subsequent preparations since the procedure is identical. The only precautions necessary concern the protection of the operator since both diazoethane and the N-nitroso-N-ethylurethan from which it is prepared are highly toxic. The entire procedure is therefore carried out in the best hood available and care is taken not to let the hands come into contact with the diazoethane or the urethan.

In a 100-cc. distilling flask connected to a long condenser with an adapter are placed 0.5 cc. of N-nitroso-N-ethylurethan, 20 cc. of absolute ether and 1 cc. of 25% potassium hydroxide in absolute methanol. The flask is then stoppered and heated with warm water. The distillate is caught in a 25-cc. Erlenmeyer flask containing 0.1233 g. of the pure di-acid. The distillation is discontinued when the drops are no longer yellow. A slow evolution of nitrogen takes place and the di-acid goes into solution. When no more reaction is apparent, the ether is evaporated and the product weighed; yield, 0.1389 g. or 99% of the tetracarbethoxy-dimethyl-dipyrrylmethane, m. p. 134°; mixed melting point with an authentic sample, 134–135°.

The rate of esterification seems to depend upon the solubility of the acid in ether. Most go rather slowly but in cases in which the acid is highly soluble, the reaction evolves nitrogen with great rapidity.

A sample of the mono-acid was esterified by the same procedure and the product shown to be identical with the starting methane by melting point and mixed melting point.

3,5,3′-Tricarbethoxy-4,4′-dimethyl-dipyrrylmethane (III).—In a 250-cc. round-bottom flask fitted with a thermometer are placed 27 g. of mono-acid II, 50 cc. of anhydrous glycerol and 0.5 cc. of quinoline. The temperature is brought rapidly to 240° using two burners and is maintained at this temperature for three minutes. The burners are then extinguished and alcohol is added in a thin stream from a wash bottle, using great caution at

(6) Fischer and Halbig, *Ann.*, **447**, 134 (1926).

first, until the temperature is brought down to 100°. The flask is then set aside to cool. Crystals begin to deposit while it is still quite hot. After standing on ice for several hours the entire mass solidifies. The product is filtered off and recrystallized from ethanol, in which it is soluble to the extent of 30 g. per liter at the boiling point and 2 g. per liter at ice box temperature. By pouring the mother liquors into water and recrystallizing the impure precipitate, a second crop is obtained; total yield, 21.0 g. or 86.5%; m. p. 187°; mixed m. p. with corresponding di-α-free methane, 150–160°. The product is recrystallized five times from ethanol for analysis.

Anal. Calcd. for $C_{20}H_{26}N_2O_6$: C, 61.52; H, 6.71; active H, 2. Found: C, 61.38; H, 6.64; active H,[7] 1.96, 2.10.

It should be remarked that the yield in this decarboxylation is quite insensitive to increased temperature. Several smaller runs were heated to 285° without appreciable loss of yield. This is surprising since such a temperature in the decarboxylation of the corresponding di-acid results in complete loss of the sample, as judged from failure to obtain any crystalline product. We conclude that the α-carbethoxy group exerts some sort of stabilizing influence on the system.

By-product from the Decarboxylation.—The alcoholic mother liquors from the crystallizations were evaporated to dryness, leaving a very tarry residue. This was recrystallized repeatedly from benzene, using charcoal in the first recrystallization, and finally yielded 0.2 g. of a pure white compound, m. p. 184–185°; mixed m. p. with the major product, 162–165°. Under the microscope the compound appeared as extremely long needles, so long that they appeared filamentous and were tangled. The analysis corresponds to that of an isomer of the main product, perhaps one in which the second ring is reversed.

Anal. Calcd. for $C_{20}H_{26}N_2O_6$: C, 61.52; H, 6.71; active H, 2; mol. wt., 390. Found: C, 61.43; H, 6.69; active H,[8] 1.88; mol. wt. (ebulliometric in $CHCl_3$), 401.

Preparation of Tetrapyrrane IV.—One gram of 3,5,3′-tricarbethoxy-4,4′-dimethyl-dipyrrylmethane (III) was dissolved in 35 cc. of boiling ethanol and 1 cc. of 40% formalin and 1 cc. of concentrated hydrochloric acid were added. In a few minutes the product began to separate and the solution had to be stirred to prevent bumping. Boiling was continued for ten minutes and the solution then cooled and filtered; yield, 0.86 g. or 85%. The product is almost totally insoluble in ethanol, chloroform, benzene and other ordinary solvents. It is soluble in pyridine, acetic acid and normal butanol at their boiling points and may be recrystallized satisfactorily from either of the latter two. It has a slight pinkish color which was not removed by recrystallization; m. p. 216–217°, with decomposition.

Anal. Calcd. for $C_{41}H_{52}N_4O_{12}$: C, 62.11; H, 6.61. Found: C, 61.93; H, 6.65.

Attempted Saponification of Tetrapyrrane IV.—Attempts to saponify tetrapyrrane IV with sodium hydroxide in aqueous alcohol and in aqueous pyridine led only to dark brown or black material from which no crystalline acid could be isolated. The product was soluble in ethanol in the cold and in most other solvents when hot except hexane.

Attempted Saponification of Dipyrrylmethane III.—Treatment of 1 g. of dipyrrylmethane III with an equimolar quantity of alkali by the method described above leads to the display of color described after Chart I. Distillation of the ethanol causes formation of a precipitate which was filtered off and recrystallized from ethanol; yield, 0.140 g. Solutions of this material have a strong purple fluorescence. The analytical data suggest that the substance is impure.

Anal. Found: C, 67.34, 67.54; H, 5.95, 5.84[9]; mol. wt. (in $CHCl_3$), 293.

The filtrate was evaporated to dryness, crystallized from 10 cc. of water, and the filtered crystals washed with cold water. More crystals were recovered from the mother liquor by heating and precipitating with ethanol; total yield of sodium salts, 0.750 g.

The free acid was prepared by acidification: 100 mg. was treated with diazoethane in ether. Evolution of nitrogen was extremely slow and the esterification incomplete. On filtering off and evaporating the ethereal solution, a few crystals were obtained; m. p. over 205°. The substance is therefore not dipyrrylmethane III.

1.5 g. of the sodium salt was crystallized twice from hot water and the acid precipitated with hydrochloric acid; yield 1.2 g. of acid. This was heated in 3 cc. of anhydrous glycerol over a free flame to complete the evolution of carbon dioxide, cooled and alcohol added; yield, 1.0 g. of yellow-green crystalline powder, which can be crystallized from ethanol, acetic acid or pyridine; m. p. over 250°. The substance is therefore not dipyrrylmethane VI.

2,8-Dicarbethoxy-3,7-dimethyl-dipyrrolopyridone-(4) (V).—One gram of 3,5,3′-tricarbethoxy-4,4′-dimethyl-dipyrrylmethane (III) was dissolved in 60 cc. of ethanol at the boiling point and 40 cc. of water added; 0.14 cc. of 1 *N* sodium hydroxide solution, 5% of the equivalent amount was added. The solution turned bright orange, then lighter to yellow. After fifteen minutes of refluxing, a precipitate started to separate and in an hour it had become quite heavy. Refluxing was continued for three hours and the solution was then evaporated to dryness. The residue was washed twice with hot water and then recrystallized from dioxane; yield, 0.30 g. or 34% of a yellow, micro-crystalline product. The new compound is very sparingly soluble in alcohol, benzene and chloroform. It crystallizes from acetic acid in large orange needles which darken at 235° and decompose at 245°. They show no extinction under crossed nicols. A sample was recrystallized six times from glacial acetic acid for analysis.

Anal. Calcd. for $C_{18}H_{20}N_2O_5$: C, 62.78; H, 5.85; mol. wt., 344. Found: C, 62.75; H, 5.73; mol. wt. (ebullioscopic in $CHCl_3$), 349.

3,7-Dimethyl-dipyrrolopyridone-(4) (VIII).—One gram of 3,3′-dicarbethoxy-4,4′-dimethyl-dipyrrylmethane (VI) was dissolved in a boiling mixture of 60 cc. of ethanol and 40 cc. of water. One equivalent of sodium hydroxide was added and refluxing continued for two and one-half hours. The solution was evaporated on a steam-bath to remove the alcohol and filtered to remove a negligible amount of tarry material. The filtrate was heated and acidified with hydrochloric acid, yielding 0.72 g. of a dark yellow acid. This was suspended in 1 cc. of dry glycerol and heated on an oil-bath until decarboxylation was complete. Ethanol was added from a wash-bottle whereupon a crystalline product separated instantly. It was recrystallized three times from glacial acetic acid for analysis. Losses in recrystallization were very high and only 30 mg. of analytical sample was obtained.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 71.97; H, 6.04. Found: C, 71.83; H, 5.97.

Saponification of 1,4,1′,4′-Tetramethyl-3,5,3′,5′-tetracarbethoxy-dipyrrylmethane (IX).—Eighty-four grams (0.171 mole) of dipyrrylmethane IX was dissolved in a liter of alcohol and 8 g. (0.20 mole) of sodium hydroxide added. The mixture was refluxed for eight hours and then evaporated to dryness. The mono- and di-sodium salts and unchanged starting compound were separated by the procedure described for the saponification products of dipyrrylmethane I, described above. The reaction is noticeably cleaner and is easier to handle since the products are less soaplike in character. The results were as follows: recovered starting compound, 13 g. or 15%; mono-acid (X), 33 g. or 49%; di-acid (XI) 5 g. or 8%.

Re-esterification.—One hundred milligram samples of the mono- and di-acids were esterified with diazo-ethane as described above. Each yielded starting compound (IX) identified by melting point and mixed melting point.

1,4,1′,4′-Tetramethyl-3,5,3′-tricarbethoxy-dipyrrylmethane (XII).—Ten and one-half grams of 1,4,1′,4′-tetra-

(7) Corwin and Ellingson, THIS JOURNAL, **64**, 2100 (1942).

(8) Kindly performed by R. C. Ellingson.

(9) This includes a small correction for oxides of nitrogen based upon the assumption that the percentage of N is 9.8.

methyl - 3,5,3′ - tricarbethoxy - 5′ - carboxyldipyrrylmethane (X) was suspended in 20 cc. of anhydrous glycerol containing ten drops of quinoline. The mixture was heated rapidly to 200° and held at this temperature for three minutes. Heating was discontinued and 30 cc. of alcohol added in a thin stream from a wash bottle. The solution was then set on ice and the product separated as an oil which crystallized slowly. It was filtered off and recrystallized from acetone; yield, 8.7 g. or 89.5%; m. p. 127–129°.

The product may be recrystallized from either acetone or methanol. From ethanol it came out as an oil which solidified slowly. A sample was recrystallized three times from methanol for analysis.

Anal. Calcd. for $C_{22}H_{33}N_3O_6$: C, 63.14; H, 7.23. Found: C, 63.36; H, 7.20.

Preparation of Tetrapyrrane XV.—Two grams of 1,4,1′,4′-tetramethyl-3,5,3′-tricarbethoxy-dipyrrylmethane (XII), 0.1 g. of paraformaldehyde, 10 drops of glacial acetic acid and 10 cc. of anhydrous butanol were refluxed together for one hour and the solution then placed in the ice box overnight. The entire mixture solidified. The snow-white product was filtered off and washed with ethanol; yield, 1.8 g. or 89%; m. p. 147–149°.

The product may be recrystallized from ethanol, methanol or dioxane. The latter is preferable and the analytical sample was prepared by recrystallizing three times from this solvent.

Anal. Calcd. for $C_{46}H_{60}N_4O_{12}$: C, 63.66; H, 7.12. Found: C, 63.77; H, 7.05.

Saponification of 1,4,1′,4′-Tetramethyl-3,5,3′-tricarbethoxy-dipyrrylmethane (XII).—Four and one hundredth grams (0.0096 mole) of dipyrrylmethane XII was dissolved in 200 cc. of 80% ethanol and 0.011 mole of sodium hydroxide added. The solution was refluxed overnight and evaporated to dryness. The residue was taken up in 100 cc. of hot water and filtered to remove a small amount of water-insoluble product. On cooling the filtrate, 3.24 g. of a soapy sodium salt was precipitated. This was dissolved in hot ethanol, acidified with hydrochloric acid to the congo red end-point and hot water added to incipient turbidity. On cooling, 2.85 g. of crystalline acid was deposited. An additional 0.80 g., somewhat less pure, was obtained on acidification of the aqueous mother liquor; total yield, 3.55 g. or 98%.

Re-esterification.—A 100-mg. sample of the acid was re-esterified with diazo-ethane by the process described above. The product melted at 126–129°; mixed m. p. with pure dipyrrylmethane XII, 127–129°.

Decarboxylation.—A 100-mg. sample of the acid was decarboxylated in glycerol and quinoline, yielding a product melting at 163–164° after two recrystallizations from acetone; mixed m. p. with 1,4,1′,4′-tetramethyl-3,3′-dicarbethoxy-dipyrrylmethane (described below), 164–165°.

1,4,1′,4′-Tetramethyl-3,3′-dicarbethoxy-dipyrrylmethane (XIII).—Two and eight-tenths grams of 1,4,1′,4′-tetramethyl - 3,3′ - dicarbethoxy - 5,5′ - dicarboxyldipyrrylmethane (XI) was suspended in 5 cc. of dry glycerol and two drops of quinoline in a Pyrex test-tube. The temperature was brought rapidly to 220° and maintained for three minutes. Cold alcohol was added cautiously in a thin stream from a wash bottle. The product started to crystallize immediately. After standing on ice for several hours, the product was filtered off and recrystallized from acetone. It deposited as beautiful, large, clear crystals; yield, 2.10 g. or 94%; m. p., 164–165°.

Anal. Calcd. for $C_{19}H_{26}N_2O_4$: C, 65.87; H, 7.57. Found: C, 65.67, 65.65; H, 7.57, 7.60.

Summary

1. An attempt to achieve a stepwise condensation of pyrrole derivatives to give linear tetrapyrryl compounds capable of producing porphyrins is described.

2. The proposed porphyrin synthesis is shown to be blocked by condensation of β-carbethoxy groups with imino nitrogens under the influence of alkali to give dipyrrolopyridones.

3. Minimum conditions under which such a synthesis could be achieved are stated as a result of these observations.

4. Conditions have been found for the selective saponification of a single carbethoxy group on two tetracarbethoxy dipyrrylmethanes.

5. A method for the identification of pyrrole and dipyrrylmethane carboxylic acids by re-esterification with diazo-ethane is reported.

6. A group of di-N-methyl dipyrrylmethane derivatives has been prepared.

7. Two new tetrapyrrane derivatives have been synthesized.

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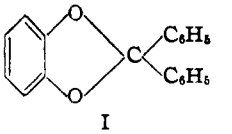
[CONTRIBUTION FROM THE DERMATOSES SECTION OF THE INDUSTRIAL HYGIENE DIVISION, BUREAU OF STATE SERVICES U. S. PUBLIC HEALTH SERVICE]

The Toxic Principles of Poison Ivy. II. Preparation and Properties of the Diphenylmethylene Ethers of Catechols[1]

BY HOWARD S. MASON

The difficulty with which 2-alkoxy derivatives of 3-alkyl-catechols are hydrolyzed[2] and the sensitivity of alkenyl-catechols to heat[3] and mineral acid have been serious hurdles to the synthesis of the toxic principles of poison ivy, 3-*n*-pentadecenyl catechols.[4] Accordingly, a derivative of catechols suitable for purposes of synthesis but cleavable under mild conditions has been sought in this investigation.

The diphenylmethylene ethers of catechol (I),



I

3-*n*-propylcatechol, and 4-*t*-butylcatechol have now been investigated from this point of view. These compounds, which may be regarded as

(1) For the first article in this series, see Mason and Schwartz, THIS JOURNAL, **64**, 3058 (1942).

(2) Majima and Takayama, *Ber.*, **53**, 1097 (1920).

(3) Majima, *ibid.*, **42**, 1418 (1909).

(4) Hill, Mattacotti and Graham, THIS JOURNAL, **56**, 2736 (1934).