842. *Porphyrins. Part I. Intramolecular Hydrogen Bonding in Pyrromethenes and Porphyrins.*

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The NH stretching frequencies in some porphyrins have been compared with those of related dipyrromethenes and dipyrromethanes. The effect of π-donor solvents on the NH frequencies of some substituted pyrroles has also been studied.

Several workers have reported that hæmatoporphyrin tends to accumulate in neoplastic, embryonic, and traumatic tissue; [1] and if large doses are given, it seems that this property could be used to assist the surgeon to delineate neoplastic tissue during cancer operations.[2] On the other hand, it has been claimed that an impurity in commercial hæmatoporphyrin is responsible,[3] and that pure hæmatoporphyrin does not thus become localised. A halogenated derivative was considered to be a likely impurity, and this has been supported by the finding that di-(2-[^{131}I]iodoethyl)deuteroporphyrin, given parenterally, became localised selectively in transplanted adenocarcinomata and in spontaneous mammary adenocarcinomata of mice.[4] Any compound which becomes concentrated in tumour tissue is clearly of interest as a lead in the search for a suitable tumour-inhibitor; moreover, hæmatoporphyrin has been found to sensitise paramecia to *X*-radiation.[5] A comprehensive study of methods for the synthesis of porphyrins in gram quantities has therefore been undertaken, and at the same time some of the properties of porphyrins of interest in this field will be examined. The present paper is a contribution to the study of intramolecular hydrogen bonding in porphyrins.

In the first systematic study of the infrared spectra of porphyrins in Nujol mull, Falk and Willis [6] found that the NH stretching vibration appeared as a very weak band at 3280—3300 cm.$^{-1}$. In dilute carbon tetrachloride solution, several porphyrins gave NH

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[1] Auler and Banzer, *Z. Krebsforsch.*, 1942, **53**, 65; Figge, Weiland, and Manganiello, *Proc. Soc. Exp. Biol.*, 1948, **68**, 640; Manganiello and Figge, *Bull. School Med. Univ. Maryland*, 1951, **36**, 3.

[2] Rassmussen-Taxdal, Ward, and Figge, *Cancer*, 1955, **8**, 78.

[3] Schwartz, Absolon, and Vermund, *Univ. Minn. Med. Bull.* 27 (Oct. 15, 1955).

[4] Altman and Salomon, *Fed. Proc.*, 1958, **17**, 181; *Nature*, 1960, **187**, 1124.

[5] Figge and Wichterman, *Science*, 1955, **122**, 468.

[6] Falk and Willis, *Austral. J. Sci. Res., A*, 1951, **4**, 579.

TABLE 1.

Infrared frequencies of the NH stretching vibrations of porphyrins (cf. I) in carbon tetrachloride solution and as hexachlorobutadiene mulls.

No.	Name	Substituents * 1	2	3	4	5	6	7	8	ν(NH) (cm.$^{-1}$) CCl_4 soln.	C_4Cl_6 mull
1	Protoporphyrin IX Me_2 ester	Me	V	Me	V	Me	P(Me)	P(Me)	Me	3323	3318
2	Mesoporphyrin IX Me_2 ester	Me	Et	Me	Et	Me	P(Me)	P(Me)	Me	3323	3320
3	Hæmatoporphyrin IX Me_2 ester	Me	Hy	Me	Hy	Me	P(Me)	P(Me)	Me	3320	3320
4	Pyrroporphyrin Me ester	Me	Et	Me	Et	Me		P(Me)	Me	3326	—
5	Phylloporphyrin Me ester †	Me	Et	Me	Et	Me		P(Me)	Me	3321	—
6	Rhodoporphyrin Me_2 ester	Me	Et	Me	Et	Me	C(Me)	P(Me)	Me	3332	—
7	Octamethylporphin	Me	Me	Me	Me	Me	Me	Me	Me	—	3316
8	Tetrabenzoporphin	Benzo		Benzo		Benzo		Benzo		—	3319
9	Coproporphyrin III Me_4 ester	Me	P(Me)	Me	P(Me)	Me	P(Me)	P(Me)	Me	—	3322
10	Uroporphyrin III Me_8 ester	A(Me)	P(Me)	A(Me)	P(Me)	A(Me)	P(Me)	P(Me)	A(Me)	—	3314
11	Tetraphenylporphin ‡									3326	3324

* P(Me) = $CH_2{\cdot}CH_2{\cdot}CO_2Me$; V = $CH{:}CH_2$; Hy = CHMe·OH; A(Me) = $CH_2{\cdot}CO_2Me$; C(Me) = CO_2Me. † Also γ-Me. ‡ α-, β-, γ-, and δ-Ph.

stretching bands around 3320 cm.$^{-1}$. As pyrrole, indole, and carbazole in dilute solution gave stretching bands at about 3500 cm.$^{-1}$, it was concluded that intramolecular hydrogen bonding must be present; but its exact nature has not been elucidated. The NH stretching frequencies for eleven porphyrins (cf. I) have now been accurately determined (Table 1) and compared with those for some dipyrromethenes (cf. II) and dipyrromethanes (cf. III) (Table 2).

In dilute solution in carbon tetrachloride, the NH stretching frequency for the porphyrins examined was almost constant at about 3324 cm.$^{-1}$ (Table 1). However, some compounds, being too insoluble in carbon tetrachloride, were examined as mulls in hexachlorobutadiene; four compounds were examined both in solution and as mulls. For the porphyrins examined in the solid state, the NH band was found to be near 3319 cm.$^{-1}$. (Hexachlorobutadiene is better [7] than Nujol for the study of the NH stretching vibrations in porphyrins

TABLE 2.

Infrared frequencies of the NH stretching vibrations of dipyrromethenes (cf. II) and of dipyrromethanes (cf. III) in carbon tetrachloride solution.

No.	Substituents 5	4	3	*ms*	3′	4′	5′	ν(NH) (cm.$^{-1}$)
	Dipyrromethenes							
1	Me	Me	Me		Me	Me	Me	3281
2	Me	Et	Me		Me	Et	Me	3279
3	Me	P(Me)	Me		Me	P(Me)	Me	3281
4	Me	CO_2Et	Me		Me	Me	Me	3246
5	Me	CO_2Et	Me		Me	Et	Me	3248
6	Me	CO_2Et	Me		Me	CO_2Et	Me	3226
7	I	Me	I		Me	Me	Me	3310
8	I	Me	I		Me	CO_2Et	Me	3292
	Dipyrromethanes							
9	Me	CO_2Et	Me		Me	CO_2Et	Me	3456; —
10	Me	COMe	Me		Me	COMe	Me	3449; —
11	CO_2Et	Me	Me		Me	Me	CO_2Et	3455; 3345
12	CO_2Et	Me	Me	Me	Me	Me	CO_2Et	3460; 3364
13	CO_2Et	Me	CO_2Et		CO_2Et	Me	CO_2Et	— ; 3394
14	CO_2Et	Me	CO_2Et		Me	CO_2Et	Me	3447; 3379

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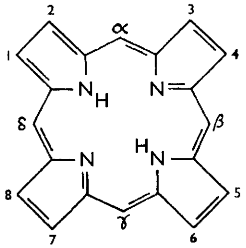
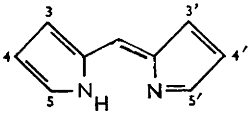
[7] Thomas and Martell, *J. Amer. Chem. Soc.*, 1956, **78**, 1338.

as the intensity of the NH bands is much greater in the former.) The NH frequency now found for tetraphenylporphin (3324 cm.$^{-1}$) in hexachlorobutadiene mull is lower than that (3350 cm.$^{-1}$) given by Thomas and Martell;[7] they used rock-salt optics and did not record their method of calibration.

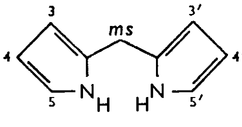
The change in the NH stretching frequency between the solid state and carbon tetrachloride solution observed in the present work is only a few cm.$^{-1}$, much smaller than was observed by Falk and Willis[6] (who used Nujol mulls). For three porphyrins in pressed potassium bromide discs Mason[8] observed a shift of only 4 cm.$^{-1}$ from the frequencies in carbon tetrachloride. It seems established, therefore, that the hydrogen bonding in porphyrins is entirely intramolecular even in the solid state.



(I)



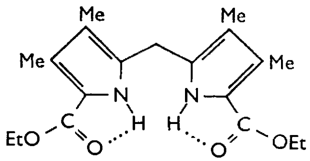
(II)



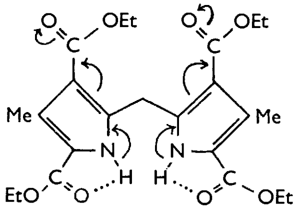
(III)

The dipyrromethenes (II) were examined in dilute carbon tetrachloride (Table 2). For alkyldipyrromethenes the NH stretching frequency was found near 3280 cm.$^{-1}$, and it may therefore be inferred that the intramolecular hydrogen bonding in these compounds is somewhat stronger than in related porphyrins. Even in relatively concentrated solution no intermolecular hydrogen bonding could be detected. The presence of an electron-attracting group (CO_2Et) in a β-position would be expected to increase the acidic nature of the NH group and hence the strength of the intramolecular hydrogen bond; this has been confirmed, for the NH stretching vibration appeared near 3247 cm.$^{-1}$ with such compounds. Two such groups further increased the strength of the hydrogen bond, as indicated by a further reduction of the NH stretching frequency to 3226 cm.$^{-1}$. A large substituent (iodine) in the 3-position decreased the strength of the intramolecular hydrogen bond, presumably by preventing coplanarity of the molecule. Moreover, an electron-attracting substituent (CO_2Et) in a β-position of such a non-planar molecule increased hydrogen bonding less than it did in a compound having no large substituent in the 3-position.

No N–H • • • N intramolecular hydrogen bonding is possible with dipyrromethanes (III), and such compounds have been found to give a free NH stretching vibration at about 3453 cm.$^{-1}$ (Table 2). However, dipyrromethanes having an α-ethoxycarbonyl group gave two NH bands. The first was the sharp peak at ~3453 cm.$^{-1}$, due to the non-bonded NH, the second a broad peak at 3394—3345 cm.$^{-1}$. The second band is presumably the stretching vibration of the NH group, which is intramolecularly hydrogen-bonded to the carbonyl group (cf. IV). A β-ethoxycarbonyl group (compound 13, Table 2) increases



(IV)



(V)

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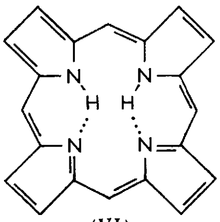
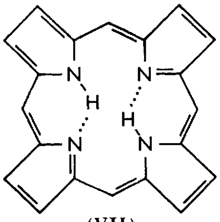
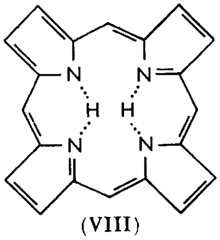
[8] Mason, *J.*, 1958, 976; see also Rimington, Mason, and Kennard, *Spectrochim. Acta*, 1958, **12**, 65.

the acidity of the NH group to such an extent that intramolecular hydrogen bonding (to α-ethoxycarbonyl) is favoured to the exclusion of a free NH (cf. V) and only one NH frequency (a bonded one) was observed.

Three intramolecularly hydrogen-bonded models may be considered for porphyrins.[8] In the first, the hydrogen atoms are attached to adjacent nitrogen atoms and hydrogen bonded to the remaining nitrogen (as VI). In the second, the hydrogen atoms are on opposite nitrogen atoms and are hydrogen bonded to the adjacent nitrogen atoms (as VII). In the third, the hydrogen atoms are symmetrically placed between each pair of nitrogen atoms (as VIII).


(VI)


(VII)


(VIII)

The dimensions of the porphyrin nucleus are not known with accuracy; but if they are taken to be very close to those of the azaporphin nucleus of phthalocyanine,[9] then these three models can be examined. Mason[8] used the bond angles found for phthalocyanine to draw certain conclusions about the hybridisation of the bonds in porphyrins; he showed that model (VI) is less stable than the others owing to the greater penetration of each hydrogen atom into the van der Waals sphere of the other. The details of Mason's arguments can be criticised for the weight he gives to bond angles rather than to bond lengths in discussing bond hybridisation in strained (five-membered) rings. Nevertheless, the same conclusion is reached from a study of a scale drawing of the molecule (Fig. 1). Indeed, a detailed consideration of the geometry of the molecule also leads to the conclusion that symmetrical hydrogen bonding (as in VIII) must also be excluded. The N • • • N distances of 2·65 and 2·76 Å found for phthalocyanine clearly involve an excessive lengthening of the N–H bond. It is generally accepted that symmetrical hydrogen bonding occurs in nickel dimethylglyoxime; but here the O–H • • • O distance is 2·45 Å, and the O–H • • • O angle is 180°.

The most reasonable model for the intramolecular hydrogen bonding in porphyrins is therefore (VII). On this basis, the situation in the porphyrins closely resembles that in 8-hydroxyquinoline. In the latter, the O • • • N distance is *ca.* 2·65 Å, the O–H • • • N angle is *ca.* 120°, and weak intramolecular hydrogen bonding has been established.[10] In the porphyrins, the N • • • N distance is 2·65 or 2·76 Å, and the N–H • • • N angle (from Fig. 1) is ∼115° or 118°. The possibility that the hydrogen bonds in (VII) are bifurcated cannot be excluded, and indeed this seems very likely. However, with N • • • N distances of 2·65 and 2·76 Å, this means that one leg of the bifurcated bond must be more important than the other.

In the dipyrromethenes (II), there is no rigid cyclic structure, and the N • • • N distance is presumably a little shorter, giving a slightly stronger intramolecular hydrogen bond than in the porphyrins.

In the above discussion, reference has been made to the stretching vibration of the NH group in pyrrole itself. In dilute carbon tetrachloride solution this appears at 3490 cm.$^{-1}$, but in concentrated solution an additional band appears at 3413 cm.$^{-1}$, the relative intensities of the two bonds varying with the concentration. This effect has been widely

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[9] Robertson, *J.*, 1936, 1195.

[10] Badger and Moritz, *J.*, 1958, 3437.

interpreted as indicating the association of pyrrole. To some extent, this is supported by the high b. p. of pyrrole (130°) relative to that of thiophen (84°) and of furan (32°). However, much better evidence was provided by a study of the effect of the solvent on the frequency of the NH stretching vibration in pyrrole.[11] A marked distinction has been clearly shown, for example, between the solvent–solute interaction which is a function of dielectric constant (carbon tetrachloride, hexane, cyclohexane), and that which is more specific, involving hydrogen bonding (acetone, pyridine, aromatic hydrocarbons). In acetone–carbon tetrachloride, for example, the NH bands of pyrrole appear at 3492 and 3390 cm.$^{-1}$; in pyridine–carbon tetrachloride they are at 3493 and 3250 cm.$^{-1}$; and in aromatic hydrocarbon solvents the NH band appears at about 3450 cm.$^{-1}$. It seems that the NH group is hydrogen-bonded to the carbonyl group in acetone, to the lone pair of electrons in pyridine, and to the π-electron system in aromatic hydrocarbons.[12]

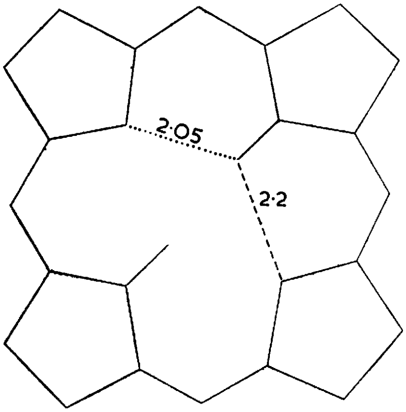

FIG. 1. A porphyrin molecule, to scale; bond lengths and bond angles as for phthalocyanine,[9] N–H bond 1 Å.

These general conclusions have been supported by nuclear magnetic resonance spectroscopy, and two models have been considered for the association of pyrrole.[13] In the " open dimer " model, the NH proton is assumed to be directly above the centre of the donor ring, the two rings being more or less perpendicular to one another. In the alternative " cyclic " model of the pyrrole dimer, both rings act as π-donors, and Happe [13] concludes that his study slightly favours the second model.

It was therefore of interest to determine the frequency of the NH stretching vibration in pyrrole when hydrogen-bonded to the π-electrons of a number of other pyrroles having no NH group, or to related aromatic systems. The infrared spectrum of a 0·01M-solution of pyrrole in carbon tetrachloride has therefore been compared with the spectra obtained from 0·01M-solutions of pyrrole in carbon tetrachloride containing varying concentrations of 1-methyl- and 1-ethyl-pyrrole, of 1-phenyl-, 1-benzyl-, and 1-1′-naphthyl-2,5-dimethylpyrrole, and of benzene, thiophen, furan, and pyridine. In all these systems, association of the " cyclic dimer " type would seem to be precluded; but in every case, two NH frequencies (bonded and non-bonded) were observed. It will be noted from the $\Delta\nu$, and from the plot of the molar concentrations of the π-donor against the relative intensities of the bonded and non-bonded NH bands (Fig. 2), that pyrrole forms a hydrogen bond with *N*-substituted pyrroles, of approximately the same strength as it does with itself. With 2,5-dimethyl-1-1′-naphthylpyrrole, this is especially noteworthy, for with this compound steric hindrance requires that the planes of the naphthalene and the pyrrole ring must be

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[11] Josien and Fuson, *J. Chem. Phys.*, 1954, **22**, 1169, 1164; Fuson, Pineau, and Josien, *J. Chim. phys.*, 1958, **55**, 454; Pineau, Fuson, and Josien, *ibid.*, 1958, **55**, 464; see also " Hydrogen Bonding," ed. Hadži, Pergamon Press, London, 1959, pp. 129, 169, 177.

[12] Cf. Jones and R. M. Badger, *J. Amer. Chem. Soc.*, 1951, **73**, 3132.

[13] Happe, *J. Phys. Chem.*, 1961, **65**, 72.

more or less at right angles to one another. These results may be taken to support the " open dimer " model for pyrrole association.

With benzene and thiophen, pyrrole forms a weaker hydrogen bond (see Fig. 2); and with pyridine it forms a much stronger hydrogen bond, which, however, must be of the N–H • • • N type. The respective gradients of the three lines are: pyridine, 1·63 ± 0·05; 1-substituted pyrroles, 0·59 ± 0·09; benzene, thiophen, 0·10 ± 0·01. The effects of the three classes of compound are also illustrated by Fig. 3. Furan acted as a weak π-donor, similar to thiophen, but quantitative results could not be obtained owing to the volatility of this material.

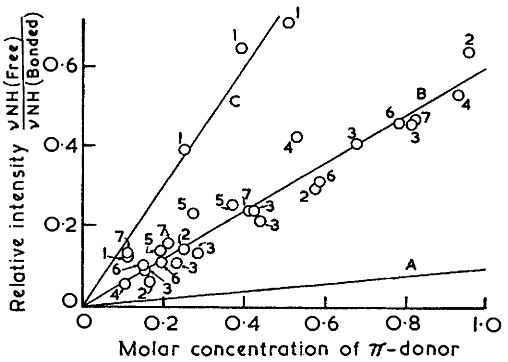


FIG. 2. Graphs showing the relation between the molar concentration of the π-donor in carbon tetrachloride and the relative intensities of the free and bonded NH band in pyrrole: (1) pyridine; (2) pyrrole; (3) 1-methylpyrrole; (4) 1-ethylpyrrole; (5) 2,5-dimethyl-1-phenylpyrrole; (6) 1-benzyl-2,5-dimethylpyrrole; (7) 2,5-dimethyl-1-1′-naphthylpyrrole.

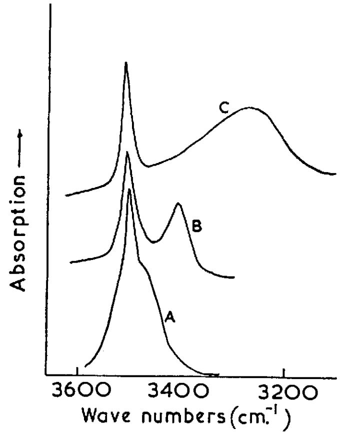


FIG. 3. Infrared absorption curves obtained (A) from pyrrole (0·01M) and thiophen (3·32M) in carbon tetrachloride; (B) from pyrrole (0·96M) in carbon tetrachloride; and (C) from pyrrole (0·01M) and pyridine (0·39M) in carbon tetrachloride.

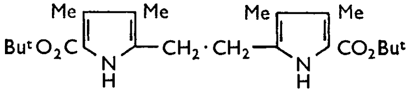
TABLE 3.

Infrared frequencies of the NH stretching vibration given by a 0·01M-solution of pyrrole in various solvents.

Solvent: CCl_4 plus stated compound	Concn. (M) of π-donor in solvent	ν(NH) (cm.$^{-1}$) Free NH	ν(NH) (cm.$^{-1}$) Bonded NH	Δν = ν(free NH) −ν(bonded NH)
—	—	3490	—	—
Pyrrole	0·05—0·96	3490	3413	77
1-Methylpyrrole	0·15—0·81	3502—3508	3413—3427	85
1-Ethylpyrrole	0·11—2·82	3501—3505	3419—3423	82
2,5-Dimethyl-1-phenylpyrrole	0·20—0·37	3505—3509	3399—3411	104
1-Benzyl-2,5-dimethylpyrrole	0·14—0·78	3506—3509	3401—3407	103
2,5-Dimethyl-1-1′-naphthylpyrrole	0·11—0·82	3504—3509	3399—3403	105
Benzene	0·34—5·17	3502—3504	3472—3480	26
Thiophen	0·58—10·38	3498—3502	3465—3471	32
Pyridine	0·11—1·21	3507—3515	3264—3268	245

Most of the dipyrromethenes and dipyrromethanes were prepared by known methods. 2-Formyl-3,5-di-iodo-4-methylpyrrole was prepared by iodination-decarboxylation of 5-formyl-3-methylpyrrole-2,4-dicarboxylic acid, and condensed with t-butyl 3,4,5-trimethylpyrrole-2-carboxylate, to give 3,5-di-iodo-3′,4,4′,5′-tetramethyldipyrromethene.

The same formylpyrrole was condensed with ethyl 2,4-dimethylpyrrole-3-carboxylate, to give ethyl 3′,5′-di-iodo-3,4′,5-trimethyldipyrromethene-4-carboxylate.



(IX)

Most of the porphyrins used were prepared from commercially available acids by esterification with diazomethane. Tetrabenzoporphin and octamethylporphin were prepared essentially by the methods given in the literature, but the opportunity has been taken to improve some of the procedures. In the preparation of the intermediate t-butyl 5-acetoxymethyl-3,4-dimethylpyrrole-2-carboxylate by the oxidation of t-butyl 3,4,5-trimethylpyrrole-2-carboxylate with lead tetra-acetate, a by-product was isolated which appears to be di-t-butyl *sym*-5,5′-ethylenebis-(3,4-dimethylpyrrole-2-carboxylate) (IX). Pyrolysis of this compound gave octamethylporphin in 15% yield, the species condensing to form the porphyrin presumably being the radical produced by scission of the " bibenzyl " type. The method for pyrolysis of t-butyl 5-acetoxymethyl-3,4-dimethylpyrrole-2-carboxylate to give octamethylporphin has been improved.

EXPERIMENTAL

Infrared Spectra.—The spectra were determined for carbon tetrachloride solutions in 3-mm. cells, or as mulls in hexachlorobutadiene, by using a Grubb–Parsons S4 double-beam spectrometer and a calcium fluoride prism. The absorption bands given by gaseous ammonia in a 10-cm. cell were used for calibration.

Materials.—Commercial samples of pyrrole, thiophen, furan, benzene, and pyridine were purified by distillation under nitrogen. 1-Methylpyrrole, b. p. 110—112° (lit.,[14] 112—113°), 1-ethylpyrrole, b. p. 131—132° (lit.,[15] 131°), 2,5-dimethyl-1-phenylpyrrole, m. p. 51° (lit.,[16] 51—52°), 1-benzyl-2,5-dimethylpyrrole, m. p. 47—48° (lit.,[16] 48°), and 2,5-dimethyl-1-1′-naphthylpyrrole, m. p. 119·5—120° (lit.,[16] 121°), were prepared by known methods. So were 3,3′,4,4′,5,5′-hexamethyldipyrromethene, m. p. 170—171° (lit.,[17] 172°), 3,3′,5,5′-tetramethyl-4,4′-diethyldipyrromethene, m. p. 150° (lit.,[18] 151°), ethyl 3,3′,4′,5,5′-pentamethyldipyrromethane-4-carboxylate, m. p. 126° (lit.,[17] 127°), ethyl 4′-ethyl-3,3′,5,5′-tetramethyldipyrromethene-4-carboxylate, m. p. 131—132° (lit.,[19] 132°), and diethyl 3,3′,5,5′-tetramethyldipyrromethene-4,4′-dicarboxylate, m. p. 190° (lit.,[20] 190°). Also diethyl 3,3′,5,5′-tetramethyldipyrromethane-4,4′-dicarboxylate, m. p. 221—223° (lit.,[21] 223·5°), tetraethyl 4,4′-dimethyldipyrromethane-3,3′,5,5′-tetracarboxylate, m. p. 134—135° (lit.,[22] 135°), triethyl 3′,4,5′-trimethyldipyrromethane-3,4′,5-tricarboxylate, m. p. 156° (lit.,[22] 157°), and 4,4′-diacetyl-3,3′,5,5′-tetramethyldipyrromethane, m. p. 265—266° (lit.,[23] 268°).

Dimethyl esters of protoporphyrin IX, mesoporphyrin IX, hæmatoporphyrin IX, and rhodoporphyrin and methyl esters of pyrroporphyrin and phylloporphyrin were prepared from the commercial acids by treatment with diazomethane in ether. All the esters had m. p.s in agreement with the literature. Commercial samples (Lights) of coproporphyrin III tetramethyl ester and uroporphyrin III octamethyl ester were used without purification. We are indebted to Mr. R. L. Laslett for gifts of *ms*-tetraphenylporphin and diethyl *ms*-3,3′,4,4′-pentamethyldipyrromethane-5,5′-dicarboxylate.

2-Formyl-3,5-di-iodo-4-methylpyrrole.—A solution of iodine (2·5 g.) and potassium iodide

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[14] Oddo, *Ber.*, 1914, **47**, 2427.
[15] Ciamician and Zanetti, *Ber.*, 1889, **22**, 659.
[16] Hazlewood, Hughes, and Lions, *J. Proc. Roy. Soc. New South Wales*, 1937, **71**, 92.
[17] Fischer and Walach, *Annalen*, 1926, **450**, 109.
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[19] Fischer and Schormuller, *Annalen*, 1929, **473**, 243.
[20] Fischer and Zerweck, *Ber.*, 1923, **56**, 526.
[21] Piloty, Krannich, and Will, *Ber.*, 1914, **47**, 2531.
[22] Corwin, Bailey, and Viohl, *J. Amer. Chem. Soc.*, 1942, **64**, 1267.
[23] Fischer and Ammann, *Ber.*, 1923, **56**, 2319.

(5 g.) in water (10 ml.) was added dropwise (at such a rate that the iodine colour did not accumulate) with stirring to a solution of 5-formyl-3-methylpyrrole-2,4-dicarboxylic acid [24] (1 g.) in 2% aqueous potassium hydroxide (25 ml.) at 65—70°. Carbon dioxide was evolved and a solid separated. The mixture was heated to 100° to discharge the iodine colour and then poured into ice–water (100 ml.). The crude product was collected, washed with water, and recrystallised from aqueous alcohol as needles, m. p. 191° (sintering 187°). After sublimation in a high vacuum and recrystallisation from aqueous alcohol, 2-*formyl*-3,5-*di-iodo*-4-*methylpyrrole* was obtained as needles, m. p. 191·5—192·5° (Found: C, 20·25; H, 1·7; I, 69·7. $C_6H_5I_2NO$ requires C, 20·0; H, 1·4; I, 70·3%). After recrystallisation from chloroform–hexane the pyrrole was obtained as prisms; when slowly heated these changed to needles at about 165° and melted at 191°. Decomposition occurred when the compound was heated above 200°.

Potassium 3,4,5-*Trimethylpyrrole*-2-*carboxylate*.—Ethyl 3,4,5-trimethylpyrrole-2-carboxylate (10 g.) was refluxed for 3 hr. with potassium hydroxide (10 g.) in anhydrous ethanol (100 ml.). The volume of the solution was reduced to 50 ml. and dry ether (500 ml.) added. The mixture was left overnight, and the product collected and washed with ether. The potassium salt (9·2 g., 87%) which formed colourless plates, darkening from 210—220°, was much more stable than the free acid or 3,4,5-trimethylpyrrole, and coloured only on long storage.

3,5-*Di-iodo*-3′,4,4′,5′-*tetramethyldipyrromethene*.—2-Formyl-3,5-di-iodo-4-methylpyrrole (0·72 g.) was dissolved in hot acetic acid (10 ml.). To the cooled solution was added a solution of potassium 3,4,5-trimethylpyrrole-2-carboxylate (0·394 g.) in cold acetic acid (2 ml.), immediately followed by 48% hydrobromic acid (2 ml.). The mixture was stirred, red needles separated, and a slight effervescence of carbon dioxide was observed. The mixture was left for 3 hr. at 0°, and the solid then collected, washed with acetic acid, then with ether, and air-dried. 3,5-*Di-iodo*-3′,4,4′,5′-*tetramethyldipyrromethene hydrobromide* (0·85 g., 94%) was obtained as bluish-red needles, blackening at 115—185°, not melting at 300°. The hydrobromide could not be recrystallised satisfactorily and was purified for analysis as follows: A suspension of it in benzene was shaken with anhydrous sodium acetate for 1 hr. The benzene solution was filtered and run on to a short column of alumina (acid-washed, grade 4). The free base was eluted with benzene–hexane (1 : 1). The hydrobromide was precipitated from the filtered eluate by the addition of 50% ethanolic hydrogen bromide (Found: N, 5·3, 5·4. $C_{13}H_{15}BrI_2N_2$ requires N, 5·3%). The *base* was isolated by evaporation of the eluate obtained as above in a stream of nitrogen at 0—10°; it crystallised as red needles with a metallic lustre, blackening at 130—145°, not melting at 300° (Found: C, 34·65; H, 3·2; N, 6·05. $C_{13}H_{14}I_2N_2$ requires C, 34·5; H, 3·1; N, 6·2%).

Ethyl 3′,5′-*Di-iodo*-3,4′,5-*trimethyldipyrromethene*-4-*carboxylate*.—Ethyl 2,4-dimethylpyrrole-3-carboxylate (0·33 g.) was added to 2-formyl-3,5-di-iodo-4-methylpyrrole (0·72 g.) in hot acetic acid (5 ml.). The solution was cooled, and 48% hydrobromic acid (2 ml.) added with stirring. The mixture was left at 0° for 3 hr., after which the solid was collected, washed with acetic acid, then with ether, and recrystallised from chloroform. *Ethyl* 3′,5′-*di-iodo*-3,4′,5-*trimethyldipyrromethene*-4-*carboxylate hydrobromide* (0·61 g., 56%) was obtained. This could not be satisfactorily purified by recrystallisation. An analytical sample was prepared as follows: The hydrobromide was suspended in chloroform and shaken with anhydrous sodium acetate for 1 hr. The chloroform layer was filtered and run through a short column of alumina (acid-washed; grade 4). A portion of the eluate was treated with 5% ethanolic hydrogen bromide; the salt separated as red needles, decomp. 175—185°, no m. p. up to 300° (Found: C, 30·5; H, 2·9; N, 4·4. $C_{15}H_{17}BrI_2N_2O_2$ requires C, 30·5; H, 2·9; N, 4·75%).

Evaporation of the remainder of the eluate gave the *base* as bright-red hair-like needles, decomp. 200°. For analysis it was recrystallised twice from benzene–hexane (Found: C, 35·6; H, 3·5; N, 5·1. $C_{15}H_{16}I_2N_2O_2$ requires C, 35·3; H, 3·2; N, 5·5%).

Diethyl 3,3′,4,4′-*Tetramethyldipyrromethane*-5,5′-*dicarboxylate*.—The following procedure was more satisfactory than that given in the literature.[17] A solution of bromine (1·8 ml.) in acetic acid (40 ml.) was added to ethyl 3,4,5-trimethylpyrrole-2-carboxylate (1·0 g.) in acetic acid (3·5 ml.), and the mixture irradiated with ultraviolet light for 3 hr. The solution was diluted with water, and the solid collected and crystallised from aqueous ethanol, to give the dipyrromethane (0·3 g., 32%) as needles, m. p. 196—197° (lit.,[17] 198°).

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[24] Fischer and Ernst, *Annalen*, 1926, **447**, 139.

t-Butyl 5-Acetoxymethyl-3,4-dimethylpyrrole-2-carboxylate.—The following conditions were more satisfactory than those of Bullock *et al.*[25] t-Butyl 3,4,5-trimethylpyrrole-2-carboxylate (20 g.) was dissolved in pure glacial acetic acid (400 ml.) containing pure acetic anhydride (2 ml.). The system was flushed with nitrogen, and lead tetra-acetate (42·4 g.) was added during ½ hr. with stirring. The mixture was stirred at room temperature for a further 3½ hr., then poured into water (3 l.) with stirring. After several hours, the crude product was collected, washed with water, and dried (26·4 g.; m. p. 118—124°). This material, which contained both the required compound and the dimer (see below), was suitable for the next stage.

In another experiment, lead tetra-acetate (21·2 g.) was added in ½ hr., with stirring, to the t-butyl ester (10 g.) in acetic acid (200 ml.) and acetic anhydride (5 ml.). The mixture was stirred at room temperature for 1½ hr. and at 50° for 1½ hr., then poured (without prior concentration; cf. Bullock *et al.*[25]) into water (1·5 l.). The resulting solid was fractionally recrystallised from aqueous acetone, and from light petroleum, to give t-butyl 5-acetoxymethyl-3,4-dimethylpyrrole-2-carboxylate (3·8 g.), m. p. 126—127° (lit.,[25] m. p. 127—128°), and a second product, m. p. 167—170° (1·8 g.). Further purification of the latter gave *di-t-butyl 5,5′-ethylenebis-(3,4-dimethylpyrrole-2-carboxylate)* (IX) as needles, m. p. 176° (Found: C, 69·1, 69·3; H, 8·4, 8·6; O, 15·4; N, 6·9%; *M*, 394. $C_{24}H_{36}N_2O_4$ requires C, 69·2; H, 8·7; O, 15·4; N, 6·7%; *M*, 416).

1,2,3,4,5,6,7,8-*Octamethylporphin.*—(i) The crude acetoxylation product above (10 g.) was suspended in ethylene glycol (50 ml.) and stirred with a stream of nitrogen. The mixture was heated until it began to effervesce, white fumes being evolved. It was then refluxed for 3 hr., with stirring by nitrogen, allowed to cool to 60°, aerated for ½ hr., and poured into methanol (1 l.). After being left overnight, the product was collected, washed with methanol and cold chloroform, and recrystallised from nitrobenzene. The resulting pure octamethylporphin (1·13 g.) had a visible spectrum identical with a specimen prepared by the method of Bullock *et al.*[25] If *o*-dichlorobenzene was used for recrystallisation [25] it reacted with the porphin.

(ii) The bis-product (IX) (0·5 g.) was pyrolysed and worked up by the general method of Bullock *et al.*[25] except that the crude product was washed twice with cold chloroform before the Soxhlet-extraction, and gave pure octamethylporphin (35·4 mg.).

Tetrabenzoporphin.—A mixture of methyl 3-oxoisoindolinylacetate (28·7 g.) and zinc acetate (21·3 g.) was divided into ten parts, each of which was pyrolysed under nitrogen. Working up followed the method of Linstead and Weiss [26] except that it was preferable to extract the product (Soxhlet) successively with chloroform, 7 : 3 benzene–pyridine, and pyridine. The final extraction was complete after two days, and cooling the pyridine extract gave pure zinc tetrabenzoporphin (3·0 g.). Its absorption spectrum in pyridine–ether had $\lambda_{\max.}$ (and log ε values in parentheses) at 404 (4·69); 427 (5·73); 454·5 (3·79); 578 (4·14); 600 (3·91); 625 (5·14).[27] Decomposition of the complex as described by Linstead and Weiss [26] gave pure tetrabenzoporphyrin.

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[25] Bullock, Johnson, Markham, and Shaw, *J.*, 1958, 1438.
[26] Linstead and Weiss, *J.*, 1950, 2975.
[27] Cf. Barrett, Linstead, Rundall, and Tuey, *J.*, 1940, 1079.