161. *Synthesis of* meso*Tetramethylchlorin.*

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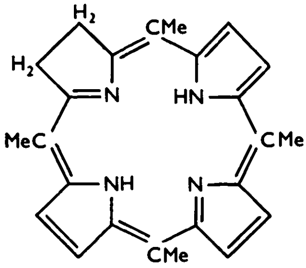
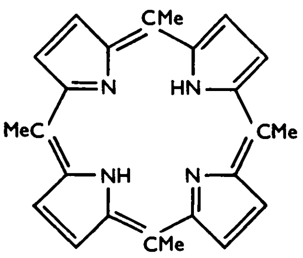
The Mannich base (VI) has been prepared from pyrrole in three stages. From it *meso*tetramethyl-chlorin (I) and -porphin (II) have been synthesised.

The synthesis of chlorin, the parent compound of the chlorophylls, and its octamethyl derivative, with full substitution of the β-positions of the pyrrole nuclei, has been recently described.[1,2] It was of interest to determine whether the same method could be applied to the preparation of a *meso*-substituted chlorin.

It was decided to prepare the unknown *meso*-tetramethylchlorin (I). The corresponding porphin (II) has been prepared[3] in low yield by the reaction of pyrrole and acetaldehyde in methanol at 100°, but analytical data have not been recorded for it nor has it been characterised.

(I)





(II)

Synthesis of the appropriate Mannich base (III) was accordingly attempted. Reaction of pyrrole, acetaldehyde, and dimethylamine afforded much polymeric material from which the desired base (III) could be isolated in variable yields not exceeding 5%. An indirect route was therefore attempted. 2-Acetylpyrrole[4] (IV) was reduced with potassium borohydride in aqueous medium (cf. Silverstein *et al.*[5]), affording the known 2-1′-hydroxyethylpyrrole[6] (V) in 87% yield. Reaction of the alcohol (V) with 1 mol. of piperidine in the presence of sodium ethoxide in boiling ethanol (cf. Silverstein *et al.*[7]) afforded the desired Mannich base (VI) in 40% yield. With an excess (15%) of piperidine the yield was raised to 63%.

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[1] Eisner and Linstead, *J.*, 1955, 3742.
[2] Eisner, Linstead, Parks, and Stephen, *J.*, 1956, 1655.
[3] Rothemund, *J. Amer. Chem. Soc.*, 1935, **57**, 2010.
[4] Oddo, *Ber.*, 1910, **43**, 1012.
[5] Silverstein, Ryskiewicz, and Chaikin, *J. Amer. Chem. Soc.*, 1954, **76**, 4485.
[6] Herz and Courtney, *ibid.*, 576.
[7] Silverstein, Ryskiewicz, Willard, and Koehler, *J. Org. Chem.*, 1955, **20**, 668.

On treatment with 1 mol. of ethylmagnesium bromide in boiling xylene or bromobenzene (cf. refs. 1, 2) the base (VI) afforded a mixture of *meso*tetramethyl-chlorin (I) and -porphin (II). Isolation and purification of the pigments proved unexpectedly difficult because of their relative insolubility, their instability, and the superficial similarity of their light absorption properties. The last fact precluded an accurate spectroscopic estimation of the yields. Purification by counter-current distribution could be applied only on a small scale, and adsorption chromatography was unsuccessful on all adsorbents tried. Preliminary purification was, however, effected by extraction with various solvents. Partition chromatography on cellulose finally achieved complete separation.

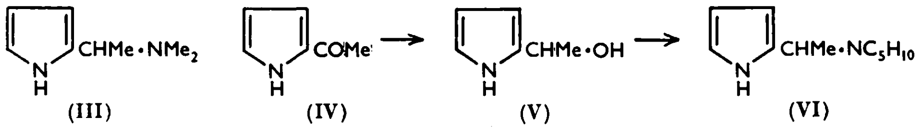

FIG. 1.

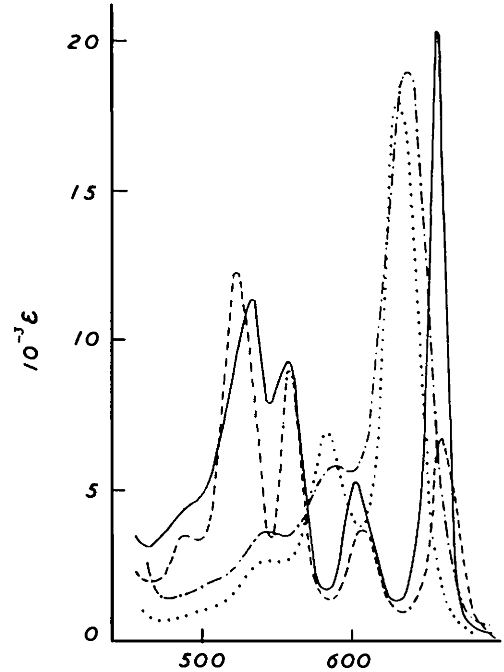

FIG. 2.

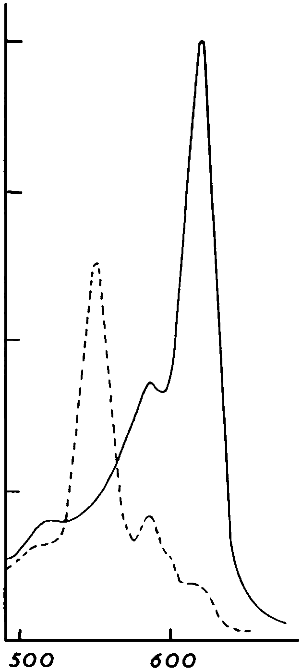

FIG. 1. *Absorption of* (i) meso*tetramethylchlorin in benzene* (——) *and in* 2N-HCl (— . —) *and* (ii) *of* meso*tetramethylporphin in chlorobenzene* (– – – –) *and* 2N-HCl (. . . . .).

FIG. 2. *Absorption of copper* meso*tetramethylchlorin in benzene* (——) *and copper* meso*tetramethylporphin in chlorobenzene* (– – – –).

The *meso*tetramethylchlorin obtained by this procedure was essentially pure although elementary analyses tended to give low values for carbon in spite of rigorous drying. Its copper derivative, prepared by the usual method, was not isolated owing to lack of material. Its light absorption and that of the metal-free chlorin (I) are given in the Table and Figures. The spectrum of the chlorin (I) is noteworthy in having a Soret band which is split into two peaks and in having a long-wavelength band of relatively low intensity.

The light absorption of *meso*tetramethylporphin (II) and of its copper derivative are given in the Table and in the Figures. The spectrum of the porphin (II) is subject to a considerable solvent effect which particularly affects the long-wavelength band; moreover, its spectral " type " does not conform to any of the classifications proposed by Stern.[8]

Although the chlorin (I) and the porphin (II) resemble each other to a marked extent, their separate identities are confirmed by the following evidence: (1) their chromatographic separation; (2) their solubilities; (3) their light-absorption properties in neutral and in acid solution; and (4) the existence of two distinct copper derivatives.

As additional proof of the structure of the chlorin (I), its dehydrogenation was investigated. The metal-free pigment (I) gave inconclusive results, chiefly owing to the difficulty of interpreting spectroscopic data. The action of 2 : 3-dichloro-5 : 6-dicyano-1 : 4-benzoquinone at room temperature appeared to produce some dehydrogenation although partial destruction of pigment took place at the same time. The copper derivative of (I) was next investigated. Excess of high-potential quinones, *e.g.*, the preceding quinone or tetrachloro-1 : 2-benzoquinone, decomposed the pigment. The action of 1 : 4-benzoquinone or of chloranil for 24 hr. at 80° caused slight decomposition (10—20%) but no dehydrogenation. However, when 1 mol. of the dicyano-quinone was used, dehydrogenation was instantaneous and the presence of the copper porphin could be shown spectroscopically. The reaction was not quantitative, owing partly to precipitation, even in very dilute solution, of solid material, possibly a quinone complex, and partly to the partial decomposition of pigment which becomes more important when excess of quinone is employed (see Experimental section).

Light-absorption data [$\lambda_{max.}$ (mμ), above ε].

(I) in C_6H_6	372·5	411 †	437 †	532·5	557	602·5	656
	31,000	113,000	78,300	11,400	10,300	5300	20,400
(I) in 2N-HCl	421 †	442 †	545	587	635		
	120,000	70,600	3600	5800	19,000		
(II) in PhCl	370—375 •	420 †	489	522	557	605·5	657·5
	21,400	282,000	3500	12,300	8950	3700	6800
(II) in C_6H_6			487	520·5	556·5	607	665
(II) in pyridine–Et_2O ‡		413 †	485	517	551	602	662
	292,000	4350	12,200	7800	2800	4450	
(II) in 2N-HCl	417·5 †	544	582	630			
	291,600	2600	6900	18,000			
Cu deriv. of (I) in C_6H_6	419 †	519	587	618			
	149,400	4000	8600	20,100			
Cu deriv. of (II) in PhCl	420 †	549	587·5				
	370,000	4200	12,600				

• Inflection. † Soret band. ‡ Knorr and Albers, *J. Chem. Phys.*, 1936, **4**, 422.

EXPERIMENTAL

2-1′-*Dimethylaminoethylpyrrole* (III).—A mixture of pyrrole (13·4 c.c.) and 33% ethanolic dimethylamine (21 g.) was added dropwise to acetaldehyde (11·2 c.c.) with stirring, at <10°. After being kept overnight at 0° the solution was acidified and extracted with ether, and the aqueous layer basified with sodium hydroxide solution and again extracted with ether. The ethereal extracts were dried and the solvent was removed under reduced pressure. Distillation of the residue afforded a forerun, b. p. 60—80°/18 mm. (0·5 g.), followed by 2-1′-*dimethylaminoethylpyrrole* (0·9 g.), b. p. 80—95°/18 mm., n_D^{23} 1·5039 (Found: C, 69·8; H, 10·5; N, 19·6. $C_8H_{14}N_2$ requires C, 69·5; H, 10·2; N, 20·3%). Its *picrate* crystallised from methanol in yellow plates, m. p. 160° (decomp.) (softens at 130°) (Found: C, 45·9; H, 4·85; N, 19·25. $C_8H_{14}N_2,C_6H_3O_7N_3$ requires C, 45·8; H, 4·7; N, 19·1%).

2-1′-*Hydroxyethylpyrrole* (V).—2-Acetylpyrrole (10 g.), suspended in water (50 c.c.), was treated with potassium borohydride (10 g., ~100% excess) in water (50 c.c.) with stirring. The suspension was stirred at room temperature for 0·5 hr., then at 50—60° for 0·75 hr., the

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[8] Stern and Wenderlein, *Z. phys. Chem.*, 1936, **176**, *A*, 98.

solid dissolving. Potassium carbonate was added to saturation, and the solution was extracted with ether. The ethereal extracts were dried (K_2CO_3) and the solvent was removed. The alcohol (V) distilled at 68°/0·8 mm., and had n_D^{24} 1·5240 (lit., b. p. 83·5°/2 mm., n_D^{23} 1·5242).

2-1'-Piperidinoethylpyrrole (VI).—The above alcohol (3·67 g., 1 mol.) and piperidine (3·3 c.c., 1 mol.) were added to a solution from sodium (0·76 g., 1 mol.) in ethanol (20 c.c.). The solution was boiled for 1 hr., the solvent removed under reduced pressure, and the residue dissolved in water and acidified. The solution was extracted with ether, basified, and re-extracted. The latter extracts were dried, the solvent was removed under reduced pressure, and the residue distilled. *2-1'-Piperidinoethylpyrrole* had b. p. 68°/0·3—0·4 mm.; m. p. 28—30° (Found: C, 74·1; H, 10·1; N, 15·4. $C_{11}H_{18}N_2$ requires C, 74·1; H, 10·2; N, 15·7%). Its picrate, m. p. 110—112°, could not be crystallised without decomposition and was not obtained pure.

Increasing the reaction period to 4 hr. did not improve the yield, but with a 15% excess of piperidine a yield of 63% was obtained.

meso*Tetramethyl-chlorin and -porphin.*—In a typical experiment the base (VI) (3·66 g.) in xylene (60 c.c.) was treated with ethereal ethylmagnesium bromide (7 c.c.; 3·142N). The solution was boiled under reflux in oxygen-free nitrogen with stirring for 17 hr. The cooled solution was filtered, the residue was washed with benzene, and the combined filtrate and washings were shaken with 2N-hydrochloric acid. The solution was basified with aqueous ammonia and extracted with benzene. Trouble was experienced owing to emulsions at this and subsequent stages, and the solution had to be filtered repeatedly.

Purification. (*a*) Countercurrent distribution. The above solution was concentrated to 40 c.c. under reduced pressure and placed in a Craig apparatus. With benzene–1% hydrochloric acid the porphin remained in the acid, and the chlorin in the benzene. After 15 transfers the contents of the last six tubes containing the crude chlorin were mixed, basified, and extracted with benzene. The combined extracts were concentrated to 40 c.c. and the process was repeated with benzene–3·2% hydrochloric acid. After 10 transfers the chlorin which had remained in the acid phase of the first four tubes was extracted into benzene after basification. The pigment was subsequently chromatographed on cellulose (see below) but less than 2 mg. of material were obtained.

(*b*) Solvent extraction. The insoluble residues from several experiments were extracted (thimble) with acetone in a stream of nitrogen. The extracts, containing the magnesium complexes, were treated with enough concentrated hydrochloric acid to effect complete conversion into the green hydrochloride and basified with ammonia solution. The precipitated metal-free pigments were extracted continuously with methanol which removed some impurities. Finally the pigments were extracted into boiling chloroform; the solution was then evaporated to dryness and used for the next stage.

(*c*) Partition chromatography. The crude pigments (above) were dissolved in a solvent mixture obtained by taking the upper phase of an equilibrated mixture of light petroleum (b. p. 100—120°)–butan-1-ol–1% hydrochloric acid (1 : 2 : 3), and chromatographed on a column (30 × 3·3 cm.) of cellulose (Whatman; standard grade), with the same solvent system as eluant. Separation into a faster-moving grass-green band of chlorin and a blue-green band of the porphin took place. These were eluted separately and treated with ammonia solution to precipitate the pigments which were filtered off.

meso*Tetramethylchlorin.* The *pigment* obtained from the partition chromatogram crystallised from benzene as small purplish-blue needles, forming red solutions in organic solvents and green solutions in mineral acids (Found: C, 77·3, 77·2, 76·85; H, 7·0, 6·9, 6·9. $C_{24}H_{24}N_4$ requires C, 78·2; H, 6·6%). It is moderately soluble in all organic solvents except alcohol and acetone.

Copper meso*tetramethylchlorin.* A solution of the chlorin (I) (0·34 mg.) in benzene (10 c.c.) was heated to boiling in a current of nitrogen and treated with a slight excess of cupric acetate in methanol (2 c.c.). It was cooled, diluted with benzene, washed with aqueous ammonia and water, and concentrated to 25 c.c. under reduced pressure. Its light absorption was determined immediately (see Table). The pigment forms a greenish-blue solution which, however, does not appear to be very stable as seen by the decrease in optical density.

meso*Tetramethylporphin.* The pigment obtained by chromatography (see above) was extracted from a thimble into boiling benzene from which it crystallised in deep blue needles (Found: C, 78·5; H, 6·3. $C_{24}H_{22}N_4$ requires C, 78·65; H, 6·05%). The *pigment*, which is sparingly soluble in most organic solvents, could be crystallised from pyridine or chloroform. It forms purplish-red solutions in organic solvents and bluish-green solutions in mineral acids.

Copper meso*tetramethylporphin.* The crude metal-free porphin (II) was placed in a thimble and extracted into boiling acetic acid containing excess of cupric acetate. The precipitated deep blue *copper derivative* was crystallised by continuous extraction into, successively, pyridine, chloroform, and benzene in which it formed red solutions (Found : C, 67·4; H, 4·9; Cu, 14·3. $C_{24}H_{20}N_4Cu$ requires C, 67·4; H, 4·7; Cu, 14·85%).

Dehydrogenation of Copper meso*Tetramethylchlorin.*—(*a*) A benzene solution of the copper derivative ($\sim 3 \times 10^{-5}$ molar) was treated respectively with 1 and 2 mols. of benzoquinone in benzene; the solutions were sealed into glass ampoules and heated for 24 hr. at 80°. Spectroscopic determination showed a recovery of 90·7 and 89·4% of starting material, with no trace of the copper porphin derivative. In a similar experiment with chloranil the respective recoveries of starting material were 84·1 and 76%.

(*b*) 2·5 c.c. of a solution of the copper pigment (30·47 mg./l.) were mixed in a stoppered quartz cell with 0·25 c.c. (1 mol.) of a solution of dichlorodicyanoquinone (175 mg./l.) and the intensities of the absorption at 618 and 549 mμ were determined. From the observed values the concentrations of the two pigments were calculated.

Time (hr.)	0·2	3	6	28
Unchanged chlorin (%)	21·3	17·0	12·9	10·5
Porphin formed (%)	59·7	54·4	47·0	37·1

Similarly, 2 c.c. of the above solution were sealed with respectively 0·2 and 0·3 c.c. (1 and 1·5 mols.) of quinone solution into ampoules. After 28 hr. at room temperature the following results were obtained :

Mols. of quinone	Unchanged chlorin (%)	Porphin formed (%)
1	7·7	38·5
1·5	7.4	20·3

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