Rational Syntheses of Chlorocruoroporphyrin (*Spirographis* Porphyrin) and Pemptoporphyrin

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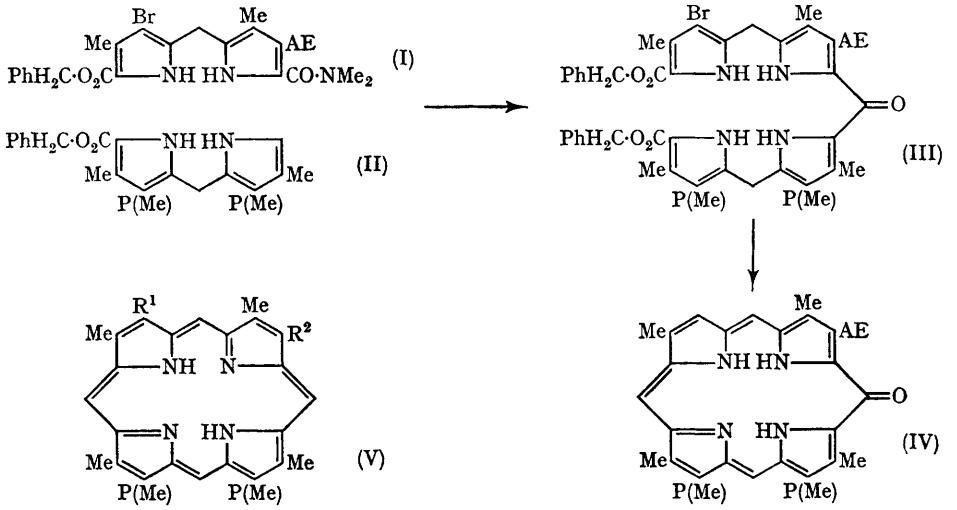
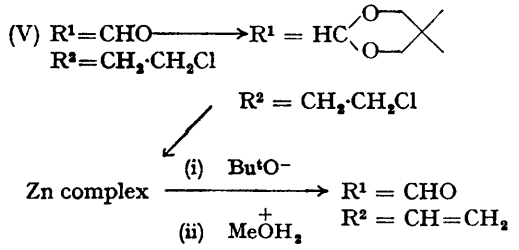
THE ferrous complex of chlorocruoroporphyrin (also known as spirographic haem) is the prosthetic group of the oxygen-carrying pigment of certain polychaete worms (*e.g.*, *Spirographis spallanzanii*) found in the Mediterranean. Chlorocruoroporphyrin dimethyl ester has been obtained from protoporphyrin-IX by partial oxidation with permanganate,[1] or recently by an ingenious photo-oxidation and subsequent transformation,[2] but neither of the methods gives totally satisfying support to the structure (V; R^1=CHO, R^2 = CH=CH_2), based largely on synthesis of certain degradation products,[3] nor does an earlier synthesis from deuteroporphyrin-IX.[4] We now report a rational synthesis of chlorocruoroporphyrin as part of our programme aimed at synthesis of porphyrin-*a*, which also contains formyl and vinyl substituents.[5] We have taken the opportunity of settling the structure of pemptoporphyrin, a faecal metabolite,[6] as (V; R^1=H, R^2=CH:CH_2) rather than (V; R^1= CH:CH_2, R^2=H) (dimethyl ester) by synthesis of both isomers.



[AE=CH_2·CH_2·O·COMe; P(Me)=CH_2·CH_2·CO_2Me]

The earlier stages of the synthesis were similar to those in our synthesis of protoporphyrin-IX by the *b*-oxobilane route,[7] except that a bromo-substituent protected a β-position. Thus the pyrromethane amide (I) was coupled (as its phosphoryl chloride complex) with the pyrromethane (II) to form a *b*-oxobilane (III), which was then converted into the oxophlorin (IV).[8] The bromine

was removed during hydrogenolysis of the benzyl esters. The oxophlorin (IV) was converted into the corresponding porphyrin (V; R^1=H, R^2=AE) by acetylation, hydrogenation, and aeration.[8] The acetoxyethyl group was transformed into chloroethyl,[7] and then the formyl group was introduced by treatment of the ferric complex with methyl dichloromethyl ether and stannic chloride.[9] Direct elimination of hydrogen chloride from the resultant formylchloroethylporphyrin (V; R^1=CHO, R^2=CH_2·CH_2Cl) or its metal complexes could not be accomplished without producing mixtures of porphyrins, and therefore the formyl group was protected as its relatively stable cyclic acetal according to the following scheme. (The dimethyl acetal was too unstable.)



The product (V; R^1=CHO, R^2 = CH:CH_2) had m.p. 281—283°,† and was identical with one of the porphyrins prepared by photo-oxidation[2] of protoporphyrin-IX (sample kindly provided by Professor H. H. Inhoffen); the m.p. is also in satisfactory agreement with that of the natural product, 285°.[3]

4-Vinyldeuteroporphyrin-IX dimethyl ester (V; R^1=H, R^2 = CH:CH_2), one of the two possible structures for pemptoporphyrin dimethyl ester, was readily accessible from the foregoing intermediate (V; R^1=H, R^2=AE) by the sequence described for protoporphyrin.[7] The n.m.r. spectrum was virtually identical with that published[10] for pemptoporphyrin dimethyl ester, but there was a small discrepancy in the m.p. 213—214°† (lit.,[10] 215–218°), and moreover Fischer and Wecker in their earlier synthesis had reported m.p. 264°, "falling to 225° after some time".[4] It was therefore essential to synthesise the 2-isomer (V; R^1 = CH:CH_2, R^2=H) for comparison, and this was done by a similar method, but using the *a*-oxobilane route[11] for synthesis of the intermediate porphyrin (V; R^1 = AE, R^2 = H). The product had m.p. 220—221°,† greatly depressed by mixing with the 4-isomer, and the n.m.r. spectrum was significantly different (see Figure), as was expected

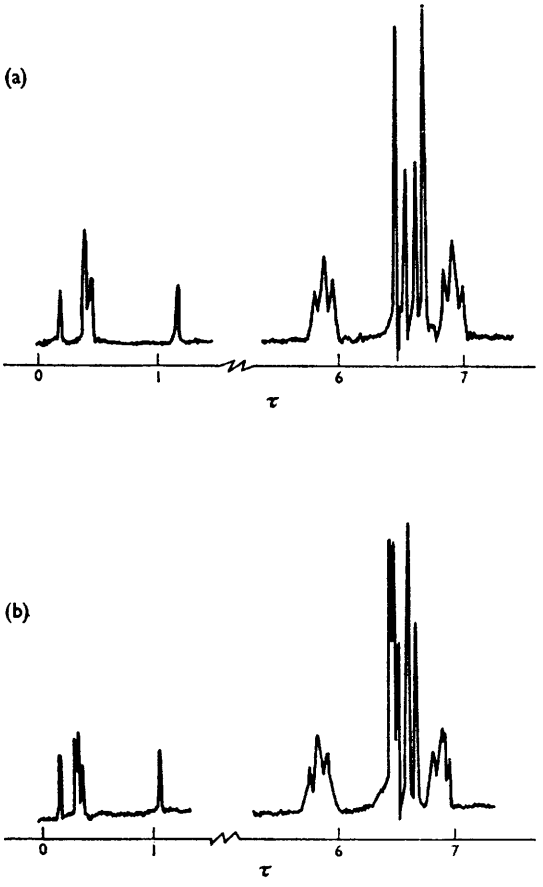


FIGURE. *N.m.r. spectra in* $CDCl_3$ *at* 100 Mc./sec.; (a) 4-vinyldeuteroporphyrin-IX dimethyl ester (0·092 M); (b) 2-vinyldeuteroporphyrin-IX dimethyl ester (0·089 M); (only the *meso*- and β-proton regions are shown).

on the basis of our recent work.[11] A pure sample of the natural product is no longer available for mixed m.p., but determinations with recovered material showed the expected depression of m.p. on

† M.p.s. were determined on a Kofler block and are corrected.

admixture of the 2-isomer and no change with the 4-isomer. Our sample of the latter was identical with material synthesized independently by Bamfield, Grigg, Kenyon, and Johnson.[12]

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