Synthesis of Deuteroporphyrin-IX and Pemptoporphyrin

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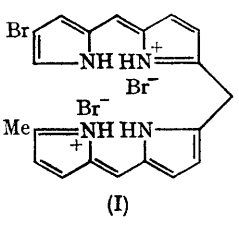
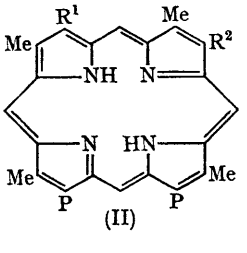
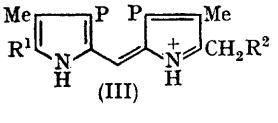
IN previous papers,[1,2] we have described the synthesis of several porphins, including degradation products of both haemin and chlorophyll, by the cyclization of 1-bromo-1,19-dideoxy-19-methyl biladiene-ac dihydrobromides (I), either by heating in *o*-dichlorobenzene, or, in certain cases, by keeping a pyridine solution at room temperature in presence of dimethyl sulphoxide. We have now extended the porphin synthesis to the preparation of deuteroporphyrin-IX (II; $R^1 = R^2 = H$) and to certain porphins containing β-vinyl substituents, including pemptoporphyrin.



(I)



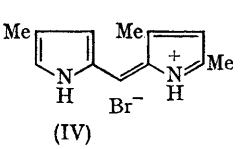
(II)



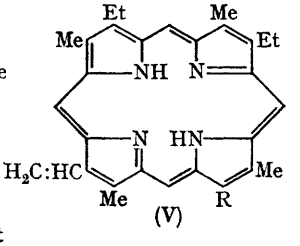
(III)

(P=$CH_2{\cdot}CH_2{\cdot}CO_2H$)

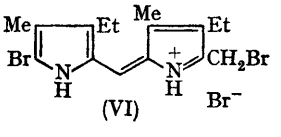
The two dipyrromethene hydrobromides required for the preparation of deuteroporphyrin-IX were (III; $R^1=R^2=Br$) and (IV), the latter being obtained by condensation of 2-formyl-4-methylpyrrole with 2,4-dimethylpyrrole. The important intermediate (III; $R^1=R^2=Br$) which is also required for syntheses of pemptoporphyrin (II; $R^1=H$, $R^2=CH:CH_2$) (see below) and *Spirographis* porphyrin (II; $R^1=CHO$, $R^2=CH:CH_2$) (see



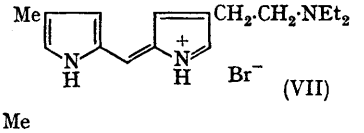
(IV)



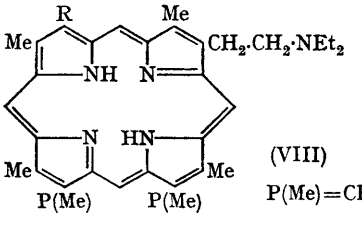
(V)



(VI)



(VII)



(VIII)

P(Me)=$CH_2{\cdot}CH_2{\cdot}CO_2Me$

below) is obtained by bromination of the dipyrromethene (III; $R^1 = CO_2H$, $R^2=H$). Condensation of (III; $R^1=R^2=Br$) and (IV) in nitromethane

in presence of stannic chloride, followed by treatment with methanolic hydrogen bromide, gave the corresponding 1,19-dideoxybiladiene-*ac* salt (56%), which was cyclized by heating in *o*-dichlorobenzene to deuteroporphyrin-IX (II; $R^1=R^2=H$).

For the preparation of β-vinylporphins we have used β-diethylaminoethyl substituents (*cf.*, ref. 3) in the intermediates, and introduced the vinyl group by Hofmann elimination as a final stage. Thus, as a model substance, 3,8-diethyl-2,7,12,17-tetramethyl-18-vinylporphin (V; R=H) has been prepared using the dipyrromethane hydrobromides (VI) and (VII) as precursors. In a parallel synthesis the zinc complex of 3,8-diethyl-2,7,12,-13,17-pentamethyl-18-vinylporphin (V; R=Me) has also been obtained.

We have extended the method to the preparation of pemptoporphyrin (II; $R^1=H$, $R^2=CH:CH_2$), isolated recently from human faeces.[4] The properties of pemptoporphyrin, particularly the spectral data, did not enable the original workers to eliminate the isomeric structure (II; $R^1=CH:CH_2$, $R^2=H$) for the natural product. However the unambiguous syntheses reported in this and the accompanying Communication by Jackson, Kenner, and Wass[5] enable the structure of pemptoporphyrin to be defined as (II; $R^1=H$, $R^2=CH:CH_2$). The requisite dipyrromethene hydrobromides for the synthesis were (III; $R^1=R^2=Br$) and (VII), which were condensed to form the 1-bromo-1,19-dideoxy-19-methylbiladiene-*ac* salt (the propionic acid chains were converted to the corresponding methyl esters in the process) which was cyclized to the corresponding porphin (VIII; $R^1=H$). Hofmann elimination then gave the dimethyl ester of pemptoporphyrin, m.p. 209—210°.

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[1] R. L. N. Harris, A. W. Johnson, and I. T. Kay, *J. Chem. Soc.* (*C*), 1966, 22.
[2] P. Bamfield, R. L. N. Harris, A. W. Johnson, I. T. Kay and K. W. Shelton, *J. Chem. Soc.* (*C*), 1966, 1436.
[3] A. M. Fargali, R. P. Evstigneeva, I. N. Khaidy, and N. A. Preobrazhenskii, *Zhur. obshchei. Khim.*, 1964, **34**, 898.
[4] S. Sano, T. Shingu, J. M. French, and E. Thonger, *Biochem. J.*, 1965, **97**, 250.
[5] A. H. Jackson, G. W. Kenner, and J. Wass, preceding Communication.