N-Methylation and Electrophilic Substitution Reactions of Octa-alkylporphins, Octaethylchlorin, and Metalloporphins

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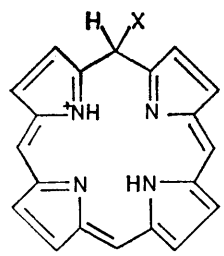
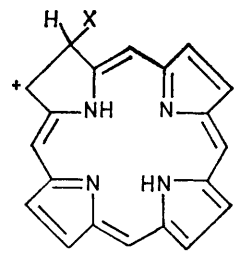
Methylation of octaethylporphin with methyl iodide yields the 21,22-dimethylporphin iodide as well as the 21-monomethyl derivative. The structure of the salt (*trans* arrangement of methyl groups) is assigned from n.m.r. data as well as evidence for chirality provided by partial resolution of the corresponding D-camphorsulphonate. Methylation of octaethylporphin with methyl fluorosulphonate gives the 21,23-dimethylporphin fluorosulphonate, probably through the intermediacy of the 21,22,23-trimethylporphin salt, suggesting that the 21- and 23-methyl substituents are *cis*-oriented. Methylation of octaethylchlorin gives the 23-monomethyl derivative (methyl fluorosulphonate) or the 22,23,24-trimethylchlorin iodide (methyl iodide). Electrophilic *meso*-substitution, exemplified by deuteriation, formylation, and nitration, takes place more readily with the metal complexes of porphins than with the free porphins; the first direct *meso*-methylation of a metalloporphin (Pd^{II} complex) is reported.

THE general trends discernible from previous studies of the reactions of porphins with electrophiles are (*a*) that reaction occurs preferentially at nitrogen (*e.g.* protonation,[1] methylation,[2,3] perbromide formation [1]); (*b*) that reaction at carbon is more difficult especially in acidic media where the porphin is present in the protonated form; and (*c*) that a vacant β-position is more reactive than a *meso*-position but reactions carried out in strong acid (*i.e.* on protonated porphins) or on metal complexes (*e.g.* copper porphins) may diminish or reverse this preference.[4] This last trend is deduced from isolated observations and may require qualification as more evidence accumulates. The first two trends are clearly related to the presence of two nucleophilic imino (-N=) nitrogen atoms in the porphins which impart properties similar to those of pyridines. Trend (*c*) is a reflection of the relative energies of the two transition states for electrophilic substitution, in which cyclic conjugation is blocked in one (1) but not in the other (2). Other canonical forms can be written for (2) but these involve cross-conjugated electronic systems, whereas (2), in which an 18 π-electron system is retained, should be the major contributor to the resonance hybrid. Clearly in acidic media *N*-protonated transition states are important.



(1)



(2)

Other more subtle aspects of porphin chemistry remain to be defined. Initially we were interested in the amount of crowding the interior of the porphin ring could withstand from the presence of *N*-alkyl substituents and the effect of the consequent steric strains on the aromaticity of the porphins. Previous work [3] had shown that aetioporphyrins I and II could be mono-*N*-methylated and -ethylated by heating the porphin with the appropriate alkyl iodide in a sealed tube. The resulting *N*-monomethyl porphins (21-methylporphins) were demethylated by heating or by the action of strong bases under anhydrous conditions, but they could be converted into zinc and copper complexes in which the *N*-methyl substituent was retained. Subsequent n.m.r. studies [5] showed that the 21-alkyl substituents gave rise to signals at $\tau > 10$, as expected for an alkyl substituent in a strongly shielded environment.

We have examined the methylation of octaethylporphin [6] using methyl iodide, and, like McEwen,[3] have shown that two products are formed. These were separated by chromatography and shown to be the 21-methyl derivative (3) and its *N*-methiodide, the 21,22-dimethylporphin (4; X = I). The visible and n.m.r. spectra of compound (3) were similar to those of the parent porphin, although the reduction in intensity of the Soret band accompanying *N*-methylation [$\varepsilon_{max.}$ 163,500 (ref. 7) reduced to 129,900] reflects the increased deviation of the ring from planarity. The protons of the 21-methyl group of (3) were, as expected, highly shielded (τ 14·7). The 21-methyl derivative (3) formed a charged zinc complex (5; X = I) analogous to the product described by McEwen.[3] The n.m.r. spectrum of compound (5; X = I) confirmed its structure and contained singlets at τ 0·35 (2H) and 1·25 (2H) associated with the *meso*-protons, together with a singlet at τ 16·05 for the 21-methyl group. The additional shielding observed for the 21-methyl protons, the large upfield shift of the protons of the

[1] H. Fischer and H. Orth, ' Die Chemie des Pyrrols,' Akademische Verlagsgesellschaft, Leipzig, 1937, vol. II, **1**, pp. 185 and 237.

[2] Preliminary communications, M. J. Broadhurst, R. Grigg, G. Shelton, and A. W. Johnson, *Chem. Comm.*, 1970, 231; R. Grigg, A. Sweeney, G. R. Dearden, A. H. Jackson, and A. W. Johnson, *ibid.*, p. 1273; R. Grigg, A. Sweeney, and A. W. Johnson, *ibid.*, p. 1237.

[3] W. K. McEwen, *J. Amer. Chem. Soc.*, 1946, **68**, 711; R. C. Ellingson and A. H. Corwin, *ibid.*, p. 1112.

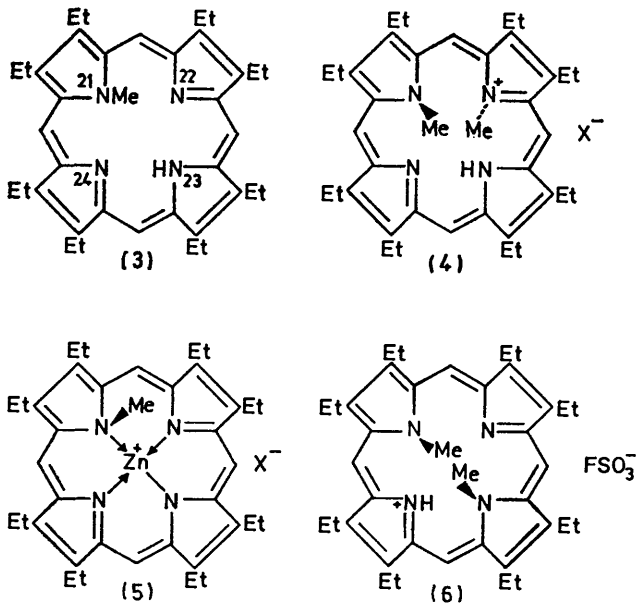
[4] W. S. Caughey, J. O. Alben, W. Y. Fujimoto, and J. L. York, *J. Org. Chem.*, 1966, **31**, 2631; H. Brockmann, K. M. Bliesener, and H. H. Inhoffen, *Annalen*, 1968, **718**, 148.

[5] W. S. Caughey and P. K. Iber, *J. Org. Chem.*, 1963, **28**, 269; C. B. Storm and A. H. Corwin, *ibid.*, 1964, **29**, 3700.

[6] H. H. Inhoffen, *Pure Appl. Chem.*, 1968, **17**, 443.

[7] H. W. Whitlock and R. Hanauer, *J. Org. Chem.*, 1968, **33**, 2169.

β-ethyl groups (CH_2 at τ 6·92; CH_3 at τ 9·1) attached to the *N*-substituted ring relative to the others (CH_2 at τ 5·76—6·26; CH_3 at τ 8·05—8·5) as compared to the parent 21-methyl compound (3), and the upfield shift of the *meso*-proton resonances conflicted with some of our observations on the related uncharged metal complexes of *N*-alkylcorroles, where the *meso*- and *N*-methyl proton resonances tended to undergo a downshift on metal (Ni^{II}) complex formation.[8] The importance of the influence of the anion on the spectral shifts in the porphin series was demonstrated by converting the iodide into the corresponding chloride complex (5; X = Cl), the n.m.r. spectrum of which illustrated the general trends observed in the corrole series since the *meso*-proton signals occurred at τ −0·22 (2H) and −0·27 (2H) and the *N*-methyl protons gave rise to signal at τ 14·60.* The differences in the n.m.r. spectra of compounds (5; X = I) and (5; X = Cl) presumably reflect a greater covalency in the iodide. Attempts were made to prepare nickel and palladium analogues of (5), but although insertion occurred on treatment of compound (3) with metal acetates in suitable solvents, the products were unstable and decomposed to metal octaethylporphins. The zinc complex (5; X = I) decomposed to zinc octaethylporphin when it was heated at 200° for a short time.



The highly crystalline salt (4; X = I) was reddish green and its electronic spectrum was typical of a porphin monocation (Figure 1). The *N*-methyl groups were assigned to adjacent rings on the basis of its n.m.r. spectrum, in which the *meso*-protons resonated at τ −0·4 (2H), −0·35 (1H), and −0·2 (1H), and a six-proton singlet at τ 15·75 indicated the presence of two similar or equivalent *N*-methyl substituents. Had methylation occurred on opposite rings [*i.e.* (6; iodide)] then the *meso*-protons should have given rise to two singlets (each 2H), or a 4H singlet assuming that the imino-proton is not fixed but shared between the

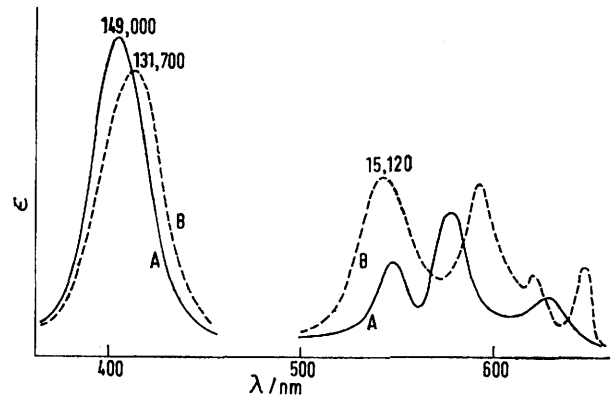


FIGURE 1 U.v. spectra ($CHCl_3$) of (A) *trans*-21,22-dimethyloctaethylporphin iodide and (B) 21,23-dimethyloctaethylporphin fluorosulphonate

two remaining nitrogen atoms.[9] The n.m.r. spectrum of the protonated form of (4; X = I) ($CF_3{\cdot}CO_2H$ solution) again showed three sharp signals (ratio 1 : 2 : 1) for the *meso*-protons, and the *N*-methyl signal remained a singlet. Solvent shifts brought about by the addition of perdeuteriobenzene failed to split the 2H *meso*-proton signal or the *N*-methyl resonance and thus supported structure (4; X = I), which has a two-fold rotation axis of symmetry if the imino-nitrogen atom is assumed to be equally shared between the unmethylated nitrogen atoms. These spectra also showed that four of the β-ethyl groups were shielded to a greater degree than the other four, caused by their attachment to the *N*-methylated rings and consequent diminished deshielding by the induced ring current. In the n.m.r. spectrum of a solution of compound (4; X = I) in deuteriochloroform, the imino-proton gave rise to a singlet resonance at τ 13·7 which was sharper than the signals usually associated with the imino-protons of porphins. Exchange with $NaOD–D_2O$ did not occur, although the exchange with $CF_3{\cdot}CO_2D$ was rapid, as shown by n.m.r. studies. The basicity of the 21,22-dimethylporphin (4; free base) was such that the compound existed as the salt even on alumina columns. Treatment of the iodide (4; X = I) with organic bases (*e.g.* piperidine) or hydroxide ions caused a marked reduction in the intensity of the Soret band ($\varepsilon_{max.}$ 149,000 to 62,950), but the shape of the spectrum suggested that the free base also contained an aromatic

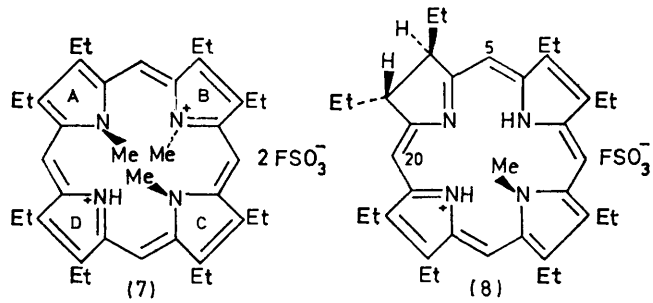
* We thank Professor A. H. Jackson and Mr. G. R. Dearden for communicating their results on related zinc 21-methylporphin chlorides which caused us to examine the chloride salt in our series.

[8] R. Grigg, A. W. Johnson, and G. Shelton, *Annalen*, 1971, **746**, 32; R. Grigg, T. J. King, and G. Shelton, *Chem. Comm.*, 1970, 56.

[9] M. J. Hamor, T. A. Hamor, and J. L. Hoard, *J. Amer. Chem. Soc.*, 1964, **86**, 1938; L. E. Webb and E. B. Fleischer, *J. Chem. Phys.*, 1965, **43**, 3100; B. F. Hoskins, S. A. Mason, and J. C. B. White, *Chem. Comm.*, 1969, 554.

chromophore. Solutions of the free base soon reverted to the salt form. This enhanced basicity of *NN'*-dialkylated macrocycles is common to the porphin, corrole, and dioxacorrole series.[10] An interpretation of the enhanced basicity in terms of current theories [11] of steric hindrance to solvation of charged species is not possible, and although steric hindrance to deprotonation is apparent from models, we have no definite evidence to support such an argument and the enhanced basicity of the dioxaporphins [12] suggests that other factors, such as ' bond fixation,' may be involved. The *trans*-configuration of the 21- and 22-methyl groups of structure (4) was demonstrated by conversion of the iodide into the D-camphor-10-sulphonate (*cf.* ref. 13), crystallisation of which effected partial resolution ($[\alpha]_D^{21}$ *ca.* +200°). The intense colour of the chloroform solutions used for rotation measurements prevented an accurate determination of this rotation. The steric influence of the first methyl group clearly favours attack from the other face of the molecule but the factors favouring formation of *trans*-21,22-dimethylporphin rather than the *trans*-21,23-isomer are not clear. However, an analogue computer study of porphins concluded that adjacent nitrogen atoms are more readily displaced than opposite nitrogen atoms.[14] When the iodide (4) was heated at its m.p. (233—238°) or in refluxing *o*-dichlorobenzene (179°), demethylation to octaethylporphin and the corresponding *N*-methyl derivative (3) occurred.

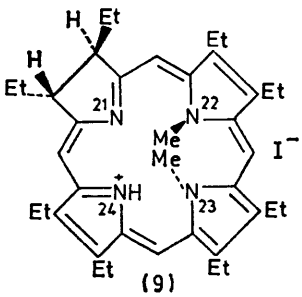
When octaethylporphin was treated with methyl fluorosulphonate [15] at room temperature for 24 h, similar methylation products (3) (22%) and (4; X = FSO_3) (28%) were obtained. However when the methylation was effected in boiling chloroform, besides the 21-methyl derivative (3), there was obtained a new *NN'*-dimethyl derivative (35%), isolated as its fluorosulphonate. The gross structure of this product was readily established by spectral measurements, *e.g.* the aromatic nature was supported by the existence of a Soret band at 402 nm ($\varepsilon_{max.}$ 131,700), although the visible spectrum was of a type which had not been observed previously in the porphin series (Figure 1). In the n.m.r. spectrum, the *N*-methyl groups were associated with a singlet (6H) at τ 13·6, and the four *meso*-protons with another singlet at τ 0·15. On this basis, the product was formulated [2] as the fluorosulphonate (6). The 21,22-dimethyl isomer (4; X = FSO_3) was unchanged in boiling chloroform, showing that it did not rearrange to compound (6) and thus ruling out the possibility of the formation of (6) by the conversion (4) ⟶ (6) under thermodynamic control. However treatment of compound (4; X = FSO_3) with more methyl fluorosulphonate gave a product, presumably the fluorosulphonate of the 21,22,23-trimethylporphin (7), which decomposed during chromatography on alumina to the 21,23-dimethylporphin salt (6). Dearden and Jackson [2,16] isolated the chloride of the 21,22,23-trimethylporphin by heating octaethylporphin in methyl fluorosulphonate for 5 days at 100° and showed that two of the *N*-methyl groups gave rise to a n.m.r. singlet peak at τ 13·92 whereas the third was associated with a singlet at τ 17·08. The definitive assignment of the stereochemistry of the two *N*-methyl groups of structure (6) must await *X*-ray crystallography, since (6) possesses a symmetry plane and is optically inactive, but we are inclined to believe that methylation on adjacent rings occurs in a *trans* manner [as in (4)], resulting in a *cis*-relationship of the *N*-methyl groups on rings A and C. The removal of an *N*-methyl group by nucleophilic attack on the 21,22,23-trimethylporphin [*i.e.* (7)] would then favour removal of the less sterically hindered ring B methyl group. A *cis*-arrangement of the *N*-methyl groups in (6) would result in greater deformation of the macrocycle than the *trans*-arrangement in (4), and this is reflected in the n.m.r. spectra of compounds (4) and (6), where there is an upfield shift of the *meso*-proton signals (τ −0·3, −0·1 to 0·15) and a downfield shift of the *N*-methyl signal (τ 15·9 to 13·6).



Treatment of *trans*-octaethylchlorin (from sodium–alcohol reduction of the porphin) with excess of methyl fluorosulphonate in methylene chloride at room temperature for 48 h gave an *N*-methyl derivative (87%) as its fluorosulphonate; in boiling chloroform solution the yield of the methylated derivative was much lower suggesting that the reaction was reversible. The product was purified by chromatography and it then showed a spectrum typical of a monoprotonated chlorin with a split Soret band ($\lambda_{max.}$ 399 and 415 nm) indicating distortion of the π-electron chromophore.[17] The n.m.r. spectrum showed that the two ethyl groups on the reduced ring were no longer equivalent (methyl triplets centred at τ 8·75 and 9·0) and whereas four of the

[10] M. J. Broadhurst, R. Grigg, A. W. Johnson, and G. Shelton, *J.C.S. Perkin I*, 1972, 143.
[11] V. Gold, *Progr. Stereochem.*, 1962, **3**, 169; C. H. Rochester and B. Rossall, *J. Chem. Soc.* (*B*), 1967, 743; *Trans. Faraday Soc.*, 1969, **65**, 1004.
[12] M. J. Broadhurst, R. Grigg, and A. W. Johnson, *J. Chem. Soc.* (*C*), 1971, 3681.
[13] R. Grigg, A. P. Johnson, A. W. Johnson, and M. J. Smith, *J. Chem. Soc.* (*C*), 1971, 2457.
[14] H. H. Corwin, J. A. Walter, and R. Singh, *J. Org. Chem.*, 1962, **27**, 4280.
[15] M. G. Ahmed, R. W. Alder, G. H. James, M. L. Sinnott, and M. C. Whiting, *Chem. Comm.*, 1968, 1533.
[16] G. R. Dearden and A. H. Jackson, *Chem. Comm.*, 1970, 205.
[17] J. E. Falk, ' Porphyrins and Metalloporphyrins,' Elsevier, Amsterdam, 1964, p. 75.

remaining ethyl groups were identical, the other two were different [methyl triplets centred at 8·15 (12H) and 8·57 (6H)]. The *meso*-proton signals occurred as two singlets at τ 0·0 and 0·8, and the accumulated n.m.r. evidence, especially the upfield shift of the protons of two of the β-ethyl substituents, suggests that methylation had occurred on the ring opposite the reduced ring, *i.e.* ring C, to give the 23-methylchlorin (8). A signal at τ 13·9 was associated with the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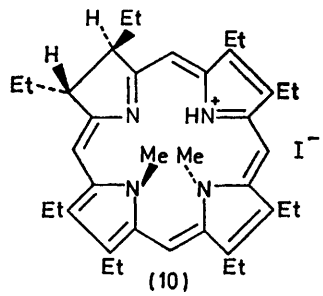
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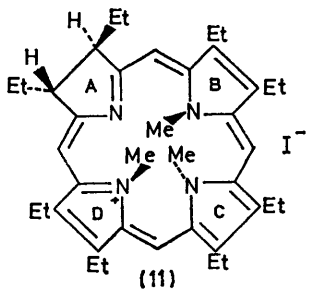
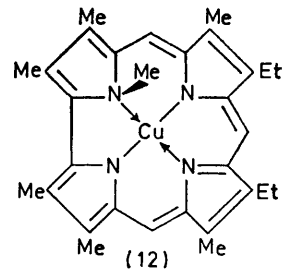

(11)

protons of the *N*-methyl group. The *N*-methylchlorin salt (8) decomposed at 195° to the parent octaethylchlorin.

When octaethylchlorin was heated in a sealed tube at 100° with methyl iodide in the presence of anhydrous potassium carbonate for 1—2 h, a mixture of two *NN'*-dimethylated octaethylchlorins and an *NN'N''*-trimethylated chlorin was obtained, we were unable to separate the mixture completely by column chromatography. However, when the reaction time was extended to 15 h the trimethylated product was isolated in 91% yield. The formation of two *NN'*-dimethylchlorins which can be converted into the same *NN'N''*-trimethylchlorin is interpreted as conversion of the 23-methylchlorin (8) into the two 22,23-dimethylchlorins (9) and (10), followed by further alkylation to give the 22,23,24-trimethylchlorin (11).

The n.m.r. spectrum of the mixture of compounds (9)—(11) indicates that (9) and (10) are formed in approximately equal amounts (*N*-methyl singlets at τ 14·65, 14·68, 14·7, and 14·75), demonstrating the absence of any marked directive steric effect by the chirality of the reduced ring. The pattern of the *N*-methyl signals of (11) in its n.m.r. spectrum resembled that of the related porphin (7), in that two of the *N*-methyl signals occurred at lower field (τ 13·3 and 13·4) than the other (τ 15·86). This pattern of signals is consistent with the *cis*-*N*-methyl substituents in rings B and D causing the chromophore to assume a bow configuration. The assignment of the site of alkylation in compounds (9), (10), and (11) again rests on n.m.r. evidence, in particular the upfield shift of the β-ethyl substituents which occurs in rings which are *N*-alkylated.

The *N*-alkylation pattern of octaethylchlorin, especially our suggestion that the reduced ring is not alkylated, calls for comment. Our earlier *X*-ray crystal structure determination of the *N*-methyl copper corrole (12)[8] indicated that the methylated nitrogen atom was essentially sp^3 hybridised and the bond lengths demonstrated that the conjugated chromophore by-passed the methylated nitrogen atom. We suggest therefore that a similar tendency for change in hybridisation occurs in the porphins and chlorins and that methylation on the reduced ring in a chlorin, both in the transition state and in the ground state of the product, would effectively block or seriously impair the cyclic delocalisation of electrons with consequent loss of aromaticity. However, methylation of any of the three remaining nitrogen atoms is energetically more favoured since an alternative pathway for conjugation through the β-positions is still available. Related cases are the ready terminal alkylation of nickel 1-methyltetradehydrocorrins (13) to give the 1,19-dimethyltetradehydrocorrin salts (14)[18] and the methylation of metal corrole ambident anions on nitrogen to give (for example) compound (12).[8]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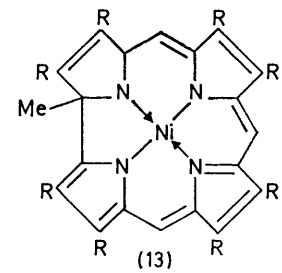
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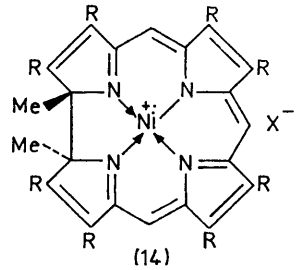
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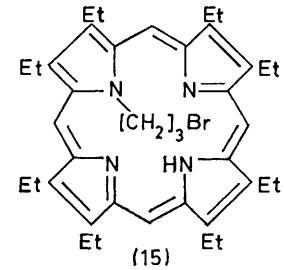

(15)

Hydrogen–deuterium exchange reactions with compound (8) and the parent octaethylchlorin show that exchange of the C-5 and C-20 *meso*-protons in deuterioacetic acid (*ca.* 0·1M-solutions) at 78° is approximately sixteen times slower for the 21-methyl compound (160 h) than for octaethylchlorin (10 h). Chlorins themselves are known to undergo deuteriation much faster than

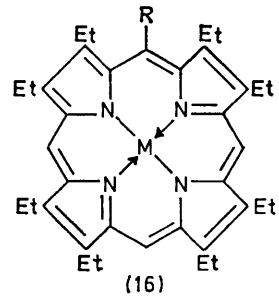
[18] R. Grigg, A. W. Johnson, and K. W. Shelton, *J. Chem. Soc.* (*C*), 1968, 1291.

porphins.[19,20] The lower rate of exchange in compound (8) possibly reflects both the increased nitrogen basicity and the effective prevention of N-23 from participating in the stabilisation of the transition state involved in *meso*-protonation.

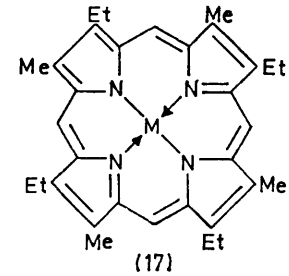
Thus our studies on the *N*-alkylation of porphins and octaethylchlorin demonstrate the great flexibility of the macrocycles and their ability to retain their aromaticity even when severely distorted by methylation of three of the four nitrogen atoms. The tendency to sp^3 hybridisation of the methylated nitrogen atoms demonstrated for the corrole (12) is, probably, also occurring in the *N*-methylated porphins and octaethylchlorin, and this has the effect of forcing conjugation to occur *via* β-positions. An attempt to produce a transannular carbon bridge by alkylation of octaethylporphin with 1,3-dibromopropane gave only the monoalkylated product (15). The n.m.r. spectrum ($CDCl_3$) of the latter showed the signals of the propyl chain at τ 14·9 (t, $N{\cdot}CH_2$), 11·5 (m, CH_2), and 8·5 (t, CH_2Br).

The biologically important porphins and chlorins occur as metal complexes but surprisingly little is known about the influence of metal ions on the chemical reactivity of the porphin ligand. We were particularly interested in electrophilic substitution reactions of metalloporphins since the *meso*-reactivity of porphins is low under acidic conditions, when *N*-protonation and consequent deactivation occurs. The situation in porphins, with two imino (=N–) nitrogens, is thus related to the difficulty experienced in achieving electrophilic substitution of pyridines. The formation of *N*-oxides of pyridines overcomes this difficulty in the pyridine series where p_π–p_π interaction of the oxygen and the pyridine ring stabilises the transition state for electrophilic substitution. The concept of transition metals fulfilling a similar role in porphin chemistry, either by discouraging *N*-protonation and/or by p_π–d_π interaction appeared attractive and has been studied.

A few examples of deuterium exchange (*e.g.* with magnesium chlorins [21]) and tritium exchange (with iron porphins [22]) have been recorded. The very mild deuteron source needed for exchange with magnesium chlorins ($CD_3{\cdot}OD$) emphasised the remarkable rate enhancement possible on insertion of a metal ion. We have now studied the deuterium exchange reactions of a series of metal derivatives of aetioporphyrin I and octaethylporphin. The metals used were Co^{II}, Ni^{II}, Pd^{II}, Pt^{II}, Rh^{III}, Fe^{III}, and Co^{III}. A chloroform solution of the metal porphin was treated with an equal volume of trifluoroacetic [^{2}H]acid and kept for 20 min at room temperature. The product was then isolated and its n.m.r. spectrum measured. In the cases of the complexes (16; M = Pd^{II} or Pt^{II}, R = H), (16; M = Pd^{II}, R = Me) (see later), and (17; M = Rh^{II}, extraplanar ligands OAc and H_2O) the fully *meso*-deuteriated products were obtained ($t_{\frac{1}{2}}$ for free octaethylporphin at 90° is 16,500 min [20]). In the case of the paramagnetic metal complexes (17; M = Cu^{II} or Fe^{III}), the mass spectra of the products provided clear evidence for exchange of all *meso*-protons and showed varying amounts of mono-, di-, and tri-deuterio-compounds. The copper porphin (17; M = Cu^{II}) underwent partial demetallation (37% estimated spectroscopically) but both the demetallated porphin and the Cu^{II} porphin had undergone deuteriation. The cobalt(II) and nickel(II) porphins (16; M = Co^{II}, R = H) and (17; M = Ni^{II}) were demetallated immediately by the acid, and the resulting metal-free porphins had not undergone any deuteriation (n.m.r. and mass spectra). The Co^{III} porphin (17; M = Co^{III}, extraplanar ligands Br and pyridine) underwent partial demetallation but no exchange was observed in either the metal-free porphin or the Co^{III} porphin (mass spectrum) isolated after the reaction. This surprising result is being more closely investigated.*



(16)



(17)

The *meso*-methyl palladium octaethylporphin (16; M = Pd^{II}, R = Me) was sufficiently soluble in $CDCl_3$–$CF_3{\cdot}CO_2D$ (1 : 1) for the n.m.r.spectrum to be determined. This again showed complete exchange of the *meso*-protons, but all the other proton signals were shifted markedly upfield, *e.g.* the *meso*-methyl protons appeared as a singlet at τ 5·65 in $CDCl_3$, but at τ 8·4 in $CDCl_3$–$CF_3{\cdot}CO_2D$. This evidence, together with the colour change (red ⟶ green-brown) when the *meso*-methyl palladium complex was dissolved in the acidic solvent, suggested that further deuteriation was occurring at one of the *meso*-positions, giving a blocked chromophore. This was verified by the spectrum of a solution in $CDCl_3$–$CF_3{\cdot}CO_2H$ (Figure 2), which showed that the product was compound (18). The quartet at τ 5·28 is assigned to the C-5 proton and the doublet at τ 8·47 to the C-5 methyl group. The simplicity of the n.m.r. spectrum indicates that specific protonation (within the limits of detection of the spectrometer, *i.e.* ⩾95%) has occurred at C-5. This specificity presumably

* Recently J. B. Paine and D. Dolphin, *J. Amer. Chem. Soc.*, 1971, **93**, 4080, have shown our failure to observe *meso*-exchange in the Co^{III} porphin case was due to dissolved oxygen in the trifluoroacetic acid causing oxidation to the π-cation radical.

[19] R. B. Woodward and V. Skaric, *J. Amer. Chem. Soc.*, 1961, **83**, 4676; R. B. Woodward, *Ind. chim. belge*, 1962, 1293.

[20] R. Bonnett, I. A. D. Gale, and G. F. Stephenson, *J. Chem. Soc.* (*C*), 1967, 1168.

[21] R. C. Dougherty, H. H. Strain, and J. J. Katz, *J. Amer. Chem. Soc.*, 1965, **87**, 104.

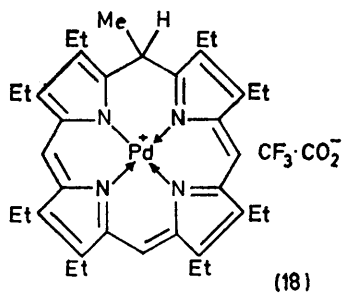
[22] C. E. Castro and H. F. Davis, *J. Amer. Chem. Soc.*, 1969, **91**, 5405.

reflects the relief of steric strain between the C-5 methyl group and the flanking β-ethyl groups which occurs in the transition state leading to protonation at C-5. Evidence for structures similar to (18) was obtained also by comparing the electronic spectra of the platinum

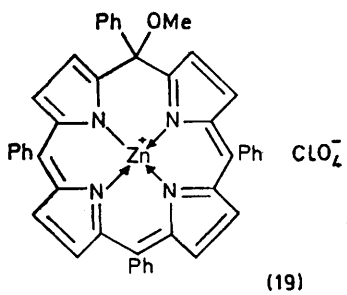
Electronic spectra of metalloporphins

(16; M = Pd^{II}, R = Me)	$\lambda_{max.}$ ($CHCl_3$) 278, 332, 408, 523, and 555 nm (ε 10,080, 11,870, 157,600, 13,560, and 18,120)
	$\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 365, 377, 570, and 908 nm (ε 32,600, 32,600, 4930, and 6940), $\lambda_{infl.}$ 329, 433, 534, and 595 nm (ε 21,400, 15,400, 4780, and 4500)
(16; M = Pd^{II}, R = H)	$\lambda_{max.}$ ($CHCl_3$) 273, 330, 394, 515, and 549 nm (ε 10,400, 11,730, 158,200, 12,720, and 39,910), $\lambda_{infl.}$ 281 nm (ε 9390)
	$\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 371, 506, 572, and 938 nm (ε 60,100, 6690, 5940, and 1250)
(16; M = Pt^{II}, R = H)	$\lambda_{max.}$ ($CHCl_3$) 293, 320, 382, 504, and 537 nm (ε 11,300, 7360, 226,000, 10,300, and 47,700), $\lambda_{infl.}$ 367 nm (ε 30,900)
	$\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 284, 293, 360, 395, 491, and 550 nm (ε 13,600, 13,900, 86,400, 23,700, 8520, and 6320)
(17; M = Rh^{III})	$\lambda_{max.}$ ($CHCl_3$) 285, 397, 515, and 548 nm (ε 12,350, 135,600, 12,050, and 28,460), $\lambda_{infl.}$ 332 and 345 nm (ε 14,800 and 16,290)
Axial ligands OAc and H_2O	$\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 356, 504, and 565 nm (ε 51,950, 6110, and 4720)

(16; M = Pt^{II}, R = H) and rhodium (17; M = Rh^{III}) porphins in acid solutions (Table). The structure (18)



(18)



(19)

which is an analogue of a benzenonium salt (*e.g.* ref. 23) is the first example of this type of intermediate resulting from electrophilic attack, to be observed in porphin chemistry; a related derivative (19) of the so-called isoporphin ring system has been isolated recently,[24] but was prepared by nucleophilic attack of methanol on a dicationic species.

The ready protonation of the palladium porphin is matched by a corresponding ease of *meso*-methylation.

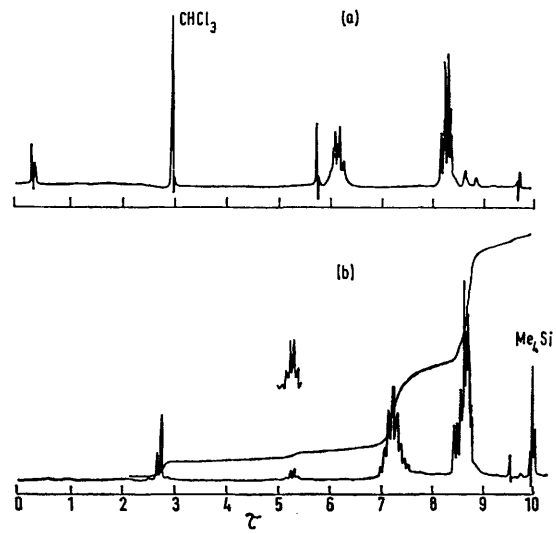


FIGURE 2 N.m.r. spectra of Pd^{II} *meso*-methyloctaethylporphin (a) in $CDCl_3$; (b) in $CDCl_3$–$CF_3{\cdot}CO_2H$

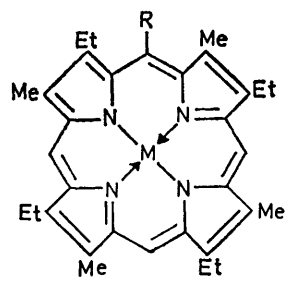
Thus, treating palladium octaethylporphin with excess of methyl fluorosulphonate in boiling chloroform for 48 h gave the *meso*-methylated palladium porphin (16; M = Pd^{II}, R = Me) (37%). The electronic spectrum showed the expected bathochromic shift in comparison with that of palladium octaethylporphin, and the n.m.r. spectrum (Figure 2a) showed only three *meso*-protons, with the *meso*-methyl protons corresponding to a sharp singlet at τ 5·65. The *meso*-methylation (at C-5) of a palladium porphin contrasts with the methylation of palladium corrole anions (20), where reaction occurred at N-21 and at C-3.[25] The direct *meso*-methylation of palladium octaethylporphin is the first example of this type of reaction although a reductive *meso*-methylation of the dianion of zinc octaethylporphin with methyl iodide to give the 5,15-dimethyl derivative has been described.[26]

Some electrophilic substitutions of porphins have been described where the presence of a complexed metal has a beneficial effect on the yield or even may change the nature of the product.[26] Thus, Vilsmeier formylation of aetioporphyrin I gives a low yield of the *meso*-chloro-derivative, whereas reaction of the nickel complex[27] or of copper(II) octaethylporphin[28] yields the *meso*-formyl derivative. We have now studied the reactivity

[23] G. A. Olah, M. B. Comisarow, E. Namanworth, and B. Ramsey, *J. Amer. Chem. Soc.*, 1967, **89**, 5259.
[24] D. Dolphin, R. H. Felton, D. C. Borg, and J. Fajer, *J. Amer. Chem. Soc.*, 1970, **92**, 743.
[25] R. Grigg, A. W. Johnson, and G. Shelton, *J. Chem. Soc.* (*C*), 1971, 2287.
[26] H. H. Inhoffen, J. W. Buchler, and P. Jäger, *Fortschr. chem. org. Naturstoffe*, 1968, **26**, 284.
[27] A. W. Johnson and D. Oldfield, *J. Chem. Soc.* (*C*), 1966, 794.
[28] H. H. Inhoffen, J. H. Fuhrhop, H. Voigt, and H. Brockmann, jun., *Annalen*, 1966, **695**, 133.

of aetioporphyrin I and a number of its metal derivatives (17; M = Zn^{II}, Cu^{II}, Ni^{II}, Co^{II}, Mn^{III}, or Fe^{III}) under identical formylation conditions [1,2-dichloroethane at 50° with equimolar amounts (5 mol. equiv.) of dimethylformamide and phosphoryl chloride for 30 min]. Aetioporphyrin I and the trivalent metal complexes (17; M = Mn^{III} or Fe^{III}) did not react under these conditions and the zinc porphin was demetallated. However both (17; M = Cu^{II}) and (17; M = Ni^{II}) gave the *meso*-monoformyl product (20; M = Cu^{II} or Ni^{II}, R = CHO). The cobalt(II) complex proved to be the most reactive of those studied (reaction essentially complete after *ca.* 3 min) and the product consisted entirely of the mixed *meso*-diformyl derivatives.

A similar comparative study was carried out for nitration with a copper(II) nitrate–acetic anhydride mixture at room temperature for 2 h. Once again the trivalent metal porphins (17; M = Mn^{III} or Fe^{III}) did not react, whereas the divalent metal complexes (17; M = Ni^{II}, Co^{II}, or Cu^{II}] gave the *meso*-mononitrometal porphin (20; M = Ni^{II}, Cu^{II}, or Co^{II}, R = NO_2) in high yield, although t.l.c. of the crude products demonstrated the presence of small amounts of dinitroderivatives. In the case of (17; M = Zn^{II}) the nitration gave a complex mixture, the main product (18%) being a *meso*-dinitro-compound (analysis), which proved too insoluble for an n.m.r. spectrum to be obtained. Aetioporphyrin I gave the expected *meso*-nitro-copper complex (20; M = Cu^{II}, R = NO_2). Our results demonstrate that incorporation of a metal ion into a



(20)

porphin promotes electrophilic substitution. The precise nature of this promoting effect is, however, not yet clear since the relative importance of a number of factors remains to be assessed. Clearly the reduced basicity of the pyrrole nitrogen atoms consequent on metal complexation will drastically (or completely) reduce the proportion of *N*-protonated species and hence facilitate electrophilic substitution. However the relative importance of other factors, such as electronegativity of the metal ion, d_π–p_π orbital interaction, and the influence of extraplanar ligands, remains to be delineated.

EXPERIMENTAL

N.m.r. spectra were determined for solutions in deuteriochloroform (except where otherwise stated) with a Perkin-Elmer RS10 instrument (60 MHz) or a Varian HA100 instrument (100 MHz) (tetramethylsilane as internal reference except where otherwise stated). U.v. and visible spectra were measured for solutions in chloroform (except where otherwise stated) with a Unicam SP 700 spectrophotometer and i.r. spectra for solutions in carbon tetrachloride (except where otherwise stated) with a Unicam SP 100 spectrophotometer. Mass spectra were obtained by direct insertion into the ion source of an A.E.I. MS 902 instrument. M.p.s were recorded with a Kofler hot-stage apparatus. Light petroleum was the fraction of b.p. 60—80°. Alumina for chromatography was Spence type H.

Methylations of Porphins and Chlorins

Octaethyl-21-methylporphin (1) *and Octaethyl-21,22-dimethylporphin Iodide* (4; X = I).—Octaethylporphin (2·25 g) was heated for 12 days with methyl iodide (50 ml; freshly distilled) under dry oxygen-free nitrogen in a sealed tube in the dark following the method of McEwen [3] with aetioporphyrin I. The excess of methyl iodide was removed by distillation and the residue (2·5 g) was chromatographed on alumina (chloroform as eluant). The first, red band yielded purple plates of *octaethyl-21-methylporphin* (1·445 g), m.p. 229—231° (from chloroform–methanol) (Found: C, 80·65; H, 8·7; N, 10·0. $C_{37}H_{48}N_4$ requires C, 81·0; H, 8·75; N, 10·2%), $\lambda_{max.}$ 412, 508, 539, 588, and 647 nm (ε 129,900, 13,520, 7360, 5120, and 3,500), $\lambda_{infl.}$ 386 nm (ε 66,780), τ 0·05 (2H) and 0·1 (2H) (4 *meso*-H, both s), 6·15 (m, 16H, CH_2·CH_3), 8·15 (18H) and 8·55 (6H) (both t, CH_2·CH_3), and 14·7 (s, 3H, NMe).

Chloroform–methanol (9 : 1) then eluted a red-green band. The solution was evaporated and the residue crystallised from methanol by addition of aqueous sodium iodide at the b.p. Recrystallisation from chloroform–light petroleum afforded purple needles of *2,3,7,8,12,13,17,18-octaethyl-21,22-dimethylporphin iodide* (920 mg), m.p. 233—238° (decomp.) (Found: C, 66·3; H, 7·45; I, 18·55; N, 8·0. $C_{38}H_{51}IN_4$ requires C, 66·1; H, 7·4; I, 18·4; N, 8·1%), $\lambda_{max.}$ 405, 545, 579, and 628 nm (ε 149,000, 8070, 12,200, and 5270), $\lambda_{max.}$ (10% piperidine in ethanol) 407, 553, 582, and 625 nm (ε 62,950, 9890, 12,190, and 10,250), τ −0·4 (2H), −0·35 (1H), and −0·2 (1H) (all s, 4 × *meso*-H), 5·9 (m, 16H, CH_2·CH_3), 7·98, 8·02, 8·3, and 8·45 (t, all 6H, CH_2·CH_3), 13·7 (s, imino-H), and 15·75 (s, 6H, 2 × NMe); when the solution was diluted with an equal volume of C_6D_6 the spectrum contained signals for *meso*-protons at −0·4 (1H), −0·3 (2H), and −0·15 (1H) (all s) and for the *N*-methyl groups at 15·7 (s); τ($CDCl_3$–CF_3·CO_2H) −0·75 (1H), −0·68 (2H), and −0·52 (1H) (all s, 4 × *meso*-H), 5·83 and 6·18 (q, both 8H, CH_2·CH_3), 8·15 (12H), 8·43 (6H), and 8·56 (6H) (all t, CH_2·CH_3), and 15·55 (s, 6H, 2 × NMe).

A solution of the salt in trifluoroacetic [^{2}H]acid was kept at room temperature for 10 min, then evaporated. The n.m.r. spectrum of the residue was identical with that already described ($CDCl_3$ solution), except that the signal at τ 13·7 had disappeared.

Iodides of Metal Cation Derivatives of Octaethyl-21-methylporphin.—(i) *Zinc complex* (5; X = I). Octaethyl-21-methylporphin (250 mg) was dissolved in chloroform (100 ml) and treated with zinc acetate (250 mg) in methanol (50 ml); the mixture was heated under reflux for 5 min, then evaporated and the residue was chromatographed on alumina. Elution with chloroform gave traces of *zinc octaethylporphin*, identified by comparison with an authentic

sample (t.l.c. and electronic spectrum). Elution with chloroform–methanol (9 : 1) then yielded a green band. This fraction was shaken with saturated aqueous sodium iodide, washed with water, and dried ($MgSO_4$). The solvent was evaporated and the residue crystallised from chloroform–light petroleum as purple needles (277 mg, 82%), m.p. (decomp.) >230° (Found: C, 59·75; H, 5·9; I, 17·5; N, 7·2. $C_{37}H_{47}IN_4Zn$ requires C, 60·05; H, 6·4; I, 17·15; N, 7·55%), $\lambda_{max.}$ 383, 432, 544, 589, and 631 nm (ε 44,800, 100,800, 8320, 12,450, and 2380), $\lambda_{infl.}$ 439 nm (ε 96,100), τ 0·35 and 1·25 (both s, both 2H, *meso*-protons), 5·76 (8H), 6·26 (4H), and 6·92 (4H) (all q, $CH_2{\cdot}CH_3$), 8·05 (6H), 8·25 (6H), 8·5 (6H), and 9·1 (6H) (all t, $CH_2{\cdot}CH_3$), and 16·06 (s, NMe). A sample was heated in the solid phase to 230° and then cooled. T.l.c. ($CHCl_3$) and the electronic spectrum of the residue showed it to consist mainly of zinc octaethylporphin.

The *chloride* salt (5; X = Cl) was prepared by dissolving the iodide (58 mg) in chloroform (50 ml) and shaking with saturated brine for 10 min. The chloroform layer was separated and evaporated to dryness and the residue crystallised from chloroform–cyclohexane (33 mg, 65%); m.p. >300° (a phase change from plates to needles commenced at *ca.* 285°) (Found: C, 68·1; H, 7·05; Cl, 5·2; N, 8·3. $C_{37}H_{47}ClN_4Zn$ requires C, 68·5; H, 7·3; Cl, 5·45; N, 8·65%).

(ii) *Attempted preparations of nickel and palladium complexes.* The metal-free macrocycle (200 mg) in chloroform (100 ml) was treated with nickel acetate (200 mg) in methanol (50 ml) and the mixture was heated under reflux for 45 min. The solvent was removed under reduced pressure and the residue chromatographed on alumina (chloroform for elution). The first, red band afforded red hairs of *nickel octaethylporphin* (48 mg, 22%), m.p. >300° (from chloroform–methanol), identical with an authentic sample (t.l.c. and electronic spectrum). The second, red band contained traces of the starting material. The main, red-green band was eluted with chloroform–methanol and the solution was shaken with saturated aqueous sodium iodide. Attempts to crystallise the salt from various solvents led only to its decomposition to nickel octaethylporphin. Solutions of the salt were stable for a few hours, but an attempt to measure the n.m.r. spectrum of a solution in deuteriopyridine was precluded by the paramagnetic nature of the species present in the solution.

Use of palladium acetate and the method described for the nickel complex gave only one isolable product, palladium octaethylporphin (72%), m.p. >300°, identical with an authentic sample (t.l.c. and electronic spectrum.)

Octaethyl-21-methylporphin (1) *and Octaethyl-21,22-dimethylporphin Fluorosulphonate* (4; X = FSO_3).—To a solution of octaethylporphin (100 mg) in freshly distilled dried chloroform (100 ml) was added methyl fluorosulphonate (5 ml). The mixture was stored in a stoppered flask at room temperature for 48 h. The solution was then washed with water (100 ml), 0·5M-ammonium hydroxide (100 ml), and water (2 × 100 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in chloroform (5 ml) and chromatographed (alumina). Elution with chloroform gave a trace of octaethylporphin, followed by a second, brown-red band which gave *N*-methyloctaethylporphin as purple needles (22·5 mg, 22%), m.p. 225—227° [from acetone–water (100 : 1)], identical with the sample obtained before. Elution with chloroform–ethanol (10 : 1) gave a green band which afforded *21,22-dimethyloctaethylporphin fluorosulphonate* as bright purple plates (35 mg, 28%), m.p. 198—199° [from dichloromethane–ether (red solution)] (Found: C, 68·55; H, 7·6; N, 8·05. $C_{38}H_{51}FN_4O_3S$ requires C, 68·85; H, 7·7; N, 8·45%), $\lambda_{max.}$ 306, 404, 543, 577, and 627 nm (ε 10,850, 132,000, 6630, 10,190, and 4410), τ −0·30 (s, 2 × *meso*-H), −0·2 and −0·1 (s, 2 × *meso*-H), 5·9 (m, 16H, $CH_2{\cdot}CH_3$), 8·1 (m, 24H, $CH_2{\cdot}CH_3$), and 15·9 (s, 6H, 2 × NMe).

Octaethyl-21,23-dimethylporphin Fluorosulphonate (6).—To a solution of octaethylporphin (100 mg) in chloroform (100 ml) was added methyl fluorosulphonate (5 ml); the mixture was heated under reflux for 100 h, care being taken to exclude moisture, The solvent was then evaporated and the residue dissolved in chloroform (5 ml) and chromatographed (alumina). Elution with chloroform gave a trace of octaethylporphin followed by *N*-methyloctaethylporphin (25 mg, 24%). Elution with chloroform–ethanol (4 : 1) gave a green-red band which afforded *21,23-dimethyloctaethylporphin fluorosulphonate* as purple plates (43 mg, 39%), m.p. >300° (from dichloromethane–ether) (Found: C, 68·55; H, 7·75; N, 8·25. $C_{38}H_{51}FN_4O_3S$ requires C, 68·85; H, 7·7; N, 8·45%), $\lambda_{max.}$ 308, 413, 542, 593, 621, and 647 nm (ε 26,390, 131,700, 15,120, 14,590, 6740, and 7380), τ 0·15 (s, 4 × *meso*-H), 6·3 (m, 16H, $CH_2{\cdot}CH_3$), 8·15 (t, 12H, $CH_2{\cdot}CH_3$ rings B/D), 8·7 (t, 12H, CH_2Me rings A/C), and 13·6 (s, 6H, 2 × NMe).

Attempted Interconversion of Octaethyl-21,22- and 21,23-dimethylporphin Fluorosulphonates.—(i) A solution of 21,22-dimethyloctaethylporphin fluorosulphonate (20 mg) in chloroform (20 ml) was heated under reflux for 100 h. T.l.c. showed the presence of only one substance which had an electronic absorption spectrum identical with that of the original salt.

(ii) A solution of 21,22-dimethyloctaethylporphin fluorosulphonate (20 mg) in chloroform (20 ml) containing methyl fluorosulphonate (1 ml) was heated under reflux for 100 h. The bright purple solution, $\lambda_{max.}$ 408, 550, and 595 nm, was evaporated and the residue dissolved in chloroform (2 ml) and then chromatoraphed on an alumina column (10 × 1 cm). Elution with chloroform gave *N*-methyloctaethylporphin; elution with chloroform–ethanol (4 : 1) gave 21,23-dimethyloctaethylporphin fluorosulphonate.

Thermolysis of Octaethyl-21,22-dimethylporphin Iodide.—The iodide (*ca.* 10 mg) was dissolved in chlorobenzene (10 ml) and the solution heated under reflux for 90 min. T.l.c. demonstrated the presence of octaethyl-21-methylporphin and octaethylporphin (comparison with authentic samples).

Octaethyl-21,22-dimethylporphyrin D-Camphor-10-sulphonate.—A solution of the foregoing iodide (350 mg) in chloroform (100 ml) was shaken several times with a saturated aqueous solution of D-camphor-10-sulphonic acid, and then washed with water, dried ($MgSO_4$), and evaporated to dryness. The residue crystallised from methylene dichloride–ether to give purple *prisms* (355 mg, 83%), m.p. *ca.* 190° (decomp.) (Found: C, 72·3; H, 8·3; N, 6·85; S, 3·9. $C_{48}H_{67}N_4O_4S$ requires C, 72·5; H, 8·35; N, 7·05; S, 4·05%), $\lambda_{max.}$ 405, 544, 577, and 626 nm (ε 151,300, 7810, 11,960, and 5200). The n.m.r. data ($CDCl_3$ and $CDCl_3$–$CF_3{\cdot}CO_2H$) were identical with those of the corresponding iodide except that signals were also observed corresponding to the D-camphor-10-sulphonate anion. A sample crystallised twice from methylene dichloride–ether showed $[\alpha]_D^{21}$ *ca.* +200°.

Octaethyl-21-(3-*bromopropyl*)*porphin* (15).—Octaethylporphyrin (500 mg) was dissolved in 1,3-dibromopropane (25 ml) containing anhydrous potassium carbonate (1 g) and the mixture was heated at 100° for 15 h in a sealed tube under nitrogen. The solvent was removed and the residue chromatographed on alumina with benzene as eluant. The first, brown band gave the *product* (141 mg, 23%), m.p. *ca.* 200° (decomp.) (from acetone–methanol) (Found: Br, 12·25; N, 8·2. $C_{39}H_{51}BrN_4$ requires Br, 12·2; N, 8·55%), $\lambda_{max.}$ 411, 509, 539, 588, and 647 nm (ε 92,500, 8690, 5080, 4010, and 2050), τ −0·3 and −0·13 (both s, both 2 × *meso*-H), 5·84 (m, 16H, $CH_2{\cdot}CH_3$), 7·9 (t, 18H, $CH_2{\cdot}CH_3$), 8·3 (t, 6H, ring A $CH_2{\cdot}CH_3$), 8·5 (t, 2H, CH_2Br), 11·5 (m, $N{\cdot}CH_2{\cdot}CH_2$), 13·2br (s, NH), 14·9 (t, 2H, NCH_2). The second, red band gave unchanged starting material (71%).

Palladium Octaethyl-5-*methylporphin* (16; M = Pd^{II}, R = Me].—To a solution of palladium(II) octaethylporphin (100 mg) in dry chloroform (100 ml) was added methyl fluorosulphonate (5 ml) and the mixture was heated under reflux for 48 h. The solution was then washed with water (100 ml), 0·5M-ammonium hydroxide (100 ml), and water again (2 × 100 ml), dried ($MgSO_4$), and evaporated. The brown residue was dissolved in chloroform (3 ml) and chromatographed on an alumina column (2 × 20 cm). Elution with benzene gave a trace amount of an unidentified green band. Elution with chloroform–benzene (1 : 1) gave a deep red band which afforded *palladium*(II) *meso-monomethyloctaethylporphin* as red needles (38 mg, 37%), m.p. >300° (from chloroform–ethanol) (Found: C, 67·95; H, 7·1; N, 8·3. $C_{37}H_{46}N_4Pd$ requires C, 68·1; H, 7·05; N, 8·6%), $\lambda_{max.}$ 278, 332·5, 408, 523, and 555 nm (ε 10,080, 11,870, 157,600, 13,560, and 18,120) $\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 365, 377, 569, and 908 nm (ε 32,600, 32,600, 4930, and 6940), $\lambda_{infl.}$ 329, 433, 534, and 595 nm (ε 21,400, 15,400, 4780, and 4500).

Elution with chloroform–ethanol (2 : 1) gave a blue solution, $\lambda_{max.}$ 404, 556, 606, and 667 nm, possibly containing a *meso*- and *N*-methylated palladium porphin.

Octaethyl-23-*methylchlorin Fluorosulphonate* (8).—(i) To a solution of octaethylchlorin [29] (200 mg) in dry, freshly distilled dichloromethane (200 ml) was added methyl fluorosulphonate (5 ml). The colour of the solution changed immediately from olive-green to blue-violet, and after 48 h in a stoppered flask at room temperature the solution was evaporated. The residue was dissolved in chloroform (3 ml) and chromatographed on an alumina column (2 × 20 cm). Elution with chloroform gave a green band which furnished purple needles of unchanged starting material, $\lambda_{max.}$ 392, 488, 497, 523, 614, and 649 nm. Elution with chloroform–ethanol (10 : 1) gave a blue-violet product which crystallised from dichloromethane–ether to give *N-methyloctaethylchlorin fluorosulphonate* as purple plates (102 mg, 87% allowing for recovered chlorin), m.p. 185—195° (Found: C, 68·8; H, 7·75; N, 8·35. $C_{37}H_{51}FN_4O_3S$ requires C, 68·4; H, 7·85; N, 8·6%), $\lambda_{max.}$ 280, 399, 415, 540, 559, and 628 nm (ε 15,200, 165,900, 153,100, 6740, 7070, and 20,500), τ 0·0 (s, 2 × *meso*-H), 0·8 (s, 2 × *meso*-H adjacent to reduced ring), 6·1 (m, 12H, $CH_2{\cdot}CH_3$), 8·15 (t, 12H, $CH_2{\cdot}CH_3$), 8·57 (t, 6H, $CH_2{\cdot}CH_3$), 8·75 (t, 3H, $CH_2{\cdot}CH_3$ of reduced ring), 9·03 (t, 3H, $CH_2{\cdot}CH_3$ of reduced ring), and 13·9 (s, NMe).

(ii) To a solution of octaethylchlorin (100 mg) in chloroform (100 ml) was added methyl fluorosulphonate (5 ml), and the mixture was heated under reflux for 1 week. T.l.c. indicated that only two substances were present, and chromatography on an alumina column gave the same products as in the previous experiment, although the actual amount of *N*-methyloctaethylchlorin fluorosulphonate produced (12 mg) was much less.

Octaethyl-22,23,24-*trimethylchlorin Iodide* (11).—Octaethylchlorin (500 mg) was dissolved in methyl iodide (25 ml) containing anhydrous potassium carbonate (1·0 g) and the mixture was heated in a sealed tube at 100° for 15 h under nitrogen. The solvent was evaporated off and the residue chromatographed on alumina. After a preliminary wash with chloroform, the column was eluted with chloroform–methanol (10 : 1). A single blue-green band was eluted, material from which was dissolved in chloroform and shaken with aqueous sodium iodide. The solution was boiled and the chloroform displaced with light petroleum; the *product* crystallised as purple prisms (546 mg, 91%), m.p. >300° (Found: C, 66·15; H, 7·9; N, 7·6. $C_{39}H_{55}IN_4$ requires C, 66·3; H, 7·85; N, 7·95%), $\lambda_{max.}$ 425, 596, and 662 nm (ε 134,000, 7720, and 11,900), $\lambda_{infl.}$ 433 and 571 nm (ε 121,400 and 6780), τ 0·45 (s, 2 × *meso*-H), 1·08 and 1·16 (both s, both *meso*-H), 5·5 (m, 2H, β-H of reduced ring), 6·45 (m, 12H, $CH_2{\cdot}CH_3$), 7·9 (m, 4H, $CH_2{\cdot}CH_3$ of reduced ring), 8·35—9·15 (m, 24H, $CH_2{\cdot}CH_3$), and 13·3, 13·4, and 15·86 (all s, 3 × NMe).

When the methylation was carried out for a shorter period (1—2 h), a mixture of di- and tri-methylated products was obtained.

Preparation and Reactions of Metalloporphins

Rhodium(III) *Aetioporphyrin I Chloride* (cf. *ref.* 30).—Aetioporphyrin I (200 mg), di-μ-chloro-bis[dicarbonylrhodium(I)] [31] (250 mg), and sodium acetate (250 mg) in glacial acetic acid (250 ml) were heated under reflux for 3 h and then poured into water (1 l). The aqueous solution was extracted with chloroform (2 × 250 ml) and the combined chloroform extracts were washed with water (3 × 200 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in chloroform (5 ml), chromatographed on alumina, and eluted with chloroform–ethanol (3 : 1) to give a red product which crystallised from chloroform–ethanol as red-brown *needles* (102 mg, 38·6%) (Found: N, 8·4. $C_{32}H_{36}ClN_4Rh,2H_2O$ requires N, 8·6%), $\lambda_{max.}$ 285, 297, 394, 513, and 545 nm (ε 12,750, 12,540, 127,100, 12,100, and 31,600), $\lambda_{infl.}$ 329 nm (ε 15,100), τ −0·34 (s, 4 × *meso*-H), 5·85 (q, 8H, $CH_2{\cdot}CH_3$), 6·3 (s, 4 × Me), 8·1 (t, 12H, $CH_2{\cdot}CH_3$), and 11·7 (m, H_2O).

Rhodium(III) *Aetioporphyrin I Acetate*.—Aetioporphyrin I (200 mg), di-μ-chloro-bis[dicarbonylrhodium(I)] (250 mg), and sodium acetate (1 g) in glacial acetic acid (500 ml) were heated under reflux for 5 h and then poured into water (1·5 l). The aqueous solution was extracted with chloroform (2 × 250 ml) and the combined extracts were washed with water (3 × 200 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in chloroform (5 ml) and chromatogtaphed on an alumina column. Elution with chloroform gave a bright orange-red fraction which afforded scarlet *needles* (138 mg, 50·5%) (from chloroform–ethanol) (Found: N, 8·6. $C_{34}H_{39}N_4O_2Rh,H_2O$

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requires N, 8·5%), $\lambda_{max.}$ 285, 397, 515, and 548 nm (ε 12,350, 135,600, 12,050, and 28,460), $\lambda_{infl.}$ 332 and 345 nm (ε 14,800 and 16,290), $\lambda_{max.}$ ($CF_3{\cdot}CO_2H$) 356, 504, and 565 nm (ε 51,950, 6110, and 4720), $\lambda_{infl.}$ 401 nm, $\nu_{max.}$ 1740 cm^{-1}, τ 0·6 (s, 4 × *meso*-H), 6·1 (q, 4 × $CH_2{\cdot}CH_3$), 6·6 (s, 4 × Me), 8·2 (t, 4 × $CH_2{\cdot}CH_3$), 10·4 (s, $CH_3{\cdot}CO$), and 13·2 (m, H_2O).

Hydrogen-deuterium Exchange Experiments.—General procedure. Deuteriotrifluoroacetic acid (3 ml) was added to a solution of metal porphin (50 mg) in chloroform (3 ml). The mixture was kept for 20 min with occasional shaking and then poured into chloroform (1 l.). The chloroform solution was washed with ammonium hydroxide (0·5M; 1 × 300 ml) and water (4 × 300 ml), dried ($MgSO_4$), and evaporated, and the residue was examined spectroscopically.

Iron(III) meso-*tetradeuterioaetioporphyrin I trifluoroacetate* was prepared thus from iron(III) aetioporphyrin I chloride. The mass spectrum showed the following deuteriation pattern; 3% $^2H_0$, 5% $^2H_1$, 13% $^2H_2$, 31% $^2H_3$, 43% $^2H_4$, and 3% $^2H_5$.

Palladium(II) *and platinum*(II) meso-*tetradeuterio-octaethylporphin* were prepared from the corresponding metal octaethylporphins. The n.m.r. spectra of the products showed the complete absence of *meso*-protons, and the electronic absorption spectra were identical with those of the starting materials.

Rhodium(III) meso-*tetradeuterioaetioporphyrin I acetate* was prepared from rhodium(III) aetioporphyrin I acetate. The n.m.r. spectrum of the product showed the complete absence of *meso*-protons, and its electronic absorption spectrum was identical with that of the starting material.

Palladium(II) 5-*methyl*-10,15,20-*trideuterio-octaethylporphin* was prepared from palladium(II) *meso*-monomethyloctaethylporphin. The n.m.r. spectrum of the product showed the complete absence of *meso*-protons and its electronic absorption spectrum was identical with that of starting material.

Copper(II) meso-*tetradeuterioaetioporphyrin*. Under the foregoing conditions the copper(II) porphin was partially demetallated (37% estimated spectroscopically), but both the porphin and the Cu^{II} porphin had undergone deuteriation. The mass spectrum of the copper complex showed the following deuteriation pattern: 2% $^2H_1$, 5% $^2H_2$, 22% $^2H_3$, 66% $^2H_4$, 2% $^2H_5$, and 2% $^2H_6$.

Formylation of Metalloporphins.—General procedure. Freshly distilled phosphoryl chloride (13·7 ml) was added dropwise to dry dimethylformamide (10 ml) cooled in an ice-bath, and the solution was kept at room temperature for 30 min. A sample (4·8 ml) was warmed on a water-bath to 50° and a solution of metal porphin (200 mg) in dry 1,2-dichloroethane (150 ml) was added dropwise with vigorous stirring, maintaining the temperature at 50—55° over a period of 15 min. The solution was then warmed for a further 30 min, a saturated solution of sodium acetate (150 ml) was added, and stirring and heating were continued for a further 2 h. The organic phase was separated and the water phase extracted with ether (2 × 100 ml), which was added to the organic layer. The organic solvents were removed under reduced pressure and the residue was dissolved in chloroform and chromatographed on an alumina column (3 × 30 cm).

Nickel(II) *aetioporphyrin I* gave a green fraction on elution with chloroform; the product, nickel(II) *meso*-monoformylaetioporphyrin I, crystallised from chloroform–ethanol in long red felted needles (155 mg, 74%) (Found: C, 70·7; H, 6·15; N, 9·72. Calc. for $C_{33}H_{36}N_4NiO$: C, 70·3; H, 6·6; N, 9·95%), $\lambda_{max.}$ 407, 428, 532, 565, and 658 nm (ε 72,300, 81,500, 4330, 6650, and 8630), $\nu_{max.}$ 1697 cm^{-1}, τ 0·8 (s, 2H) and 0·85 (s, 1H) (*meso*-protons) and −1·6 (s. 1H, CHO).

Copper(II) *aetioporphyrin I* gave, on elution with benzene–chloroform (5 : 1), unchanged starting material followed by a green-red fraction which afforded copper(II) *meso*-monoformylaetioporphyrin I as deep red needles (121 mg, 57%) (from chloroform–ethanol) (Found: C, 69·45; H, 6·15; N, 10·0. Calc. for $C_{33}H_{36}CuN_4O$: C, 69·8; H, 6·35; N, 9·95%), $\lambda_{max.}$ 326, 401, 526, 561, and 638 nm (ε 15,510, 200,500, 8600, 13,140, and 3960), $\lambda_{infl.}$ 320 nm (ε 14,500), $\nu_{max.}$ 1699 $cm.^{-1}$. Elution with chloroform–ethanol (20 : 1) removed a deep red fraction which crystallised from chloroform–ethanol to give maroon needles (5 mg), $\lambda_{max.}$ 326, 401, 525, 563, and 639 nm (ε 14,160, 184,000, 7900, 13,140, and 3540), $\lambda_{infl.}$ 322 nm (ε 13,310), $\nu_{max.}$ 1637br and 1701 (sharp) cm^{-1}.

Cobalt(II) *aetioporphyrin I* gave, on elution with chloroform–benzene (1 : 1), a green fraction which crystallised from chloroform–ethanol to give a mixture of isomers of *cobalt*(II) meso-*diformylaetioporphyrin* I (179 mg, 85%) (Found: C, 68·9; H, 5·95; N, 8·9. $C_{34}H_{36}CoN_6O_2$ requires C, 69·0; H, 6·1; N, 9·4%), $\lambda_{max.}$ 313, 402, 425, 528, 564, and 643 nm (ε 12,190, 61,950, 69,760, 4450, 5040, and 7840), $\nu_{max.}$ 1622 and 1703 cm^{-1}, $\nu_{infl.}$ 1666 cm^{-1}, *M* (mass spectrum), 591.

Zinc(II) *aetioporphyrin I* gave, on elution with chloroform, a red fraction which proved to be aetioporphyrin I. No other product was present.

Manganese(III) aetioporphyrin I hydroxide, iron(III) aetioporphyrin I chloride, and aetioporphyrin I all failed to react under the foregoing conditions.

Nitrations of Metalloporphins.—General procedure. A solution of copper(II) nitrate trihydrate (22·5 mg, 1·2 mol. equiv.) in acetic anhydride (10 ml) was added to the metalloporphin (100 mg) in glacial acetic acid (100 ml) and chloroform (50 ml), and the mixture was stirred for 2 h at room temperature. It was then poured into water (500 ml) and extracted with chloroform (250 ml). The chloroform solution was washed with water (3 × 100 ml), saturated sodium hydrogen carbonate solution (1 × 300 ml), and water again (2 × 100 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in chloroform (5 ml) and chromatographed on an alumina column (3 × 30 cm).

Nickel(II) *aetioporphyrin I* gave, on elution with benzene, a deep red fraction which was further purified by chromatography on a silica column (2 × 20 cm). The deep red band gave nickel(II) *meso*-mononitroaetioporphyrin I as deep red needles (140 mg, 64·5%) (from chloroform–light petroleum) (Found: C, 66·5; H, 5·9; N, 12·3. Calc. for $C_{32}H_{35}N_5NiO_2$: C, 66·3; H, 6·05; N, 12·1%), $\lambda_{max.}$ 291, 395, 523, and 560 nm (ε 9450, 145,800, 8950, and 20,600), $\lambda_{infl.}$ 349 nm (ε 13,450), $\nu_{max.}$ 1378 and 1536 cm^{-1}, τ 0·7 (s, 2H), and 0·8 (s, 1H) (*meso*-protons).

Cobalt(II) *aetioporphyrin I* gave, on elution with benzene, a red-brown fraction which was further purified by chromatography on a silica column (2 × 20 cm) and then crystallised from chloroform–light petroleum to give *cobalt*(II) meso-*mononitroaetioporphyrin I* as purple needles (170 mg, 74·8%) (Found: C, 66·5; H, 6·45; N, 12·4. $C_{32}H_{35}CoN_5O_2$ requires C, 66·3; H, 6·05; N, 12·1%), $\lambda_{max.}$ 385,

528, and 560 nm (ε 77,400, 10,020, and 16,580), $\nu_{max.}$ 1378 and 1540 cm^{-1}.

Copper(II) *aetioporphyrin I* gave, on elution with benzene, a bright red fraction which was further purified by chromatography on a silica column (2 × 20 cm). Copper(II) *meso*-mononitroaetioporphyrin I [32] crystallised from chloroform–light petroleum as red needles (158 mg, 66·2%).

Aetioporphyrin I similarly gave copper(II) *meso*-mononitroaetioporphyrin I (92 mg, 38%) (Found: C, 66·1; H, 5·7; N, 12·4. Calc. for $C_{32}H_{35}CuN_5O_2$: C, 65·8; H, 6·05; N, 12·0%), identical with the product obtained from copper(II) aetioporphyrin I.

Zinc(II) *aetioporphyrin I* gave, on elution with benzene, a brown-red fraction which was further purified by chromatography on a silica column (2 × 20 cm) and crystallised from chloroform–ethanol to give *zinc*(II) meso-*dinitroaetioporphyrin I* (42 mg, 18%) (Found: C, 60·5; H, 5·25; N, 13·1. $C_{32}H_{34}N_6O_4Zn$ requires C, 60·8; H, 5·4; N, 13·3%), $\lambda_{max.}$ 347, 401, 543, and 580 nm (ε 26,000, 202,000, 14,150, and 13,800), $\nu_{max.}$ 1380 and 1537 cm^{-1}.

Manganese(III) *aetioporphyrin I hydroxide* gave *manganese*(III) *aetioporphyrin I nitrate* as blue-black prisms (29 mg, 27%) (Found: C, 62·3; H, 6·7; N, 11·4. $C_{32}H_{36}MnN_5O_3,H_2O$ requires C, 62·9; H, 6·2; N, 11·5%), $\lambda_{max.}$ 362, 429, 477, 567, and 600 nm (ε 75,700, 14,070, 41,200, 9590, and 4390). A second band was eluted (56%) which proved to be unchanged starting material.

Iron(III) *aetioporphyrin I chloride* gave *iron*(III) *aetioporphyrin I nitrate* as purple-black prisms (138 mg, 68%) (Found: C, 64·6; H, 6·15; Cl, 0·0; N, 11·5. $C_{32}H_{35}FeN_5O_3$ requires C, 64·7; H, 6·05; N, 11·8%), $\lambda_{max.}$ 382, 565, and 590 nm (ε 53,950, 7200, and 6190), $\lambda_{infl.}$ 355 nm (ε 43,460).

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