Electrophilic Substitution Reactions of Metalloporphins

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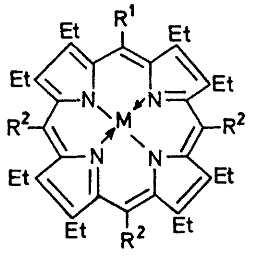
Summary Methylation, protonation, deuteriation, and formylation studies on a wide range of metalloporphins are reported and these results contrasted with the behaviour of metal-free porphins.

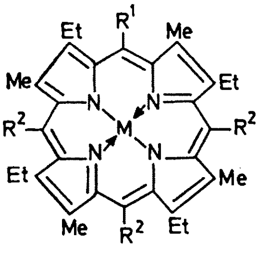
PORPHINS, metalloporphins, and related polypyrrolic macrocycles are ambident nucleophiles capable of undergoing reactions with electrophiles at several sites such as nitrogen, β-carbon, *meso*-carbon, and metal (in metalloporphins). In general, in the absence of activating substituents,[1] electrophilic substitution at *meso*-carbon in metal-free porphins is difficult, whereas reaction at nitrogen occurs much more readily. This preference for reaction at nitrogen is a consequence of the presence of two –N= atoms in the porphin skeleton which confer on the porphin ring properties related to those of pyridine, such as ready reaction of electrophiles at –N= *e.g.* protonation,[2] perbromide formation,[2] alkylation,[3,4] and reluctance to undergo electrophilic deuteriation at *meso*-[5] and β-carbon[6] owing to the formation of *N*-protonated species.

Insertion of a metal into a porphin results in the involvement of the lone pair of electrons on –N= in complex formation and reduces the basicity/nucleophilicity of the porphin nitrogen atoms. Neutral metalloporphins might therefore be expected to undergo electrophilic attack at carbon more readily than the parent porphins, and the presence of the metal should discourage attack at nitrogen.† Methylation of palladium octaethylporphyrin with methyl fluorosulphonate[7] in boiling chloroform gave the *meso*-methyl palladium porphin (I; M=Pd, R^1 = Me, R^2 = H; 36%), m.p. >300°. A second, as yet unidentified, charged product was also isolated. This is the first example of the direct *meso*-methylation of a porphin[8] and emphasises the reactivity differences between porphins and metalloporphins.

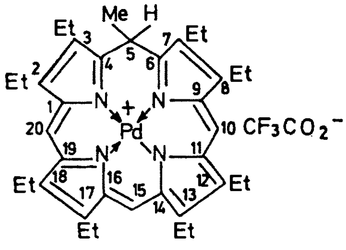
Deuterium exchange studies of the *meso*-[5] and β-protons[6] of porphins in acidic media have shown such exchange processes to be slow but recently partial exchange of the *meso*-protons of an Fe^{II} porphin in deuterioacetic acid was reported.[9] We have studied deuteriation reactions of a series of metallaoocta-alkylporphins (I; M = Co^{II}, Ni^{II}, Pt^{II}, Pd^{II}, $R^1 = R^2$ = H) and (II; M = Cu^{II}, Co^{III},‡ Fe^{III},‡ Rh^{III},‡ $R^1 = R^2$ = H) in 50:50 deuteriotrifluoroacetic acid–chloroform at room temperature. The Co^{II} and Ni^{II} porphins were rapidly demetallated and no exchange of the *meso*-protons occurred. The Co^{III} porphin underwent partial demetallation but no exchange was observed in either the metal-free porphin or the Co^{III} porphin isolated after the attempted deuteriation. All the other metalloporphins underwent rapid exchange (< 20 min) leading to complete deuteriation (n.m.r. evidence) at all four *meso*-positions to give (I; M = Pt^{II}, Pd^{II}, $R^1 = R^2$ = D) and (II; M = Rh^{III}, $R^1 = R^2$ = D). The Fe^{III} porphin was examined by mass spectrometry and found to have the following deuteriation pattern: 3%D_0, 5%D_1, 13%D_2, 31%D_3, 43%D_4, and 3%D_5. The Cu^{II} porphin underwent partial demetallation (37% estimated spectroscopically), but both the demetallated porphin and the Cu^{II} porphin had undergone deuteriation. The deuteriation pattern for the Cu^{II} porphin was 2%D_1, 5%D_2, 22%D_3, 66%D_4, 2%D_5, and 2%D_6. Under similar conditions (I; M = Pd^{II}, R^1 = Me, R^2 = H) gave the *meso*-trideuterio-product (I; M = Pd^{II}, R^1 = Me, R^2 = D). In comparison with these rapid deuteriations, the *meso*-protons of octaethylporphyrin have a half-life of 275 hr. at 90° in deuteriotrifluoroacetic acid.[5] The n.m.r. spectrum of (I; M = Pd^{II}, R^1 = Me, R^2 = H) in trifluoroacetic acid showed it to exist in the



(I)



(II)



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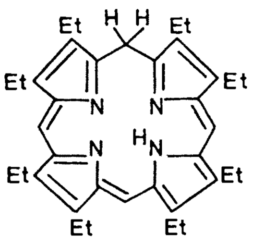

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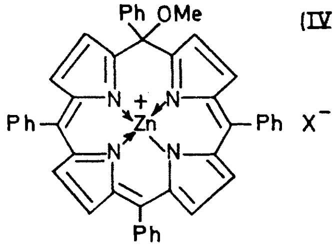

(V)

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† The metal could merely function as a "protecting" group on all four nitrogen atoms, exerting only an inductive effect, or, it could influence the transition state in electrophilic substitution by *dπ–pπ* overlap. An analogy in the pyridine series is the pyridine *N*-oxides involving *pπ–pπ* overlap of the ring with the oxygen atom.

‡ Axial ligands for Co ^{III}:Br and pyridine: Rh^{III}:OAc and H_2O: Fe^{III}:Cl and H_2O: and for Mn^{III}:OH and H_2O.

meso-protonated form (III) with signals at τ 2·68(s, 1H, C-15 proton), 2·76 (s, 2H, C-10 and C-20 protons), 5·28 (q, 1H, C-5 proton), and 8·47 (d, 3H, C-5 methyl). The protonated macrocycle (III) is related to the benzenonium ions[10] and may be regarded both as the intermediate in an electrophilic substitution reaction, and as a palladium complex of the unknown isoporphyrin (IV).[11] A related zinc complex (V) has recently been reported as the product from the nucleophilic attack of methanol on the corresponding zinc dicationic species.[12]

Although it has not proved possible to obtain the n.m.r. spectra of (I; M = $\mathrm{Pt^{II}}$, $\mathrm{Pd^{II}}$, $R^1 = R^2 = H$) and (II; M = $\mathrm{Rh^{III}}$, $R^1 = R^2 = H$) in trifluoroacetic acid, comparison of the u.v. spectra of these metalloporphins with that of (I; M = $\mathrm{Pd^{II}}$, R^1 = Me, R^2 = H) provides compelling evidence for the presence of species with interrupted π-electron chromophores (Table).

Other electrophilic substitution reactions of metalloporphins have been studied and the general trends are illustrated by formylation studies. Aetioporphyrin I and a number of its metal complexes (II; M = $\mathrm{Zn^{II}}$, $\mathrm{Cu^{II}}$, $\mathrm{Ni^{II}}$, $\mathrm{Co^{II}}$, $\mathrm{Mn^{III}}$,‡ $\mathrm{Fe^{III}}$, $R^1 = R^2 = H$) were formylated in 1,2-dichloroethane at 50° with equimolar amounts (5 mol.) of dimethylformamide and phosphorus oxychloride for 30 min. Under these conditions aetioporphyrin I and (II; M = $\mathrm{Mn^{III}}$, $\mathrm{Fe^{III}}$, $R^1 = R^2 = H$) failed to react while (II; M = $\mathrm{Zn^{II}}$ was demetallated. In contrast, both (II; M = $\mathrm{Cu^{II}}$) and (II; M = $\mathrm{Ni^{II}}$) gave the *meso*-monoformyl product (II; M = $\mathrm{Cu^{II}}$, $\mathrm{Ni^{II}}$, R^1 = CHO, R^2 = H) in 74 and 57% yield, respectively, together with small amounts of starting material. The cobalt porphin (II; M = $\mathrm{Co^{II}}$) reacted much more rapidly and gave a mixture of *meso*-diformyl derivatives.

Electronic spectra of metalloporphins

(I) M=$\mathrm{Pd^{II}}$ R^1 = Me, R^2 = H	λ_{max} ($CHCl_3$) 278, 332, 408, 523, and 555 nm ϵ, 10,080, 11,870, 157,600, 13,560, and 18,120, resp. λ_{max} (T.F.A.) 365, 377, 570, and 908 nm. ϵ, 32,600, 32,600, 4930, and 6940, resp. $\lambda_{infl.}$, 329, 433, 534, and 595 nm. $\epsilon_{infl.}$, 21,400, 15,400, 4780, and 4500, resp.
(I) M=$\mathrm{Pd^{II}}$ $R^1=R^2=H$	λ_{max} ($CHCl_3$) 273, 330, 394, 515, and 549 nm. ϵ, 10,400, 11,730, 158,200, 12,720, and 39,910, resp. $\lambda_{infl.}$, 281 nm, $\epsilon_{infl.}$, 9390. λ_{max} (T.F.A.) 371, 506, 572, and 938 nm. ϵ, 60,100, 6690, 5940, and 1250, resp.
(I) M = $\mathrm{Pt^{II}}$ $R^1 = R^2 = H$	λ_{max} ($CHCl_3$) 293, 320, 382, 504, and 537 nm. ϵ, 11,300, 7360, 226,000, 10,300, and 47,700, resp. $\lambda_{infl.}$, 367 nm, ϵ, 30,900. λ_{max} (T.F.A.) 284, 293, 360, 395, 491, and 550 nm. ϵ, 13,600, 13,900, 86,400, 23,700, 8520, and 6320, resp.
(II) M = $\mathrm{Rh^{III}}$ $R^1 = R^2 = H$ Axial ligands= OAc and H_2O	λ_{max} ($CHCl_3$) 285, 397, 515, and 548 nm. ϵ, 12,350, 135,600, 12,050, and 28,460, resp. $\lambda_{infl.}$, 332 and 345 nm, $\epsilon_{infl.}$, 14,800 and 16,290, resp. λ_{max} (T.F.A.)356, 504, and 565 nm. ϵ, 51,950, 6110, and 4,720, resp.

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