Electrophilic Attack at the Porphyrin Periphery. *meso*- *vs*. β-Deuteriation

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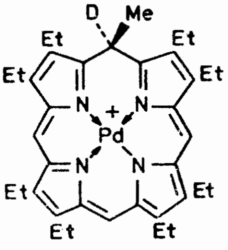
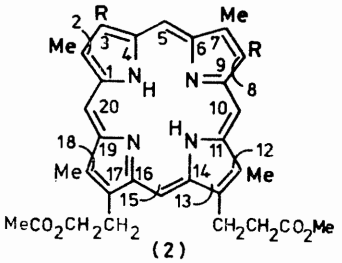
Summary Deuteroporphyrin IX undergoes faster deuteriation at the *meso*-positions than at the β-positions in deuterioacetic acid whilst in its metal complexes the order is reversed; protoporphyrin IX undergoes deuteriation at the *meso*-position in preference to the vinyl positions.

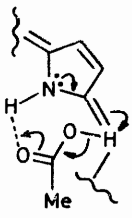
THE presence of two imino nitrogen atoms in the porphyrin core results in ready *N*-protonation of free base porphyrins in strong acids giving the di-*N*-protonated porphyrins which undergo slow *meso*-deuteriation.[1] A similar deactivation of the β-positions of free base porphyrins and corroles in strong acid has been noted.[2,3] In contrast the metalloporphyrins, where *N*-protonation is discouraged, undergo rapid *meso*-deuteriation[4,5] and clean formation of the deuteriated intermediate (1) is observed in deuteriotrifluoroacetic acid.[5] Free base porphyrins show similar exchange behaviour in weak acids.[6]



(1)



(2)
a; R = H
b; R = CH=CH2



(3)

Bromination,[7,8] sulphonation,[9] and acylation studies[10] have led to the conclusion that β-positions are more reactive towards electrophilic attack than *meso*-positions.† However, nitration of deuteroporphyrin IX (2a) occurs only at the *meso*-position[8] whilst formylation under Vilsmeir conditions often leads to mixtures of β- and *meso*-formylated products.[11] We now report the observation that in boiling deuterioacetic acid the *meso*-protons of deuteroporphyrin IX exchange at a faster rate ($t_{\frac{1}{2}} = 0{\cdot}5$ h) than the β-protons ($t_{\frac{1}{2}} = 1{\cdot}2$ h).‡ In contrast, the nickel complex of (2a) undergoes faster exchange at the β-positions ($t_{\frac{1}{2}} = 1{\cdot}25$ h) than the *meso*-positions ($t_{\frac{1}{2}} = 6{\cdot}6$ h). A similar result was obtained with the palladium complex of (2a)

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† These studies relate to β-alkylporphyrins and the effect of π-conjugating substituents remains to be evaluated, *e.g.* R. B. Woodward and V. Skaric, *J. Amer. Chem. Soc.*, 1961, **83**, 4676.

‡ $t_{\frac{1}{2}}$ values refer to the overall rate of exchange of all β- or all *meso*-protons.

[$t_{\frac{1}{2}}$ (β-H) = 1·05 h; $t_{\frac{1}{2}}$ (*meso*-H) = 8·75 h]. The cobalt(III) complex of (**2a**) also gave qualitatively the same result. Furthermore it was noticed that one *meso*-proton exchanged at a faster rate than the remaining *meso*-protons. A complete assignment of the n.m.r. spectra of (**2a**) and of the nickel and palladium complexes of (**2a**) was therefore undertaken by decoupling and nuclear Overhauser effect studies at 360 MHz. The assignments for the metal complexes are shown in the Figure and the n.m.r. studies lead to the conclusion that in (**2a**)§ and its nickel(II) and palladium(II) complexes the C(10)-*meso*-proton exchanges at a faster rate than the C(5)-, C(15)-, and C(20)-*meso*-protons, *e.g.* for nickel deuteroporphyrin IX in boiling CH_3CO_2D, $t_{\frac{1}{2}}$ for the C(10)-*meso*-proton is 2·75 h. A preference for electrophilic substitution at the C(10)-*meso*-position has been observed in deuterohaemin.[12]

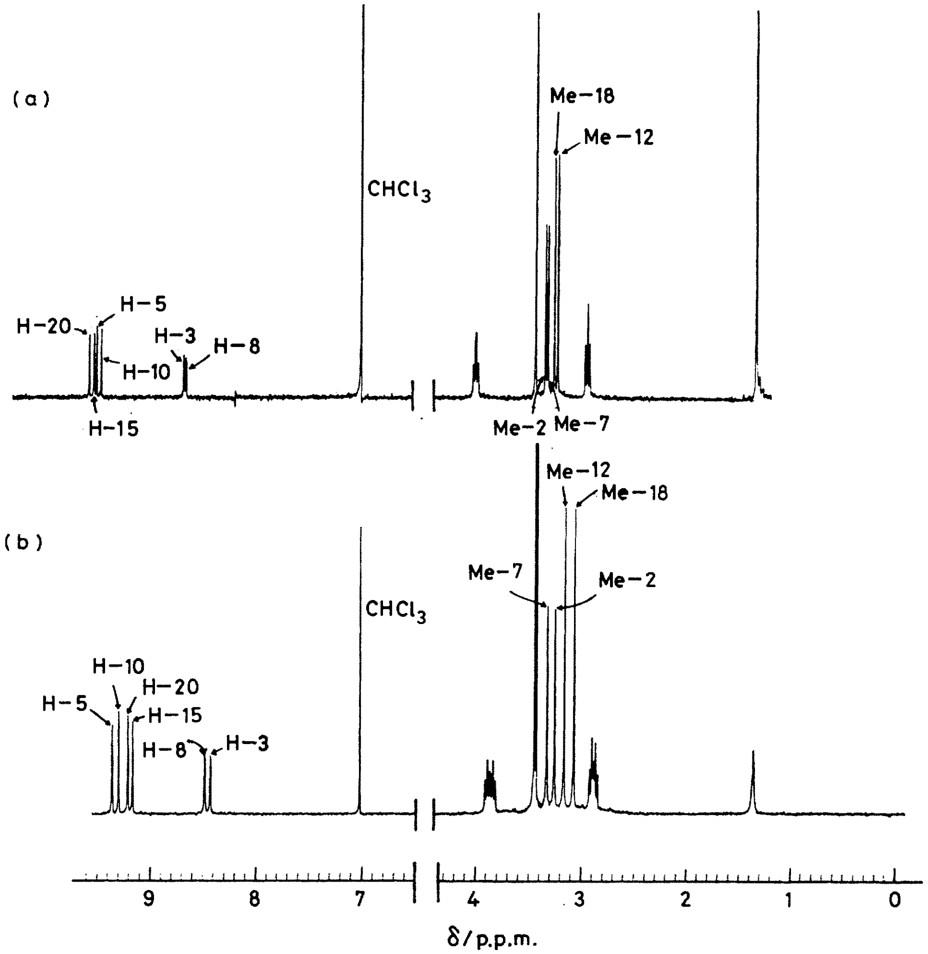

FIGURE. ^{1}H N.m.r. spectra of (a) Ni^{II} ($4{\cdot}2 \times 10^{-3}$ M) and (b) Pd^{II} ($3{\cdot}1 \times 10^{-2}$ M) complexes of (**2a**) at 360 MHz.

Attempts to study *meso*- *vs*. vinyl-proton exchange rates in protoporphyrin IX (**2b**) and its metal complexes were less successful due to their instability in hot CH_3CO_2D. However, after 2 h in boiling CH_3CO_2D the *meso*-protons of (**2b**) had exchanged to the extent of *ca*. 95% whilst the vinyl protons had undergone very little exchange (*ca*. 5%). This contrasts with the observations that protohaemin dimethyl ester [Fe^{III} complex of (**2b**)] undergoes selective nitration[13] and formylation[12] at the terminal position of the vinyl groups.¶

Insertion of nickel(II) or palladium(II) into (**2a**) has little effect on the rate of exchange of the β-protons but signifi-

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§ Chemical shifts (p.p.m. from Me_4Si) in $CDCl_3$ for (**2a**) at a concentration of 2·5 mg ml^{-1} are 10·05 (H-10), 10·09 (H-5), 10·12 (H-15), and 10·16 (H-20).

¶ D. L. Budd, G. N. La Mar, K. C. Langry, K. M. Smith, and R. Neyyir-Mazhir, *J. Amer. Chem. Soc.*, in the press, observe that the terminal methylene protons of the vinyl groups in (**2b**) exchange at a faster rate than the *meso*-protons in *o*-dichlorobenzene containing $MeC_6H_4SO_3D$-*p* at 95 °C. In this work, using a much stronger acid, the species undergoing exchange must be the protonated porphyrin.

cantly alters the *meso*-proton exchange rate. A possible explanation for the contrasting behaviour of free base- and metallo-porphyrins is that hydrogen-bonding involving the amino nitrogen atoms in the porphyrin core plays an essential role in lowering the energy of the transition state for *meso*-protonation. A simple possible model is (**3**) (partial formulae). Tilting of the pyrrole ring out of the porphyrin plane[14] facilitates the hydrogen-bonding process and in (**3**) *meso*-protonation is geometrically realisable whilst β-protonation is not. In metalloporphyrins the inner amino hydrogens are no longer present. The reported selective *meso*-nitration of (**2a**)[8] probably involves the porphyrin cation radical.[15]

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[14] The easy deformation of the porphyrin ring is shown by *X*-ray studies (J. L. Hoard, in 'Porphyrins and Metalloporphyrins,' ed. K. M. Smith, Elsevier, Amsterdam, 1975, ch. 8) and *N*-alkylation studies (*e.g.* ref. 5).

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