Control of Reactivity at the Porphyrin Periphery by Metal Ion Co-ordination: a General Method for Specific Nitration at the β-Pyrrolic Position of 5,10,15,20-Tetraarylporphyrins

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The site of nitration by nitrogen dioxide on a range of metalloporphyrins has been found to be dependent on the co-ordinated metal; copper(II), nickel(II), and palladium(II) complexes are nitrated specifically on the porphyrin β-pyrrolic position while magnesium(II), zinc(II), chloroiron(III), and cobalt(II) complexes also give products which result from reaction at the *meso*-position.

Reactions at the periphery of metalloporphyrins occur preferentially on the bridging *meso* positions and the few exceptions have been readily explained as arising from considerable steric impediment to such attack.[1] Calculations and a frontier orbital rationalization have been advanced to account for this selectivity.[2] We now report however that the preferred site of nitration of a range of 5,10,15,20-tetraarylporphyrins can be controlled by the simple process of varying the co-ordinated metal; this has allowed the development of a general method for specific nitration at a β-pyrrolic position of these porphyrins. This process is the result of electronic effects rather than overriding steric factors.

Treatment of a range of metallo-5,10,15,20-tetraphenylporphyrins (**1**) with nitrogen dioxide (2.05 equiv.) in trichloroethylene, CH_2Cl_2, benzene, benzene–hexane, or CH_2Cl_2–MeCN resulted in a rapid irreversible reaction at room temperature. Variation of the co-ordinated metal has a profound effect on the extent of β-nitration (Table 1), which was essentially the same in each solvent system.

The magnesium(II) and zinc(II) chelates gave mainly the bilinone (**2**)[3,4] and other non-porphyrin products resulting from initial reaction at the *meso*-position (Scheme 1). This observation established that attack at the *meso*-position is not prevented by the aryl substituent. The extent of β-nitration increased with the electronegativity of the central metal and in the cases of the nickel(II), copper(II), and palladium(II) complexes regiospecific reaction at the β-pyrrolic position was observed to afford the corresponding 2-nitroporphyrin (**3**).†

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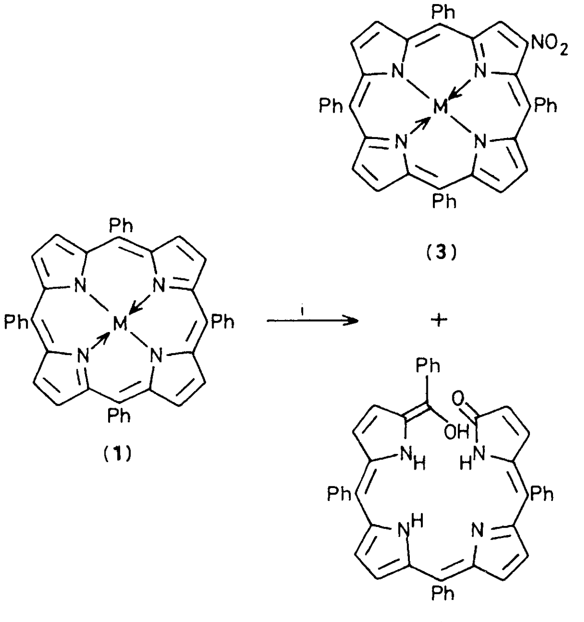
† All new porphyrins have been adequately characterized by analytical and/or spectroscopic means.

Table 1. Effect of co-ordinated metal on the site of nitration of metallo-5,10,15,20-tetraphenylporphyrins.[a]

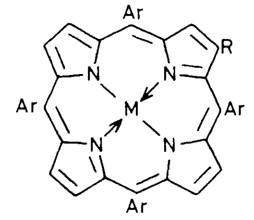
Co-ordinated metal	% Nitration at β-pyrrolic position[b,c]	Pauling electronegativity
Mg^{II}	24	1.31
Zn^{II}	26	1.65
$Fe^{III}Cl$	53	1.83
Co^{II}	80	1.88
Cu^{II}	100	1.90
Ni^{II}	100	1.91
Pd^{II}	100	2.20

[a] See text for reaction conditions. [b] Other products are ring-opened compounds arising from reaction at a *meso*-position. [c] Small amounts (<5%) of dinitrated compounds were also obtained.



Scheme 1. i, $NO_2^{\bullet}$, protic work-up.

The generality of the use of metal chelation to direct radical nitration to either the *meso* or the β-pyrrolic position in 5,10,15,20-tetra-arylporphyrins was shown by reactions on 5,10,15,20-tetra-*p*-chlorophenylporphyrin (**4**), 5,10,15,20-tetra-*m*-methoxyphenylporphyrin (**5**), 2-nitro-5,10,15,20-tetraphenylporphyrin (**6**), and 2-methyl-5,10,15,20-tetraphenylporphyrin (**7**) complexes. In each of these cases the copper(II) complex was cleanly and specifically nitrated on the β-pyrrolic positions to give (2-nitro-5,10,15,20-tetra-*p*-chlorophenylporphyrinato)copper(II) (93% isolated yield), (2-nitro-5,10,15,20-tetra-*m*-methoxyphenyl porphyrinato)-copper(II) (91%), an isomeric mixture of 2,7-, 2,8-, 2,12-, and 2,18-dinitro-5,10,15,20-tetraphenylporphyrin copper(II) complexes (38:19:23:20; 80% after demetallation), and an isomeric mixture of nitro-2-methyl-5,10,15,20-tetraphenylporphyrin copper(II) complexes [3-, 7-, 8-, 12-, 13-, 17-, 18-substitution (7:18:5:20:7:24:19); 68% after demetallation]. The separation and structural assignment of these disubstituted compounds will be reported elsewhere. By comparison, nitration of zinc(II) complexes of (**4**) and (**5**) gave only low yields of the corresponding 2-nitrotetra-arylporphyrins (9% and 14%, respectively), while nitration of the zinc(II) complex of (**6**) gave an isomeric mixture of dinitroporphyrins (18%); in each of these cases the major products were ring-opened compounds arising from initial reaction at a *meso*-position, again showing that steric factors are small. These yields were unaltered when the reaction mixture was allowed to stand for extended periods before work-up, showing that the reaction is under kinetic control. The basis for the metal-ion dependent selectivity follows from the mechanism of the reaction; initial oxidation of the porphyrine by $NO_2\cdot$ to a porphyrin π-cation radical, followed by a radical combination with further $NO_2\cdot$ and proton loss.[5]



(**4**) R = H, Ar = p-ClC_6H_4
(**5**) R = H, Ar = m-$MeOC_6H_4$
(**6**) R = NO_2 Ar = Ph
(**7**) R = Me, Ar = Ph

Metalloporphyrin π-cation radicals in which an electron has been removed from the highest-lying orbital have spin distribution of either a_{1u} or a_{2u} symmetry.[6] Reaction of a radical with a metalloporphyrin π-cation radical of a_{1u} symmetry, electron spin density only on the α- and β-pyrrolic positions, would lead to specific β-substitution. These conditions have been overlooked in previous rationalizations of porphyrin reactivity,[1,2] and are probably met in the case of Cu^{II}, Ni^{II}, and Pd^{II} complexes in the present study. The predominant *meso*-reactions of the Zn^{II} and Mg^{II} chelates are in accord with their π-cation radicals being of the a_{2u} type,[6] with spin density mainly on the *meso*-positions and inner nitrogens with small density at the pyrrolic positions.

The route outlined in this communication provides a general method for efficient synthesis of 2-nitrotetra-arylporphyrins and thereby allows convenient entry into several other classes of β-functionalised porphyrins by manipulation of the nitro group.[7,8]

The effect of metal co-ordination on the reactions of several other porphyrin systems is under investigation.

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