Reactions of Nitrous Acid and Nitric Oxide with Porphyrins and Haems. Nitrosylhaems as Nitrosating Agents

By Raymond Bonnett,* Antonios A. Charalambides, Ronald A. Martin, Keith D. Sales, and Brian W. Fitzsimmons†

(*Department of Chemistry, Queen Mary College, Mile End Road, London* E1 4NS; and †*Department of Chemistry, Birkbeck College, Malet Street, London* WC1E 7HX)

Summary Attempted nitrosation of octaethylporphyrin, mesoporphyrin dimethyl ester, and octaethylhaemin with acidified nitrite solutions gives *meso*-nitro derivatives, and nitrosylation of octaethylhaemin and protohaemin dimethyl ester gives the corresponding nitrosylhaems; under suitable conditions the latter substances nitrosate secondary amines.

Sodium nitrite is added to certain processed meats in strictly limited amounts as an antibacterial and cosmetic agent.[1] The colour produced may reasonably be attributed to denatured nitrosylmyoglobin.[2] In order to understand better the reactions which may occur, we examined the interaction of acidified nitrite solutions and of NO with appropriate model porphyrins and haems and report the observations here.

Octaethylporphyrin reacts with $NaNO_2$ in $HOAc–H_2SO_4–H_2O$ (20 °C, 1·5 h) to give 5-nitro-octaethylporphyrin[3] (40%). Mesoporphyrin dimethyl ester (in $CHCl_3–HOAc–H_2O$) similarly gives the *meso*-nitro derivative[3] (65%, isomers).[4] Disubstituted products have also been detected, but we have not observed nitroso derivatives (reported[5] for a reaction with etioporphyrin I). The reactions of protoporphyrin (and protohaemin) are more complex: attack is thought[6] to occur at the vinyl groups to give products that are under study.

Octaethylhaemin in $CHCl_3–HOAc–H_2O$ reacts with $NaNO_2$ to give 5-nitro-octaethylhaemin (43% conversion).

NO reacts with octaethylhaemin [or methoxo-iron(III) octaethylporphyrin or the μ-oxo dimer] in aqueous tetrahydrofuran (THF) under nitrogen to give nitrosyloctaethylhaem, $C_{36}H_{44}N_5OFe$, λ_{max} ($CHCl_3$) 389 (ϵ 83,500), 478 (10,200), 531 (9300), and 557 nm (9400); ν_{max} (CsI) 1670 cm^{-1} (Fe–NO).‡ Magnetic susceptibility measurements indicate one unpaired electron (μ 2·4 B.M.). Similarly protohaemin dimethyl ester gives nitrosylprotohaem dimethyl ester,

---

‡ A nitrosyl complex (called a Type II preparation to distinguish it from the NO reaction) can also be prepared using $NaNO_2$–HCl as the reagent.[6] The Type II preparation has i.r. bands at 1880, 1670, and 1295 cm^{-1}: it is unstable, and may well be a mixture.

$C_{36}H_{36}FeN_5O_5$. The e.s.r. spectrum of a polycrystalline sample of this compound is typical of a radical in a rhombic environment, with g values of 2·097, 2·052, and 2·010. The spectrum of a solution in degassed acetone shows some resolution of the nitrogen hyperfine coupling and has parameters very similar to those reported[7] for nitrosyltetraphenylhaem in solution.

The Mössbauer spectra of nitrosyloctaethylhaem and of nitrosylprotohaem dimethyl ester consist of simple quadrupole doublets (δ 0·377, ΔE 1·220; and δ 0·365, ΔE 1·377 mm s^{-1}, respectively, where δ is relative to natural iron). The data suggest a similarity to certain other FeL_4NO complexes which have $S = \frac{1}{2}$ and comparable chemical isomeric shifts [*e.g.* $Fe(S_2CNEt_2)_2NO$, δ 0·34 mm s^{-1}].[8] Such compounds are considered to involve the NO^+ ion and are, in a formal sense, derivatives of Fe^I. While it is misleading to assign valency to iron in the nitrosylhaems since the odd electron is clearly delocalised,[9] the NO group appears to have some cationoid character.

The nitrosylhaems are able to nitrosate secondary amines under favourable conditions. For example, transnitrosation of Ph_2NH in THF (60 °C, 1 h) has been observed both with nitrosyloctaethylhaem (36%) and with nitrosylprotohaem dimethyl ester (37%).

We conclude that for haem systems attack by nitrosating species may occur at both the porphyrinate ligand (*meso*-positions and vinyl groups) and at the metal, and that the nitrosylhaem system formed by reaction at the metal may itself function, directly or indirectly, as a nitrosating agent under favourable conditions.

We thank the Ministry of Agriculture, Fisheries and Food for support.

(*Received, 7th August* 1975; *Com.* 914.)

---

[1] K. Möhler, Proceedings of the International Symposium on Nitrite in Meat Products, Zeist, 1973, Centre for Agricultural Publishing and Documentation, Wageningen, 1974, p. 13; J. Meester, *ibid.*, p. 265.

[2] *Cf.* J. Haldane, *J. Hygiene*, 1901, **1**, 115.

[3] R. Bonnett and G. F. Stephenson, *J. Org. Chem.*, 1965, **30**, 2791.

[4] For related observations see H. Fischer and W. Klendauer, *Annalen*, 1941, **547**, 123; A. W. Johnson and D. Oldfield, *J. Chem. Soc.*, 1965, 4303.

[5] H. Fischer and W. Neumann, *Annalen*, 1932, **494**, 225.

[6] R. A. Martin, Ph.D. Thesis, University of London, 1975.

[7] B. B. Wayland and L. W. Olson, *J.C.S. Chem. Comm.*, 1973, 897.

[8] C. E. Johnson, R. Rickards, and H. A. O. Hill, *J. Chem. Phys.*, 1969, **50**, 2594.

[9] L. C. Dickinson and J. C. W. Chien, *Biochem. Biophys. Res. Comm.*, 1974, **59**, 1292; *cf.* D. M. P. Mingos and J. A. Ibers, *Inorg. Chem.*, 1971, **10**, 1479.